

Visiting Friends and Relatives (VFRs) travelers and imported malaria in the Palermo district (Sicily)

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Abstract

Introduction. Although Italy has been malaria-free since 1970, the infection is commonly introduced into the country by travelers and immigrants from endemic areas. The term VFRs refers to immigrants from malaria-endemic countries who are regularly resident in a malaria-free area, and who travel to their countries of origin to visit friends and relatives (VFRs). This group is at special risk of malaria as they are unaware of having lost their transitory immunity to the disease.

Methods. We conducted a retrospective study at the International Travelers Department of Palermo (Italy), examining records of malaria cases (67) reported over the period from 1998 to 2013.

Results. VFRs represent the highest number of cases (77.6%), followed by workers (16.4%) and tourists (6.0%). All female patients and patients under the age of 18 were VFRs. *Plasmodium falciparum* was the most frequently-identified species. In all cases, chemoprophylaxis was not taken or was incomplete.

Conclusions. VFRs are at high risk of contracting malaria. This is probably related to an inequality in health care available to immigrants, as well as to ethnic and cultural conditions.

Key words

- visiting friends and relatives
- imported malaria
- travelers
- Sicily
- VFRs

INTRODUCTION

Malaria remains a major public health problem in certain areas of the world. The World Health Organization (WHO) estimates that people living in 107 countries are at risk of malaria transmission. In 2010, an estimated 3.3 billion people were considered at risk of the disease, especially in Sub-Saharan Africa, where 81% of cases and 91% of deaths are estimated to have occurred. Children under five years of age and pregnant women are most severely affected [1].

EU Member States have been malaria-free since 1975, although *Anopheles* mosquito vectors are still present. Sporadic local transmission of malaria (including airport malaria) has been reported over the last 10 years in several EU countries such as Bulgaria, France, Germany, Greece, Italy and Spain [2]. However, the disease is often introduced to Europe by travel and migration [3-5]. It represents a serious health hazard for travelers to endemic areas. International travel is growing rapidly worldwide, and this growth is particularly fast in the world's emerging regions

and tropical and subtropical areas. This is reflected in a significant number of imported malaria cases in countries in which the disease is not endemic [6]. The increase in international travel together with the large influx of immigrants from malaria-endemic countries has had a significant impact on malaria cases in developed countries. Between 2001 and 2010, 45 countries in the European Region reported a decline in imported malaria cases and deaths, possibly due to malaria control activities in endemic countries and a possible under-reporting of cases. However, malaria remains an important travel health issue in the Mediterranean regions, given the large number of imported cases. It is estimated that every year 10-15 million international travelers from Europe visit 15 malaria-endemic areas, and 12000-15000 cases of malaria are imported into European Union countries, with an average fatality rate of 0.4-3% [7].

The proportion of imported malaria cases in Europe due to immigrants has increased during the last few years from 14% in research published more than 10

years ago, to 86% in more recent studies [8]. Nearly 43% of malaria cases registered in Europe occurred in non-nationals. In immigrants, malaria is usually characterized by a milder clinical presentation, lower parasitemia levels and shorter fever duration than in non-immune travelers. These differences are explained by the fact that residents in endemic areas acquire a certain degree of immunity after repeated exposure to the parasite, and the frequency and severity of malarial episodes decreases with age [9]. It is thought that immunity diminishes once exposure to the parasite ceases.

There is a specific group of immigrants who, once settled in the host country, travel to their countries of origin to visit friends and relatives (VFRs). They have been described as being at higher risk than other types of travelers of certain travel-related illnesses, especially infectious diseases. Malaria incidence rates in particular are much higher in VFRs. This is because VFR immigrants are more likely to visit rural locations and tend to stay longer in endemic areas. Furthermore, they have a lower perception of malaria risk, and they are less likely to take adequate protective measures (chemoprophylaxis, repellents, bed nets and air conditioning) [10, 11]. They account for up to 70% of cases in several reports. It is known that partial immunity to malaria in VFRs who are resident outside malaria areas wanes with time, resulting in a more serious clinical presentation of the disease, especially after 12 years [12].

Several studies have demonstrated a lower use of malaria chemoprophylaxis in VFRs, probably also due to socio-economic factors, to confirm the higher risk of disease in this particular group of travelers [13, 14].

In Italy, the number of cases of imported malaria among immigrants showed a rising trend from 1990, reaching a peak in 1999 [15] and then subsequently declining. Nevertheless, this group still accounts for approximately 70% of reported cases [16]. Malaria is more frequently observed in immigrants who are settled in Italy and who occasionally travel to endemic areas to visit friends and relatives (VFRs) rather than in those arriving for the first time [12].

The objective of the present study is to investigate the trend in imported malaria notifications over 15 years from 1998 to 2013, analyzing cases reported in a Mediterranean area that has experienced massive immigration (Palermo, Italy), with particular reference to epidemiologic differences among the various types of travelers.

METHODS

The area involved in the investigation was the Western Sicily Health District. In Italy, malaria cases are reported by the Local National Health Service Department to the Department for Prevention of the Ministry of Health through the Regional Health Office. A malaria case report entails filling out a standard form, which is accompanied by peripheral blood-smears (thin and thick films are sent to *Istituto Superiore di Sanità* – The National Institute of Health - for diagnosis confirmation). Through the Regional

Health Office, the Regional Governments are responsible for ensuring the delivery of a benefits package via a network of population-based health management organizations, District Health Units (*Aziende Sanitarie Provinciali* – ASPs) and public and private accredited hospitals. ASPs are primarily concerned with protecting and promoting public health, and are responsible for achieving the health objectives and targets established by national and regional planning.

In this retrospective, descriptive study, we examine all the malaria cases recorded at the International Travelers Department of the ASP of Palermo from January 1, 1998 to March 31, 2013. Data sources were sheet notifications of the malaria cases reported to the Department of Preventive Medicine. A database was designed and completed after the retrospective review, and the main parameters collected were as follows: administrative (number of clinical interventions, dates of admission and discharge and admission service); demographical (date of birth, sex, nationality, occupation, country of origin and residence); data related to their stay in the endemic country (country, duration, date of departure and date of entry in Italy, reasons for traveling); parasitological diagnosis (*Plasmodium* species); treatment; and intake or not of prophylaxis. The diagnosed cases were divided into three groups, regardless of whether or not they were Italian travelers: 1) people traveling to endemic areas to visit relatives and friends (VFRs), 2) people traveling for tourism, and 3) people traveling for work, business, cooperation or other.

The most relevant microbiological data were the type of species detected. The diagnostic criteria included the microscope observation of parasites and species identification on Giemsa-stained thick and thin blood films. When the morphological characteristics of parasites were indeterminate, they were considered *Plasmodium* spp.

Statistical analysis

Data were collected and analysed by IBM SPSS Software version 21.0 (SPSS, Inc., Chicago, Ill, US) and Epi Info software, version 3.2.2, (Centers for Disease Control and Prevention). Statistical analysis of quantitative and qualitative data, including descriptive statistics, was performed for all the items. Frequency analysis was performed with chi-square test. Where parametric analysis was appropriate, univariate analysis of variance (ANOVA) with Bonferroni post hoc comparison was used to compare the results among the traveler groups. All *P* values were two-sided and *P* values less than 0.05 were considered to indicate statistical significance.

RESULTS

Demographic and clinical characteristics of the patients are reported in Table 1. Sixty-seven cases of diagnosed malaria were notified between 1998 and 2013. Twenty-one patients (31.3%) were female, 46 were male (68.7%). The mean age was 31.4 years (\pm 17.8; median 35 years; range 1-72 years) and sixteen patients were under the age of 18.

Plasmodium falciparum was the most frequently identified species, detected in 42 cases (62.7%). *Plasmodium vivax* was identified in 13 patients (19.4%) and *Plasmodium malariae* in 2 (3.0%). No *Plasmodium ovale* species were identified. The smear did not reveal the species in 10 cases (14.9%), even though parasites were detected by the thick drop test (*Plasmodium* spp). There was no significant difference in case frequency during the fifteen years of the study.

For the whole period of study, case distribution per month was as follows: 11 cases in May (16.4%), 10 cases in October (14.9%), 8 cases in April (11.9%), 7 cases in September (10.4%), 6 cases in January and July (9%), 5 cases in February (7.4%), 4 cases in August and March (6%) 3 cases in June (4.5%), 2 cases in December (3.0%), and 1 case in November (1.5%).

There was no statistically significant relationship between the type of *Plasmodium* species detected, and the age of the patients, their gender and the year or the month of infection.

Twenty-four patients (35.8%) had Italian nationality. The remaining forty-three non-Italian patients (64.2%) were immigrants: 23 of them were citizens of West African countries (Ivory Coast and Ghana), and 11 were Asiatic citizens (Sri Lanka). It was also noted that 79.1% of the patients had traveled to an African country (35.9% to Equatorial Guinea) and the remaining 20.9% to an Asiatic country.

Seventeen of the 67 travelers (25.4%) came from Ghana, 15 (22.4%) from the Ivory Coast, 11 (16.4%) from Sri Lanka, 3 (4.4%) from Kenya and Congo, 2 (3.0%) from Nigeria, Bangladesh, Burkina Faso and Benin, and 1 (1.5%) from Botswana, Cameroon, Equatorial Guinea, Ethiopia, India, Mali, Senegal, Sudan, Togo and Zambia.

As expected, there was a significant correlation ($P < 0.0005$) between the *Plasmodium* species isolated and endemic countries where malaria was acquired: approximately 57% of *Plasmodium falciparum* species were isolated in patients who came from Ghana and the Ivory Coast, whereas 70% of *Plasmodium vivax* species were detected in travelers from Sri Lanka.

As far as reasons for traveling were concerned, VFRs made up the biggest group of patients (52; 77.6%), while 11 patients (16.4%) had traveled for work, and a minority group had done so for tourism (4; 6.0%).

There was a significant difference in mean age among the different groups of travelers ($P < 0.0005$): at the post hoc analysis, patients in the VFR group were younger (26.9 ± 16.4 yrs; range 1-55 yrs) than those in the other two groups, namely "working travelers" (46.4 ± 13.3 yrs; range 31-69 yrs) ($P = 0.001$) and "tourist travelers" (47.5 ± 16.3 yrs; range 38-72 yrs) ($P = 0.042$). Sixteen patients were under 18, and they were all in the VFR traveler group. With respect to gender distribution, all twenty-one female patients were VFRs, without significant differences regarding the country they had visited (Figure 1).

There was no statistically significant difference between type of traveler group and country they had visited.

Regarding the 24 Italian citizen patients, 9 (37.5%)

were VFRs, while 11 (45.8%) had traveled for work and 4 (16.7%) for tourism. The overall mean age was 31.4 years ($SD \pm 23.1$; range 1-72; median 35.5) without significant difference with respect to nationality. However, the Italian citizen VFR travellers (7 females and 2 males) were all under 18 and were born in Italy to non-European parents.

The mean length of stay in the visited country was 48.7 (± 39.3) days, with significant statistical difference among types of traveler groups ($P = 0.01$). The VFR group had a longer stay of 55.4 (± 40.5) days compared to the working group (31.1 ± 25.3 days) ($P = 0.017$) and tourist group (10.5 ± 3.1 days) ($P = 0.005$).

Sixty patients (90%) received the appropriate treatment for *Plasmodium* species and their clinical presentation. Mefloquine was the most frequently used drug (50%).

Patient records reported that 3.3% of the tourists, 10% of the business travelers and 86.7% of the VFRs had not taken chemoprophylaxis, while 28.6% of the tourists and 71.4% of the business travelers had not

Table 1

Demographic and clinical characteristics of imported malaria cases

Parameter	Tourist	Worker	VFRs
Patients, N.	4	11	52
Age, mean years (SD)	47.5 (16.4)	46.4 (13.3)	26.9 (16.4)
Under 18 patients	0	0	16
Gender M/F	4/0	11/0	31/21
Length of stay (days) mean (SD)	10.5 (3.1)	31.1 (25.3)	55.4 (40.5)
Nationality			
Italian	4 (16.7%)	11 (45.8%)	9 (37.5%)
Asiatic	0	0	14 (100%)
African	0	0	29 (100%)
Continent visited			
Asiatic	0	0	14 (100%)
African	4 (7.5%)	11 (20.8%)	38 (71.7%)
Correct prophylaxis			
Yes	0	0	0
No	2 (28.6%)	5 (71.4%)	0
Not taken	2 (3.3%)	6 (10%)	52 (86.7%)
Plasmodium species			
<i>P. falciparum</i>	4 (9.5%)	10 (23.8%)	28 (66.7%)
<i>P. malariae</i>	0	0	2 (100%)
<i>P. ovale</i>	0	0	0
<i>P. vivax</i>	0	1 (7.7%)	12 (92.3%)
<i>Plasmodium</i> spp.	0	0	10 (100%)

VFRs = visiting friends and relatives.

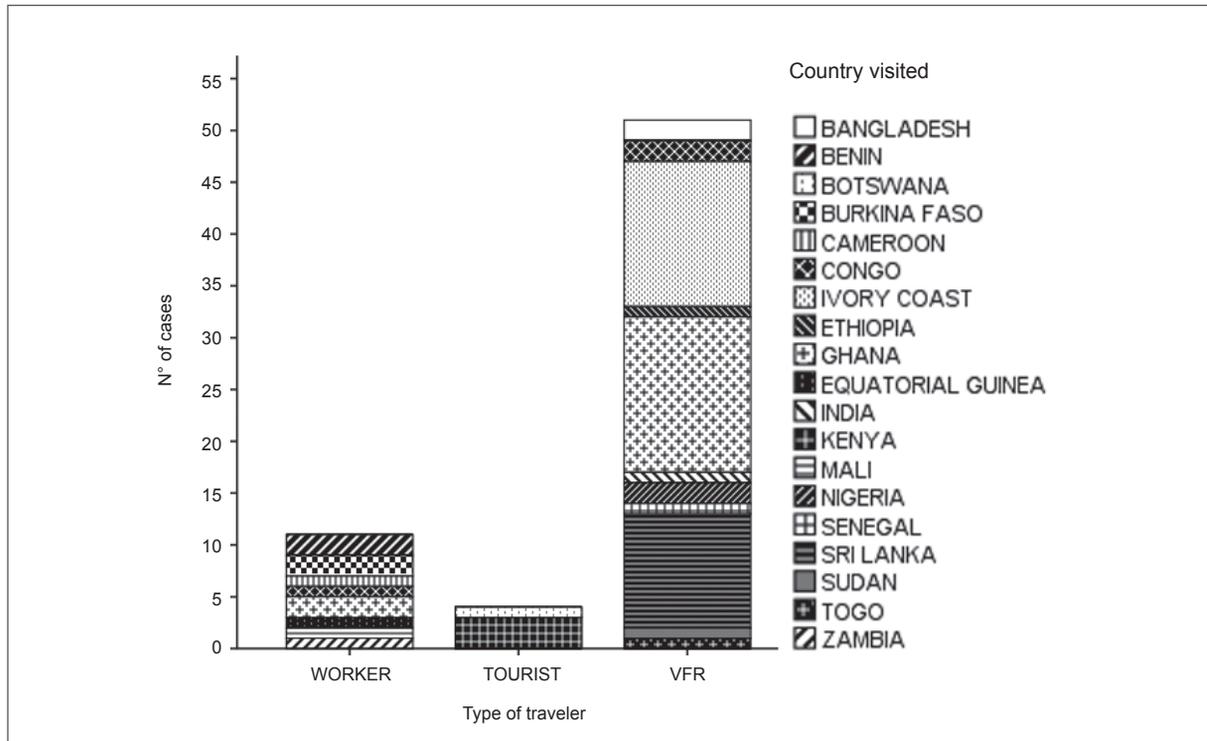


Figure 1
Frequency of imported malaria in traveler groups by nationality.

taken the correct chemoprophylaxis (Table 1).

Two deaths attributed to *P. falciparum* were reported. Both patients (one male and one female) were VFRs, over 18 years of age and had traveled to Africa.

DISCUSSION

There are now more than 114 000 immigrants living in Sicily, representing 2.9% of the national population.

In 2007, the number of females overtook the males, revealing that migration no longer involved only male workers but also women and their families. The female ratio grew further in 2008, reaching 2.6% (representing over 60 000 resident immigrant women). As for children, babies with both parents foreign-born accounted for 15% of total births in 2012 (source: Istituto Nazionale di Statistica (ISTAT), "Birth and Fertility Rates Among the Resident Population 2012" - *Natalità e fecondità della popolazione residente*). The number of foreign children in Italy rose from 412 432 in January 2004 to 932 000 in January 2010, representing 8% of the Italian child population (source: Total Resident Population ISTAT, 1st January, 2010).

Over the last decade, the foreign population resident in Sicily has doubled from 49 399 to 125 015 (an increase of 153.1%). More than half of the foreigners are resident in the provinces of Palermo, Messina and Catania (respectively 21.4 %, 19.3% and 16.7 % of the total number), with 73.3% of the province's foreign population living in the city of Palermo (2011, Population Census-ISTAT). There are 23812 immigrants registered as resident in Palermo and its districts, and the city has the highest percentage of female immigrants in Sicily (57.7%). They come from several different

countries of origin, from the African continent to Latin America, from Asia to Europe: the Ivory Coast (13.9%), Tunisia (12.5%), Morocco (12.5%), Ghana (10.7%), Romania (10.5%), Bangladesh (4.8%) and countries of the former Yugoslavia (4.6%).

Migration could increase the risk of malaria transmission, and lead to it being reintroduced in areas where it has previously been eradicated. The risk of malaria being reintroduced in Italy can be calculated by determining receptivity (influenced by the presence, density and biological characteristics of the vector), infectivity (degree of susceptibility of the different species of mosquitoes to *Plasmodium*) and vulnerability (the number of gametocyte carriers imported in the area). Some rural areas of Central and Southern Italy (Tuscany, Calabria, Sicily and Sardinia) have high receptivity due to the presence of the potential vectors of malaria, *Anopheles labranchiae* and *A. superpictus*. *Anopheles labranchiae* is probably more susceptible to infection by *Plasmodium vivax* and less so to *P. falciparum*. The vulnerability of *Anopheles labranchiae* is low due to the modest presence of gametocyte carriers (imported cases) during the season when climatic conditions are more favorable for transmission. Although it is unlikely that endemic malaria will return to Italy or other Mediterranean countries, constant monitoring and surveillance is essential [17].

Malaria cases imported by immigrants can play an important role in non-vectorial transmission in non-endemic areas through other transmission mechanisms such as blood transfusions, organ transplantation, congenital transmission or occupational exposure [18, 19].

This study has described the epidemiology of malaria

by taking into account notifications of imported malaria in the Western Sicily Health District over a period of 15 years (from 1998 to 2013), analyzing epidemiological changes with particular reference to differences among various types of traveler groups.

The number of notifications of imported malaria is lower in November and December and higher in May and October, probably due to the proportion of people traveling in those periods of the year.

As already reported by other studies, cases of imported malaria are for the most part due to infections by *P. falciparum* and related to travel in Western Africa [5, 20].

Immigrants classified as VFRs represent the highest number of cases (about 78%), followed by work travelers, as described in previous papers [12, 21-23]. Furthermore, as reported in the literature [24], children accounted for around 24% of all imported malaria cases and all of them were VFRs.

The VFR group has been described as being at higher risk than other types of travelers of travel-related illnesses, especially infectious diseases [11, 25].

In our study, all the females and the patients under 18 years of age were VFRs; this suggests that female immigrants and younger age groups are at an increased risk of contracting malaria. This could also be related to ethnic and cultural conditions, and to inappropriate information on malaria prevention.

About two million Italians travel to African countries and around one and a half million visit Asia each year. About 110 000-150 000 of them (7-8% of total travelers) are visiting friends and family (data source: Bank of Italy, National Observatory of Tourism, Data on International Tourism in Italy. http://www.ontit.it/opencms/opencms/ont/it/statistiche/banca_italia/index.html).

Our study reveals that more than 70% of malaria cases are imported by VFRs, which is a much higher percentage than we would expect when we compare this category of traveler with travelers for work, tourism or other. 30% were females, as reported in previous studies [26], but they all belonged to the VFR group and, in particular, 8 of them were less than 18 years old. Our findings suggest that the number of people at risk of contracting malaria is growing among second generation immigrants, and in particular among females and children.

As reported in a previous paper [25], this study confirms that there is an inequality in the health care advice offered to Italian citizens regarding pre-travel medicine and other issues concerning travel to malaria-endemic areas. It would be opportune to find better ways of tracing these new immigrant families, and direct them to international health and travel medicine centers, through the creation of communication channels that will help to prevent travel-related infection.

Limitations of the study are the retrospective nature of the survey itself, the limited sample size and the fact that there is no detailed information about the stay or any high-risk behavior the travellers may have been involved in during their visit; moreover, there is no information on the total number of international travelers flying to countries where malaria is endemic, which could be useful in estimating the global crude inci-

dence rate and crude incidence of *P. falciparum* malaria cases. Furthermore, the case reporting system might be biased due to the hierarchic reporting process from District Health Units to Regional Health Offices. This could lead to an underestimation of notified cases.

In any case, this study confirms the complete lack of attention to chemoprophylaxis in all groups of travelers, regardless of the country visited and the length of stay.

CONCLUSIONS

Immigration is a growing phenomenon in Italy and in Sicily in particular, due to its proximity to the African continent. The results of this study suggest that there has been an increase in imported cases in VFRs, probably because they often go to visit their families in areas with endemic malaria, in low-income countries, and stay for longer periods of time (consequently they are at higher risk of mosquito bites, and adherence to chemoprophylaxis is worse).

Until effective prevention by vaccine becomes available, it is advisable that all international health authorities strengthen their health monitoring networks, and upgrade the tools they use to diffuse information on the prevention of malaria to VFRs, and to females and children in particular.

This is important because patients with *P. vivax* malaria could act as reservoirs for autochthonous transmission in Europe.

In conclusion, a correct and global approach to preventing malaria should consider the need to increase awareness of the malaria risk and provide up-to-date information on the presence, distribution and prevalence of malaria before the journey, thus improving compliance with adequate chemoprophylaxis and encouraging travelers to take measures to protect themselves against mosquito bites.

Although globally there has been a decline in malaria cases in endemic areas over the past decade, WHO statistics show that the number of imported malaria cases in Europe is increasing. This situation calls for an intensification in local malaria surveillance measures for travelers and immigrants [23].

Authors' contribution statement

The Authors have contributed equally to the work and in particular to the conception, design and drafting of the manuscript (AC, PI, and CD), to the acquisition of data and the literature review (CD and NC) and to the analysis of data (PDC and AC). All the authors contributed to the concept of the study and have read the final manuscript.

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 conduct and findings of this study.

Received on 4 June 2014.

Accepted on 20 November 2014.

REFERENCES

1. WHO. *World Malaria Report*. Geneva, World Health Organization, 2010. Available at: http://www.who.int/malaria/world_malaria_report_2010/en/index.html.
2. ECDC. *Meeting report consultation on plasmodium vivax transmission risk in Europe*. Stockholm, 17-18 January 2012. Available at: <http://ecdc2007.ecdc.europa.eu/en/publications/Publications/MER-Malaria-meeting.pdf>.
3. Rey S, Zuza I, Martínez-Mondéjar B, Rubio JM, Merino FJ. Imported malaria in an area in southern Madrid, 2005-2008. *Malar J* 2010;9:290. DOI: 10.1186/1475-2875-9-290
4. Stark K, Schöneberg I. Increase in malaria cases imported from Pakistan to Germany in 2012. *Euro Surveill* 2012;17(47). pii: 20320.
5. Millet JP, García de Olalla P, Carrillo-Santistevé P, Gascón J, Treviño B, Muñoz J, Gómez I Prat J, Cabezas J, González Cordon A, Caylà JA. Imported malaria in a cosmopolitan European city: a mirror image of the world epidemiological situation. *Malar J* 2008;7:56. DOI: 10.1186/1475-2875-7-56.
6. Monge-Maillou B, López-Vélez R. Migration and malaria in Europe. *Mediterr J Hematol Infect Dis* 2012;4(1):e2012014. DOI: 10.4084/MJHID.2012.014
7. Odolini S, Gautret P, Parola P. Epidemiology of imported malaria in the Mediterranean region. *Mediterr J Hematol Infect Dis* 2012;4(1):e2012031. DOI: 10.4084/MJHID.2012.031
8. Asklung HH, Bruneel F, Burchard G, Castelli F, Chiodini PL, Grobusch MP, Lopez-Vélez R, Paul M, Petersen E, Popescu C, Ramharter M, Schlagenhaut P, European Society for Clinical Microbiology and Infectious Diseases Study Group on Clinical Parasitology. Management of imported malaria in Europe. *Malar J* 2012;11:328. DOI: 10.1186/1475-2875-11-328
9. Salvadó E, Pinazo MJ, Muñoz J, Alonso D, Naniche D, Mayor A, Quintó L, Gascón J. Clinical presentation and complications of Plasmodium falciparum malaria in two populations: travelers and immigrants. *Enferm Infecc Microbiol Clin* 2008;26:282-4.
10. Bacaner N, Stauffer B, Boulware DR, Walker PF, Keystone JS. Travel medicine considerations for North American immigrants visiting friends and relatives. *JAMA* 2004;291:2856-64. DOI: 10.1001/jama.291.23.2856
11. Angell SY, Cetron MS. Health disparities among travelers visiting friends and relatives abroad. *Ann Intern Med* 2005;142:67-72. DOI: 10.7326/0003-4819-142-1-200501040-00013
12. Mascarello M, Gobbi F, Angheben A, Concia E, Marocco S, Anselmi M, Monteiro G, Rossanese A, Bisoffi Z. Imported malaria in immigrants to Italy: a changing pattern observed in north eastern Italy. *J Travel Med* 2009;16:317-21. DOI: 10.1111/j.1708-8305.2009.00321.x
13. Baggett HC, Graham S, Kozarsky PE, Gallagher N, Blumensaat S, Bateman J, Edelson PJ, Arguin PM, Steele S, Russell M, Reed C. Pre-travel health preparation among US residents traveling to India to VFRs: importance of ethnicity in defining VFRs. *J Travel Med* 2009;16:112-8. DOI: 10.1111/j.1708-8305.2008.00284.x
14. Pavli A, Maltezou HC. Malaria and travellers visiting friends and relatives. *Travel Med Infect Dis* 2010;8:161-8. DOI: 10.1016/j.tmaid.2010.01.003
15. Romi R, Boccolini D, Majori G. Malaria incidence and mortality in Italy in 1999-2000. *Euro Surveill* 2001;6:143-7.
16. Boccolini D, Romi R, D'Amato S. Sorveglianza della malaria in Italia e analisi della casistica del quinquennio 2002-2006. *Giornale Italiano di Medicina Tropicale* 2007;12:5-12.
17. Romi R, Boccolini D, Vallorani R, Severini F, Toma L, Cocchi M, Tamburro A, Messeri G, Crisci A, Angeli L, Costantini R, Raffaelli I, Pontuale G, Thiéry I, Landier A, Le Goff G, Fausto AM, Di Luca M. Assessment of the risk of malaria re-introduction in the Maremma plain (Central Italy) using a multi-factorial approach. *Malar J* 2012;11:98. DOI: 10.1186/1475-2875-11-98
18. Bruneel F, Thellier M, Eloy O, Mazier D, Boulard G, Danis M, Bédos JP. Transfusion-transmitted malaria. *Intensive Care Med* 2004;30:1851-2. DOI: 10.1007/s00134-004-2366-6
19. Menichetti F, Bindi ML, Tascini C, Urbani L, Biancofiore G, Doria R, Esposito M, Mozzo R, Catalano G, Filippini F. Fever, mental impairment, acute anemia, and renal failure in patient undergoing orthotopic liver transplantation: posttransplantation malaria. *Liver Transpl* 2006;12:674-6. DOI: 10.1002/lt.20730
20. Driessen GJ, Pereira RR, Brabin BJ, Hartwig NG. Imported malaria in children: a national surveillance in the Netherlands and a review of European studies. *Eur J Public Health* 2008;18:184-8. DOI: 10.1093/eurpub/ckm101
21. Romi R, Sabatinelli G, Majori G. Malaria epidemiological situation in Italy and evaluation of malaria incidence in Italian travelers. *J Travel Med* 2001;8:6-11. DOI: 10.2310/7060.2001.5140
22. Romi R, Boccolini D, D'Amato S, Cenci C, Pompa MG, Majori G. Malaria surveillance in Italy: the 2000-2008 national pattern of imported cases. *Giornale Italiano Di Medicina Tropicale* 2010;15:35-38.
23. Gautret P, Cramer JP, Field V, Caumes E, Jensenius M, Gkrania-Klotsas E, de Vries PJ, Grobusch MP, Lopez-Vélez R, Castelli F, Schlagenhaut P, Hervius Asklung H, von Sonnenburg F, Lalloo DG, Loutan L, Rapp C, Basto F, Santos O'Connor F, Weld L, Parola P; EuroTravNet Network. Infectious diseases among travellers and migrants in Europe, EuroTravNet 2010. *Euro Surveill* 2012;17(26). pii:20205.
24. Ladhani S, Aibara RJ, Riordan FA, Shingadia D. Imported malaria in children: a review of clinical studies. *Lancet Infect Dis* 2007;7:349-57. DOI: 10.1016/S1473-3099(07)70110-X
25. Han P, Yanni E, Jentes ES, Hamer DH, Chen LH, Wilson ME, Macleod WB, Ooi WW, Kogelman L, Karchmer AW, Barnett ED. Health challenges of young travelers visiting friends and relatives compared with those traveling for other purposes. *Pediatr Infect Dis J* 2012;31:915-9. DOI: 10.1097/INF.0b013e318259efbe
26. Romi R, Boccolini D, D'Amato S, Cenci C, Peragallo M, D'Ancona F, Pompa MG, Majori G. Incidence of malaria and risk factors in Italian travelers to malaria endemic countries. *Travel Med Infect Dis* 2010;8:144-54. DOI: 10.1016/j.tmaid.2010.02.001