Epidemiology of Imported Malaria Cases in Japan, 2006–2014: A Sentinel Traveler Surveillance Approach

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Abstract. Malaria continues to be imported into Japan. To better assess the risk of imported malaria, we describe malaria species, suspected country/area of infection (accounting for the number of travelers), demographic characteristics, clinical manifestation, and healthcare access, based on the national surveillance data from 2006 to 2014. Among 557 cases, the median age was 33 years (range: 1–83 years), and 76% were male; 306 (55%) were classified as Japanese based on the reported name. The majority were *Plasmodium falciparum* infections (58%), followed by *Plasmodium vivax* infections (30%). Most *P. falciparum* cases were acquired in Africa and *P. vivax* in Asia/Oceania. Notification rates per 10,000 Japanese travelers for *P. falciparum* were highest for Africa, *P. vivax* were highest for Asia/Oceania, and high for both species for Papua New Guinea. Ten percent of the cases were clinically severe at the time of notification. Nearly 80% of severe cases were *P. falciparum* infections, and among *P. falciparum* cases, Japanese ethnicity was associated with severe case status ($P = 0.03$). *Plasmodium falciparum* cases among Japanese cases showed that older age (≥ 50 years) was associated with severe case status (odds ratio = 5.4; 95% confidence interval = 1.9–15.2), adjusted for sex and healthcare access. More informative assessments are possible by accounting for the number of travelers. Older Japanese represent an important demographic to target prevention and early treatment efforts for malaria.

INTRODUCTION

Malaria is a potentially life-threatening disease, estimated to affect 214 million people and causing 438,000 deaths globally per year.¹ This mosquito-borne disease is caused by five *Plasmodium* species, namely *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae*, *Plasmodium ovale*, and *Plasmodium knowlesi*. *Plasmodium falciparum* infection is commonly associated with severe and fatal malaria and is thus a public health concern, not only for persons residing in endemic areas but also for travelers. Susceptible, nonimmune travelers visiting endemic areas, in fact, appear to be at a higher risk for more severe outcomes due to malaria than persons born and raised in endemic countries.^{2,3} People traveling from nonendemic areas to endemic areas can be affected during sightseeing, during business trips, during their study abroad, while visiting friends and relatives (VFR), and during other activities. The VFR group, in fact, accounts for a substantial proportion of malaria cases in Europe and North America.^{4,5} However, the case fatality rate due to malaria among the VFR group has been reported to be considerably lower than that among the non-VFR group in Europe.⁵ A “semi-immune” state may contribute to the lower case fatality rate among the VFR group, possibly a survivor cohort from previous infection(s).

No domestically acquired case of malaria has been reported in Japan for several decades. Despite steady decrease in the reported number of malaria cases and deaths in endemic countries, malaria cases continue to be imported into Japan. The reasons for such continued importation may include increase in the number of Japanese tourists traveling to endemic areas,⁶ overall increase in the number of travelers to Japan,⁷ and/or a surveillance artifact. In this study, based on

the national Japanese surveillance data, we describe the distributions of imported malaria cases over time and space, accounting for the number of travelers as a proxy denominator. We also compared severe versus nonsevere malaria cases to assess for correlates of severe malaria.

MATERIALS AND METHODS

Data collection. Malaria is a notifiable disease in Japan, requiring an immediate report after diagnosis, according to the Infectious Diseases Control Law. Case-based data are reported via the National Epidemiological Surveillance of Infectious Disease (NESID) system to the Ministry of Health, Labour and Welfare. We extracted NESID data for malaria cases reported between 2006 and 2014 in Japan. Variables used in analysis included malaria species, travel destination (suspected country of infection), demographic characteristics (age, sex, name, and occupational status), signs and symptoms, and dates of onset, initial consultation, and diagnosis. The annual number of fatal malaria cases was extracted from the Vital Statistics report of Japan.⁸ Data regarding overseas travel among Japanese nationals between 2006 and 2014 were obtained from the Japan Association of Travel Agents.⁶ Where traveler data for a specific country and year were not available, the number of travelers was estimated using the average of the two years closest to the missing year for the same country.

Definitions. A case was defined as malaria infection confirmed using blood film microscopy or polymerase chain reaction (PCR) after the development of illness compatible with malaria. A severe infection was defined, based on the World Health Organization guidelines,³ as a case with one or more of the following: 1) development of any of the following (selected from a checklist on the surveillance report form): impaired consciousness, hypoglycaemia, acute renal failure, pulmonary edema/acute respiratory distress syndrome (ARDS), or significant bleeding; 2) development of any of the following (recorded as free text on the surveillance report form): prostration, multiple convulsions, acidosis, jaundice, shock, or

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hyperparasitemia; or 3) death. To classify cases into Japanese and non-Japanese groups, Japanese ethnicity was inferred from the names of recorded cases (i.e., written characters in the cases' names, e.g., "katakana" characters are specifically designated for non-Japanese names).

Statistical analysis. We described cases by year, malaria species, and demographic and clinical characteristics. We also assessed the suspected location of infection (excluding those who traveled to multiple countries), by malaria species and Japanese ethnicity. For those of Japanese ethnicity, we assessed the estimated notification rate per 10,000 travelers as Japanese traveler data were available. To calculate the notification rate of malaria infections among Japanese travelers, the number of reported Japanese cases imported from a specific country was divided by the total number of Japanese travelers who visited the country in the same year(s).

We analyzed clinical data using the R statistical software (version 3.3.1, Vienna, Austria). Time from onset to consultation and diagnosis were compared among Japanese versus non-Japanese ethnicity using the Mann-Whitney *U* test with statistical significance set at $P < 0.05$. Stratified by Japanese ethnicity, severe versus nonsevere cases were compared using univariate and multivariate logistic regression with odds ratios (ORs) and 95% confidence intervals (CIs). Although this was an exploratory analysis, variables hypothesized to be a priori clinically important were included in the multivariate model (i.e., age, sex, and onset to consultation).

Ethical considerations. All the information was collected in compliance with the Infectious Diseases Control Law. Using national surveillance data for public health purposes does not require informed consent from the patients or ethical approval from the associated institutions.

RESULTS

Reported malaria cases by year and by *Plasmodium* species. A total of 557 cases were reported between 2006 and 2014, including 306 Japanese, 240 non-Japanese, and 11 unspecified (Figure 1). *Plasmodium falciparum* infections accounted for the greatest proportion in both Japanese and non-Japanese (183/306 [60%]; 132/240 [55%], respectively), followed by *P. vivax* (Japanese: 78/306 [25%]; non-Japanese: 85/240 [35%]), *P. ovale* (Japanese: 20/306 [7%]; non-Japanese: 4/240 [2%]), and *P. malariae* (Japanese: 11/306 [4%]; non-Japanese: 0/240 [0%]); 33 cases were unknown (Japanese: 14/306 [5%]; non-Japanese: 19/240 [8%]). There was no report of *P. knowlesi* infection. Species were confirmed by microscopy (544/557 [98%]) and/or PCR (39/557 [7%]).

Demographic and clinical characteristics of malaria cases. The median age of cases was 33 years (interquartile range [IQR]: 26–42 years), and most were male (425/557 [76%], Table 1). A large proportion of cases resided in Japan (525/557 [94%]), and only 22/557 (4%) reported overseas residence. Among Japanese cases, students (59/306 [19%]) and those working for international cooperation/development assistance (36/306 [12%]) made up a larger proportion of cases than among non-Japanese cases (23/240 [10%] and 7/240 [3%], respectively).

Clinical information was available for 549 cases, including three cases with unspecified ethnicity (Japanese versus non-Japanese), of which 54 were severe cases at the time of reporting (Table 2). Characteristics of severe cases

FIGURE 1. Number of reported malaria cases, by species, Japan, 2006–2014. (A) Japanese. (B) non-Japanese.

included acute renal failure (31/54 [57%]), impaired consciousness (21/54 [39%]), bleeding (11/54 [20%]), jaundice (4/54 [7%]), and pulmonary oedema/ARDS (3/54 [6%]). By ethnicity, 37/306 (12%) Japanese and 17/240 (7%) non-Japanese cases were severe cases (χ^2 test, $P = 0.05$). Among the 54 severe cases, majority were *P. falciparum* infected (42 *P. falciparum*, six *P. vivax*, and six unknown). There was a single fatal case at the time of notification; however, according to data based on Vital Statistics, five malaria deaths were reported during the study period.

Geographic distributions of cases by malaria species and Japanese versus non-Japanese ethnicity. The geographic distribution of *P. falciparum* infections (291) for both Japanese (Figure 2A; 162) and non-Japanese cases (Figure 2B; 129) indicated that the majority were associated with travel to Africa (Japanese: 147/162 [91%]; non-Japanese: 112/129 [87%]). Only few cases were linked to travel to Asia (Japanese: 9; non-Japanese: 16). Both groups included cases with travel to Papua New Guinea, located in Oceania (Japanese: 4; non-Japanese: 1). Accounting for the number of travelers, the notification rates per 10,000 Japanese travelers were ≥ 1 for African countries (Benin, Central African Republic, Congo, Guinea, Mali, Niger, Rwanda, Sierra Leone, Tanzania, Togo, and Uganda) and Papua New Guinea (Figure 2A).

Asia constituted the majority of infections with *P. vivax*, both for Japanese and non-Japanese cases (35/70 [50%] and 66/82 [81%], respectively) (Figure 3). Among Japanese cases, notifications outside of Asia were as follows: Oceania (16; 13 cases from Papua New Guinea), Africa (10), and Latin America (9). The notification rate per 10,000 Japanese travelers was ≥ 1 (Figure 3A) for Papua New Guinea, Timor-Leste, Vanuatu, Rwanda, and Uganda. Similarly, among non-Japanese cases (Figure 3B), there were fewer cases from

TABLE 1
Demographic characteristics of reported malaria cases, by Japanese vs. non-Japanese ethnicity, Japan 2006–2014

	Japanese N = 306	Non-Japanese N = 240	Total* N = 557
	n (%)	n (%)	n (%)†
Age (years)			
Median (IQR)‡	31.0 (24.0–40.0)	36.0 (27.0–43.0)	33.0 (26.0–42.0)
Sex			
Male	213 (70)	205 (85)	425 (76)
Affiliation			
Student	59 (19)	23 (10)	82 (15)
Company employee	42 (14)	28 (12)	70 (13)
International cooperation/development assistance	36 (12)	7 (3)	43 (8)
Educational or research personnel	19 (6)	12 (5)	31 (6)
Self-used	8 (3)	12 (5)	20 (4)
Public official	7 (2)	4 (2)	11 (2)
Health care workers	8 (3)	1 (0)	9 (2)
Media	5 (2)	1 (0)	6 (1)
Others	42 (14)	75 (31)	119 (21)
Unemployed	55 (18)	36 (15)	92 (17)
Unspecified	25 (8)	41 (17)	74 (13)

* Sum of Japanese and non-Japanese cases does not add up to total because of missing data.

† Except for age.

‡ IQR = interquartile range.

Africa (5) relative to Papua New Guinea (7). Twenty one cases were reported from Pakistan, all from non-Japanese cases, and 18 of those cases were reported between 2011 and 2014 (6, 5, 3, and 4, respectively).

All 24 *P. ovale* cases (20 Japanese and four non-Japanese cases) were associated with travel to Africa, with Uganda, Ghana, and Zambia contributing the most Japanese cases (8, 4, and 3, respectively). All 11 *P. malariae* infections were reported among Japanese cases.

Healthcare access and characteristics of severe versus nonsevere cases. Among 275 *P. falciparum* cases with information known regarding their names and time from onset to consultation, in terms of healthcare access, non-Japanese cases (median 3 day, IQR 2–5 days) experienced a longer time

from onset to consultation than Japanese cases (median 2 days, IQR 1–4 days, Mann-Whitney *U* test, *P* < 0.01). The median time from consultation to diagnosis was zero (range 0–13) for Japanese and zero (range 0–16) for non-Japanese cases and not statistically different.

Among *P. falciparum* cases, severe case status was associated with ethnicity (31/183 [17%] Japanese and 11/132 [8%] non-Japanese cases were severe [χ^2 test, *P* = 0.03]) as well as older age (26/271 [10%] among < 50-year olds versus 16/44 [36%] among $\geq$ 50-year olds were severe [χ^2 test, *P* < 0.01]). Stratified by Japanese ethnicity, severe cases were skewed toward those aged $\geq$ 50 years among Japanese cases, but not among non-Japanese cases (Figure 4). Thus, the analysis was restricted to *P. falciparum* cases and stratified by Japanese ethnicity (Table 3). Among Japanese cases, older age ($\geq$ 50 years) was significantly related to severe case status (OR = 8.0; 95% CI = 3.3–19.1) (Table 3). A multivariate analysis including age, sex, and time from onset to consultation showed that older age remained associated with severe status (adjusted OR [aOR] = 5.4; 95% CI = 1.9–15.2); there was a nonsignificant increase in odds of severity with time from onset to consultation of two or more days (aOR = 2.3; 95% CI = 0.8–6.9). By contrast, among non-Japanese cases, there were fewer severe cases, neither age, sex nor time from onset to consultation was related to severity. Among Japanese cases, results were similar when age was treated as a continuous variable, with each increase in year being significantly associated with severity (aOR = 1.06; 95% CI = 1.02–1.09; *P* < 0.01).

Although the number of severe cases with *P. vivax* infection was too few for a full analysis (six severe cases and 157 nonsevere cases), a larger proportion of Japanese cases presented as severe cases than non-Japanese cases (OR = 2.2; 95% CI = 1.0–4.7) (4/78 versus 2/85). All cases with *P. ovale* (24) and *P. malariae* (11) infections were nonsevere.

DISCUSSION

This study describes the epidemiology of malaria cases officially reported in Japan between 2006 and 2014. All cases

TABLE 2

Clinical signs and symptoms of reported malaria cases, by Japanese vs. non-Japanese ethnicity, Japan 2006–2014

	Japanese N = 306	Non-Japanese N = 240	Total N = 546
	n (%)	n (%)	n (%)
Signs/symptoms			
Fever	303 (99)	236 (98)	539 (99)
Chill	175 (57)	144 (60)	319 (58)
Headache	176 (58)	139 (58)	315 (58)
Arthralgia	85 (28)	58 (24)	143 (26)
Splenomegaly	67 (22)	54 (23)	121 (22)
Anemia	54 (18)	41 (17)	95 (17)
DIC	36 (12)	15 (6)	51 (9)
Acute renal failure	21 (7)	10 (4)	31 (6)
Impaired consciousness	18 (6)	3 (1)	21 (4)
Bleeding	6 (2)	5 (2)	11 (2)
Jaundice	4 (1)	0 (0)	4 (1)
Pulmonary edema/ARDS	3 (1)	0 (0)	3 (1)
Hypoglycemia	0 (0)	0 (0)	0 (0)
Death	1 (< 1)	0 (0)	1 (< 1)
Severe cases*	37 (12)	17 (7)	54 (10)

ARDS = acute respiratory distress syndrome; DIC = disseminated intravascular coagulation.

* Severe cases defined as those who developed at least one of the following: acute renal failure, impaired consciousness, bleeding, jaundice, pulmonary edema/ARDS, hypoglycemia, prostration, multiple convulsions, acidosis, shock, hyperparasitemia, or death. None of the cases had prostration, multiple convulsions, acidosis, hyperparasitemia, or shock written on the surveillance report form.

A Japanese, number of cases and notification rate per 10,000 travelers **B** Non-Japanese, number of cases

FIGURE 2. Geographic distribution of *Plasmodium falciparum* cases, Japan 2006–2014. (A) Japanese, the number of cases and notification rate per 10,000 travelers. (B) Non-Japanese, the number of cases. Solid circles indicate the number of cases. Color codes indicate notification rate per 10,000 travelers: light yellow (< 0.01), yellow (0.01–0.09), orange (0.10–0.99), and red (≥ 1.00). Countries with solid circles but no color codes indicate areas where no traveler data were available. This figure appears in color at www.ajtmh.org.

were imported, and *P. falciparum* and *P. vivax* were the predominant species throughout the study period. Most Japanese and non-Japanese cases with *P. falciparum* were associated with travel to Africa, likely reflecting high prevalence

of *P. falciparum* infections in Africa.^{9,10} In fact, *P. falciparum* case notification rate per 10,000 Japanese travelers was highest for Africa and was also considerably higher than *P. vivax* notifications from Africa, both in absolute number of cases and

A Japanese, number of cases and notification rate per 10,000 travelers **B** Non-Japanese, number of cases

FIGURE 3. Geographic distribution of *Plasmodium vivax* cases, Japan 2006–2014. (A) Japanese, number of cases and notification rate per 10,000 travelers. (B) Non-Japanese, number of cases. Solid circles indicate number of cases. Color codes indicate notification rate per 10,000 travelers: light yellow (< 0.01), yellow (0.01–0.09), orange (0.10–0.99), and red (≥ 1.00). Countries with solid circles but no color codes indicate areas where no traveler data were available. This figure appears in color at www.ajtmh.org.

rate per 10,000 Japanese travelers. On the contrary, most *P. vivax* cases were reported from Asia, Oceania, and Latin America, and the notification rate per 10,000 Japanese travelers for *P. vivax* was greater for these regions overall relative to Africa. These findings are consistent with previously reported

distributions of *P. vivax*.¹¹ Although the number of travelers was unknown for non-Japanese cases, most *P. falciparum* cases were associated with Africa whereas those due to *P. vivax* were from Asia. Interestingly, there was high notification rate among Japanese travelers for Papua New Guinea for both

FIGURE 4. Age distribution of reported *Plasmodium falciparum* cases by ethnicity and severity, Japan 2006–2014. (A) Japanese. (B) non-Japanese; gray indicates nonsevere, and black indicates severe cases.

species—reports from Papua New Guinea have indicated high malaria activity for both species,^{12–14} and the risk appears to be similar for travelers. Although interpretation requires caution, the fact that *P. falciparum* was identified at relatively high proportions per Japanese travelers outside of Africa, such as Papua New Guinea, is valuable information for domestic physicians.

Severe cases accounted for 10% of all cases, and most were due to *P. falciparum* infections. We found that Japanese ethnicity was associated with severe case status despite their faster access to medical care (Table 3). Similarly, among cases with *P. vivax* infections, the proportion of Japanese cases with severe case status was higher relative to that of non-Japanese cases. This may be because most Japanese are not immune to malaria, consistent with other studies in Europe describing more severe cases or deaths in travelers originating from nonendemic countries than among VFRs or those born in endemic countries.^{15,16} Although such apparent difference in risk may be due to host genetics such as the sickle cell gene found in malaria-endemic populations, the protective effect of the sickle cell trait against severe or fatal malaria has been associated more with infants, and development of clinical immunity from infection(s) may be an additional protective factor.¹⁷ In particular, older age was strongly associated with severity among Japanese cases, with a dose-response trend (Figure 4). This is also in line with a previous report showing that fatality from *P. falciparum* in those aged 50–65 and > 65 years were higher (4.6 times and 10.7 times,

respectively) than those aged 18–35 years.¹⁶ Immune status may also explain why Japanese cases showed increased proportion of severe cases with delayed consultation but not non-Japanese cases.

Nearly 60% of malaria cases were Japanese cases. This is in contrast to the findings from Europe and North America where the proportion of malaria cases who are VFRs is high (e.g., VFRs account for more than 80% of malaria cases in the United Kingdom and more than 80% of *P. falciparum* cases in France⁵). This differential may be due to the underlying difference in the population composition of Europe and Japan—in Japan, the population of migrants from sub-Saharan Africa represents only approximately 10,000 among the 127 million Japanese population (< 0.01%). However, the total number of immigrants is steadily increasing by 1–5% per year, and non-Japanese malaria cases may increase in the future. Among Japanese cases, students and those engaged in international cooperation/development assistance were common, indicating further needs for pretravel preparation for malaria prevention among those groups.

Although the reported number of cases was few, there was an increase in the number of non-Japanese *P. vivax* cases from Pakistan since 2011. This is consistent with studies reporting an increasing number of *P. vivax* infections from Pakistan in 2011 and 2012 through GeoSentinel and Euro-TravNet¹⁸ and among people returning from Pakistan to Germany and the United Kingdom.^{19,20} Furthermore, during the study period, whereas there was a steady increase in the number of immigrants both from Pakistan and India to Japan (annual increases of 3.8% and 4.2%, respectively),²¹ there was no increase in cases from India (17 cases in 2006–2010 and 17 in 2011–2014). The increase in notifications from Pakistan may be attributable to an increase in *P. vivax* cases in Pakistan after devastating floods in September 2010, 2011,²² as well as in 2013 and 2014.^{23,24} Public health authorities and clinicians in nonendemic countries should thus closely monitor trends in the number of imported malaria cases not only by region but also by specific country.

There are several important limitations in this study. First, as the numbers of travelers for non-Japanese nationals were not available for analysis, we could not assess trends accounting for the number of travelers among non-Japanese cases. Furthermore, information such as periods of stay and specific activities at the destination site (which could differ between countries or regions among cases) were unknown. For the severity assessment, because the national surveillance database does not require reporting of nationality, we presumed Japanese ethnicity based on the written characters of names. Thus, misclassification of foreigners' ethnicity into the Japanese group could have occurred if they reported their names in Japanese style (misclassification in the other direction is believed less likely); however, such misclassification would likely have underestimated the true association between severe status and Japanese ethnicity. In addition, signs and symptoms were those at the time of notification, and cases were not systematically followed over time; if the degree of follow-up time was different between Japanese and non-Japanese cases, such differential could under or overestimate our findings. However, at the time of notification, as the time from onset to notification for Japanese cases was shorter than that for non-Japanese cases, longer follow-up time since onset would not be able to explain the higher frequency of severe

TABLE 3
Comparison of characteristics between severe and nonsevere *Plasmodium falciparum* cases, by Japanese vs. non-Japanese ethnicity

	Total n (%)	Severe n (%)	Nonsevere n (%)	OR*	95% CI†	aOR‡	95% CI
Japanese (N = 183)							
Age (years)							
< 50	152 (83)	16 (52)	136 (89)		Reference	—	—
≥ 50	31 (17)	15 (48)	16 (11)	8.0	3.3–19.1	5.4	1.9–15.2
Sex							
Female	61 (33)	7 (23)	54 (36)		Reference	—	—
Male	122 (67)	24 (77)	98 (64)	1.9	0.8–4.7	1.0	0.3–2.8
Onset to consultation (days)							
0–1	59 (36)	5 (22)	54 (39)		Reference	—	—
2–3	60 (37)	10 (43)	50 (36)	2.2	0.7–6.8	2.3§	0.8–6.9
≥ 4	43 (27)	8 (35)	35 (25)	2.5	0.7–8.2	—	—
Non-Japanese (N = 132)							
Age (years)							
< 50	119 (90)	10 (91)	109 (90)		Reference	—	—
≥ 50	13 (10)	1 (9)	12 (10)	0.9	0.1–7.7	—	—
Sex							
Female	12 (9)	1 (9)	11 (9)		Reference	—	—
Male	120 (91)	10 (91)	110 (91)	1.0	0.1–8.6	—	—
Onset to consultation (days)							
0–1	19 (17)	2 (22)	17 (16)		Reference	—	—
2–3	45 (40)	2 (22)	43 (41)	0.4	0.1–3.0	—	—
≥ 4	49 (43)	5 (56)	44 (42)	1.0	0.2–5.5	—	—

* OR = odds ratio; aOR = adjusted OR.

† CI = confidence interval.

‡ Adjusted for each other for variables listed (age, sex and onset to consultation); because of the small number of severe cases among non-Japanese cases, only univariate results are presented.

§ Categorized dichotomously (0–1, ≥ 2) based on univariate analysis results.

cases among Japanese cases. Potential misclassification of species was also considered to be a possibility. For example, as genetic diagnosis is required to differentiate *P. knowlesi* from *P. malariae*,²⁵ underreporting or misclassification of potentially more severe *P. knowlesi* infections may have been possible; however, among the 11 *P. malariae* cases, none were severe. Lastly, as information regarding some symptoms indicative of severe infections (e.g., severe anemia and hyperparasitemia) were not available, this study may underestimate the severity of infection. In addition, as notification of malaria requires immediate reporting after diagnosis, the number of deaths reported under surveillance was fewer than that reported under Vital Statistics.

For more informative assessments based on the surveillance data, some simple updates could be considered. For example, rather than presuming ethnicity based on the names of patients, recording nationality would be more informative. Furthermore, information regarding the use of prophylactic medications, as a potential protective factor, would also be useful when assessing correlates of severity. Such information is easy to collect during consultation and could be considered for inclusion to the national surveillance reporting criteria.

In conclusion, the number of imported malaria cases in Japan has not decreased despite declining trends in endemic countries. Similar to other reports, we found that Japanese, that is, persons from nonendemic areas likely with lower immunity against malaria, were associated with more severe malaria infection. Thus, more attention should be paid to preventing severe cases among Japanese travelers. In addition, even if the number of imported cases is small, the risk among travelers to certain areas may be high—such findings require further investigation, and potentially warrant information sharing with travelers and professionals in travel medicine. As globalization continues with travel to malaria-endemic

areas, risk communication, prompt healthcare access, and treatment initiation are especially important for travelers from nonendemic areas.

Received March 7, 2017. Accepted for publication June 15, 2017.

Published online August 21, 2017.

Acknowledgments: We are thankful to all the staff members of local governments and clinicians for providing surveillance data on malaria infection via NESID. We appreciate Dr. Mateusz M. Plucinski (Malaria Branch, Centers for Disease Control and Prevention), Dr. Munehisa Fukusumi (IDSC, NIID, Japan), and Dr. Yumiko Saito-Nakano (Department of Parasitology, NIID, Japan) for their valuable input and discussion.

Financial support: This study was partly supported by the Research on Emerging and Re-emerging Infectious Diseases and Immunization (H29-shinkougousei-shitei-001).

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