Imported Falciparum Malaria in Europe: Sentinel Surveillance Data from the European Network on Surveillance of Imported Infectious Diseases

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Malaria continues to have a high morbidity rate associated among European travelers. Thorough recording of epidemiological and clinical aspects of imported malaria has been helpful in the detection of new outbreaks and areas of developing drug resistance. Sentinel surveillance of data collected prospectively since 1999 has begun within TropNetEurop, a European network focusing on imported infectious diseases. TropNetEurop appears to cover ~10% of all patients with malaria seen in Europe. Reports of 1659 immigrants and European patients with *Plasmodium falciparum* malaria were analyzed for epidemiological information and data on clinical features. Regional data were quite diverse, reflecting local patterns of immigration and international travel. By far, the most infections were imported from West Africa. Europeans had more clinical complications; consequently, all deaths occurred in this group. Compared with European standards, the mortality rate was low (0.6% in Europeans). Data from TropNetEurop member sites can contribute to our understanding of the epidemiological and clinical findings regarding imported falciparum malaria.

Malaria presents a serious health hazard for travelers to areas of endemicity. In recent decades, the growing popularity of international air travel to tropical destinations has brought a steady increase in the number of imported

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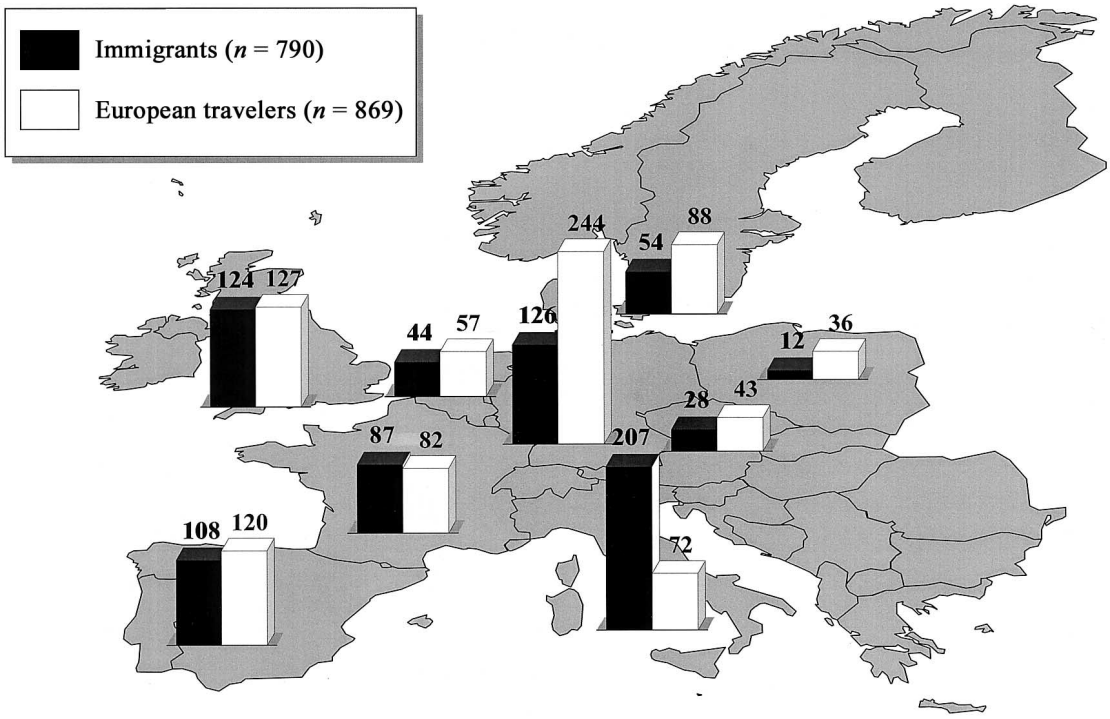

Figure 1. Importation of cases of falciparum malaria to Europe—distribution of reports among European Network on Surveillance of Imported Infectious Diseases sites.

cases of malaria in countries in which the disease is not endemic [1–6].

Health practitioners in the Western world face a broad spectrum of characteristics when encountering patients with malaria, from the moderately compromised individual with few nonspecific symptoms (primarily the semi-immune immigrant) to the critically ill nonimmune traveler. Although malaria is a notifiable disease in almost all European countries, reliable estimates of the true number of imported cases are difficult to obtain because significant underreporting occurs. On average, the number of reported cases adds up to 11,000 patients per year in European Union countries, with the numbers of patients with falciparum malaria estimated at ~8000 per year [7]. Significant underreporting is assumed. Furthermore, details on patients' travel history, symptoms, and the clinical course of the disease after treatment may be available for single countries but not for all of Europe.

Because there is a general lack of surveillance data on imported cases of infectious diseases in Europe, the European Network on Imported Infectious Disease Surveillance (TropNetEurop), was founded in February 1999 as an electronic network of clinical sites related to imported infectious diseases. The network is designed to effectively detect, at their point of entry into the domestic population, emerging infections with potential regional, national, or global impact. Sentinel surveillance reporting is performed by participating sites by use of a standardized and computerized reporting system. Immediate transmission of anonymous patient and laboratory data to the central database ensures timely detection of sentinel events. The comprehensive collection of data on notifiable and nonnotifiable infectious diseases among travelers makes it possible to identify needs for further surveillance and investigation and also provides the potential for future case-control studies by identification of specific risk factors. Primary objectives of TropNetEurop are (1) to construct and maintain a collaborative research network of clinical sites in Europe that deal with imported infectious diseases, and (2) to establish and maintain a clinical network for effective sentinel surveillance of imported infectious diseases in Europe. Membership is self-selected by participating centers and is monitored by the steering committee of the network. Although the organization of the network does not guarantee a representative data collection for Europe, most referral centers in Europe are represented. From the beginning, malaria has been one of the major targets within this network of 36 clinical sites throughout 14 European countries. This report summarizes results from the first 2 years of sentinel surveillance for imported malaria.

PATIENTS, MATERIALS, AND METHODS

Member sites of the TropNetEurop network cover ~51,000 patients per year. During the period 1999–2000, 1659 patients with

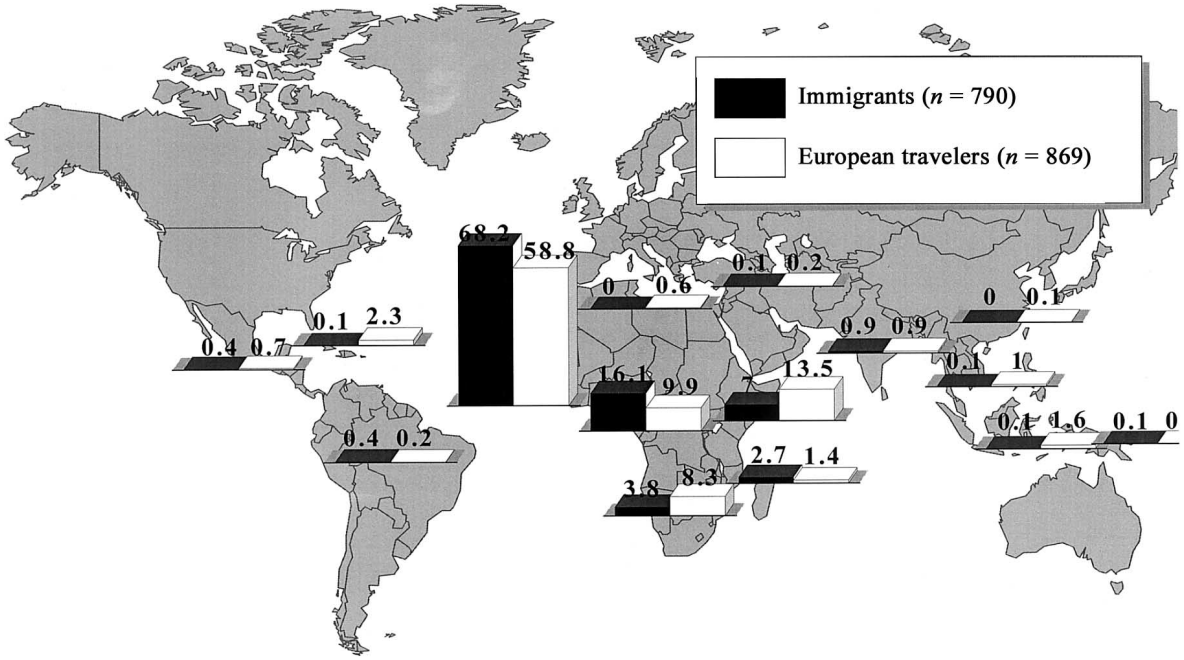

Figure 2. Type of traveler and geographical region where infection with falciparum malaria occurred [%]

falciparum malaria were reported by 31 sites within the network. For every patient, the final diagnosis was qualified by the reporting center as "probable," "suspected," or "confirmed." A standardized and anonymous questionnaire was used for data submission. Reported patients were classified according to 2 categories: (1) patient classification (immigrants, refugees, and foreign visitors to Europe were considered one group, and students, tourists, business travelers, expatriates, military, and missionaries in the other group), and (2) reason for travel (e.g., tourism, business, immigration, research/education, missionary/volunteer/humanitarian aid, or visiting relatives/friends). Travel and case histories were analyzed for clinical and epidemiological features of the infection. Presenting symptoms were analyzed, taking multiple entries by patients into account. Individual data points were stored in a computerized database (Access; Microsoft) and were analyzed by Epi Info (World Health Organization and Centers for Disease Control and Prevention). Data on patients who were repeatedly admitted for recrudescent falciparum malaria were analyzed only once to determine epidemiological background, whereas data on all patients admitted were considered for clinical analysis.

RESULTS

Of the 1659 patients with falciparum malaria reported during the evaluated period, mixed infections occurred in 27 (*Plasmodium falciparum* and *Plasmodium vivax* in 11 patients, *P. falciparum* and *Plasmodium ovale* in 10, and *P. falciparum* and *Plasmodium malariae* in 6. For further analysis, patients were classified into 2 groups: (1) immigrants, per definition including semi-immune patients, and (2) European travelers. Immigrants accounted for 790 patients (47.6%); 557 (70.5%) were male and 233 (29.5%) were female. The definition "European traveler" was fulfilled by 869 patients (52.4%); 563 (64.8%) were male and 306 (35.2%) were female. The distribution of reports from different European regions to TropNetEurop is shown in figure 1.

The average age of reported patients was 30.7 years (median, 36 years; range, 3–67 years) for those in the immigrant group and 35.8 years (median, 37 years; range, 1–86 years) among the European travelers. Reasons for travel were diverse in both groups. Europeans traveled either for tourism (59.6%, $n = 518$), visits to relatives or friends (VRFs; 21.6%, $n = 188$), business (15.8%, $n = 137$), missionary work (7.5%, $n = 65$), or other reasons. Immigrants traveled to visit relatives or friends (68.8%, $n = 544$); for immigration (13.7%, $n = 108$), tourism (9.3%, $n = 73$), or business (5.9%, $n = 47$); or for other reasons. Use of malaria chemoprophylaxis was not frequent in either group: 525 (60.4%) of the European travelers and 572 (72.4%) of the immigrants traveled without using it. Geographical regions where infection with falciparum malaria occurred are shown in figure 2. While West Africa was, by far, the largest contributor of patients to both groups, European patients presented relatively more frequently after travel to East Africa, South Africa, and the Caribbean. Presenting signs and symptoms in all patients with falciparum malaria are shown in table 1. The majority experienced a combination of fever, headache, and fatigue. However, other symptoms were frequently noted.

Table 1. Signs and symptoms in European travelers and immigrants with falciparum malaria.

Sign or symptom	Immigrants (n = 790)	European travelers (n = 869)
Fever	603 (76.3)	704 (81)
Headache	388 (49.1)	432 (49.7)
Fatigue	189 (23.9)	302 (34.8)
Myalgia, arthralgia	136 (17.2)	202 (23.2)
Diarrhea	77 (9.7)	121 (13.9)
Vomiting	96 (12.2)	104 (11.9)
Respiratory complaints	21 (2.7)	30 (3.5)
Neurological complaints	10 (1.3)	22 (2.5)
Skin affections	10 (1.3)	11 (1.3)
Otitis	56 (7.1)	8 (0.9)
Other	157 (19.9)	153 (17.6)
None	49 (6.2)	0

NOTE. Data are no. (%) of patients. Multiple entries are possible.

Treatment did not differ between European travelers and immigrants. A wide variety of antimalarials were used according to national guidelines, availability, and individual patient factors. The drugs most frequently used, alone or in combination, were quinine (65%, n = 1078), mefloquine (11.9%, n = 197), atovaquone/proguanil (7.6%, n = 126), and sulfadoxine/pyrimethamine (2.5%, n = 41). Clinical complications were reported in 55 European travelers (6.3%) and 29 immigrants (3.7%). The reported complications were quite diverse and included probable drug side effects, hyperparasitemia, and a variety of organ manifestations, such as cerebral malaria. Five patients died; all 5 were Europeans returning from African countries. Thus, the mortality rate among patents reported by TropNetEurop sites was 0.3% for all reported patients and 0.6% for Europeans. Case-fatality rates among patients with complications were 5.9% for the whole group and 9.1% for Europeans only.

DISCUSSION

Several factors appear to determine the incidence of imported cases of malaria, including areas of endemicity visited, intensity of exposure, and success of prophylactic measures. For continental European travelers, tropical Africa, an area where disease endemicity is generally high and stable, is the major site of infection with *P. falciparum* [1, 2, 4]. Exposure to anopheline vectors that carry malaria parasites is affected by the duration and type of travel and by the efficacy of antimosquito measures. The awareness of clinicians who deal with febrile patients returning from travel to malarious areas and their prescription practices regarding chemoprophylactic drugs can both be improved by regular epidemiological and clinical information. Depending on the regional impact of immigrants and the amount of travel in the local population, data from national sources in Europe can be heavily skewed toward one or the other group (figure 1). Judging from the data provided by national systems of disease notification, TropNetEurop covers ~10% of all patients with malaria seen in Europe [7]. It is also the only clinical network that collects data on imported cases of infectious diseases at a European level. As such, the network has the capacity to provide valuable information for clinical practice and pretravel counseling.

West Africa contributed, by far, the greatest number of malaria-infected patients to TropNetEurop sites: 534 (68.2%) of all immigrants and 511 (58.8%) of European travelers were infected there (figure 2). Relatively more tourists were infected in East and South Africa. However, it is difficult to contrive risk estimates from these data. Patient numbers reported throughout the network lack a true denominator basis because no data are available regarding the travel activities of the population that contributed the patient collective. A large number of patients returning from West Africa with falciparum malaria may only reflect increased travel activity to that area and not an increased risk for infection. However, reports of the World Tourism Organization (WTO) from 1999 and 2000 show that only 0.6%–2.4% of European travelers to potentially malarious areas chose West Africa as their destination [8, 9]. This suggests a comparatively high relative risk of acquiring falciparum malaria in West Africa. In comparison, the WTO reports that 16%–21% of travelers from the same collective visited Southeast Asia. Because only very few patients were reported from this area, the relative risk appears to be very low. Obviously, the risk of infection is highest for travelers to tropical Africa. These findings are comparable to those of previous investigations from various countries where malaria is not endemic [4, 10, 11]. Many immigrants enter the European continent illegally. Because reliable data are not available for movements of this group, areas where immigrants would be at high risk for malaria can only be guessed. The comparatively high percentage of patients with malaria among travelers returning from the Caribbean (2.3%) reflects an outbreak of falciparum malaria on the east coast of the Dominican Republic that was detected and reported by TropNetEurop [12]. This area previously was malaria free; control measures taken by local authorities stopped the outbreak within 3 months.

Only a minority of patients took drugs or drug combinations appropriate for the drug-resistance situation of malaria parasites at the respective destination [13]. A high percentage of the malaria cases discussed in the present study could have been avoided by use of an appropriate malaria prophylaxis regimen.

Not surprisingly, the course of illness tended to be milder in immigrants compared with Europeans (table 1), although

available data are not sufficient to show clear differences. A large number of patients in the former group were semi-immune inhabitants of areas of endemicity, whereas European patients were all nonimmune. Forty-nine immigrants showed no symptoms at all and had malaria diagnosed by positive blood smear results during routine investigations. It is notable, however, that 3.7% of immigrants developed complications during the clinical course of their disease. Although this percentage is clearly lower than that for European patients (6.3%), some immigrants were critically ill when presenting at the reporting centers. Compared with European standards [7] and with findings of reports published elsewhere [10], the mortality rate of patients was low (0.6% in European travelers). This may be attributed to the fact that TropNetEurop is a network of specialized clinics that have ample experience in dealing with complicated cases of malaria.

In conclusion, data reported by member sites of TropNetEurop can contribute to our understanding of the epidemiological and clinical characteristics of imported falciparum malaria. It is obvious that the network cannot guarantee representative data collection throughout Europe, because membership is self-selected. In most European countries, however, medical services for immigrants and returning travelers are primarily offered at specialized centers. The capacity of the network to detect and report outbreaks within a very short time has been demonstrated elsewhere [12]. Continuous monitoring of reported data will add information on epidemiological changes in areas of endemicity, information that is urgently needed in a setting of increasing travel activity and migration.

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