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Travelers' risk of malaria by destination country: A study from Japan

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Summary *Background:* Country-specific information on the incidence of malaria in travelers provides the most reliable data on which to base the pre-travel risk assessment. Some such studies have been conducted among Western travelers; however, to our knowledge, there have been no reports on Japanese travelers.
Methods: Malaria cases that were diagnosed between April 1999 and December 2005 and were reported to the national infectious disease surveillance body were used as the numerators after grouped into countries of disease acquisition. The denominators, the numbers of Japanese travelers visiting individual countries were derived from the recipient countries and obtained through a Japanese organization.
Results: In addition to the well-documented high risks in sub-Saharan countries, our study showed that travelers to Papua New Guinea were exposed to a significantly high risk of malaria. In Asia, Myanmar had the highest risk. Generally, malaria incidence rates among Japanese travelers were lower than those previously reported on Western travelers. However, the rates were rather comparable to the data obtained recently.
Conclusions: These malaria incidence data in travelers should be taken into consideration for pre-travel risk assessment. They need to be constantly updated, and at the same time, limitations in data interpretation that are inherent in various study methodologies should also be clarified.

Introduction

A decline in overseas travel from Japan was observed between 2001 and 2003 during a period of conflict in the Middle East following the September 11th attacks against the US in 2001 and subsequent epidemic of severe acute

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respiratory syndrome (SARS) in 2003. Overseas travel has since recovered and 17.535 million international trips were made in 2006, the highest ever in Japanese history apart from in 2000 when 17.819 million travelers were recorded. A significant proportion of travelers visit areas of risk for malaria, yet our previous studies have shown protection against malaria to be suboptimal in Japanese travelers.[1–3]

In Western countries, chemoprophylaxis is the mainstay of malaria preventive measures for travelers to high-risk areas. However, a high proportion of users report adverse drug events, with a predominance of neuropsychiatric adverse events among mefloquine users.[4] The benefits of chemoprophylaxis use to prevent malaria need to be carefully weighed against the risk of adverse drug events. This is particularly pertinent for travelers from Japan where mefloquine is the only drug licensed for malaria prophylaxis. Country-specific information on the incidence of malaria in travelers provides the most reliable data on which to base the pre-travel risk assessment. Some such studies have been conducted among Western travelers; however, to our knowledge, there have been no reports on Japanese travelers.

Materials and methods

Malaria has been a notifiable disease in Japan since April 1999 under the Infectious Disease Control Law, and reports of smear- and/or polymerase chain reaction-confirmed malaria cases are recorded at the Infectious Disease Surveillance Center, National Institute of Infectious Disease, Tokyo.[5] Nationality, place of birth, or details of residence are not documented on the reporting form; however, the main country of residence in the preceding several years is recorded. For the purposes of this study, Japanese travelers were defined as those who had been resident in Japan during the previous several years. Malaria cases, diagnosed between April 1999 and December 2005, were only included if a single country could be identified as the source of infection, and these served as the numerators.

The denominators were the numbers of Japanese travelers visiting individual countries, and these data were obtained from the Japan National Tourist Organization (JNTO, Tokyo, Japan).[6] The JNTO compiles data on tourism from the World Tourism Organization (UNWTO), the Pacific Asia Travel Association (PATA), and the national tourism offices of individual countries. Japanese nationals or those who had been resident in Japan prior to travel were defined as Japanese travelers by the recipient countries. Most recipient countries defined the number of Japanese visitors as that of arrivals at national borders, except for Mali and Chad, which used the number of arrivals at hotels. Countries were only included if denominator data were available for at least four years of the study period (April 1999—December 2005). For countries where data were not available for the entire study period, the denominator was estimated, based on the numbers traveling in other years. A malaria incidence rate was calculated as the number of malaria cases per 100,000 travelers to the country.

Results

Among the countries of sub-Saharan Africa, Uganda, Ghana, and Mali had a malaria incidence rate greater than 100 per 100,000 travelers (see Table 1). The rate in Nigeria was two to threefold less than in these countries. High rates were noted in the Central African Republic and Chad, however, there was only one case of malaria from each of these countries. Rates could not be calculated for the West African countries of Burkina Faso, Côte d'Ivore, Senegal, or Cameroon due to a lack of denominator data, although cases of malaria were imported from these countries (7, 5, 5, 5 cases, respectively). The lowest rates were from South Africa and Kenya. *Plasmodium falciparum* malaria accounted for all, or the majority of infections from the African countries, except for Ethiopia where the infections were split almost equally between those due to *P. falciparum* and *Plasmodium vivax*.

Incidence rates in Asia were much lower than in African countries. Myanmar had the highest rate, followed by India and Pakistan. Indonesia yielded the highest number of imported malaria cases, but with a large number of travelers to this country, the incidence rate was low. Fewer malaria cases were imported from Thailand and with a higher volume of travel than Indonesia, the incidence rate was lower. Overall, *P. vivax* was the dominant species, accounting for 84%, 77%, 71%, 64%, and 57% of infections from India, Indonesia, Thailand, Myanmar, and the Philippines, respectively.

In Oceania, Papua New Guinea was the only country that could be analyzed and where a high incidence rate was found, comparable to some African countries. However, unlike the African countries, *P. vivax* infections predominated (70%). Six travelers acquired malaria in the Solomon Islands, two infections were due to *P. falciparum* and four due to *P. vivax*; however, denominator data for this country were incomplete.

Brazil was the only Latin American country to be analyzed and this revealed a low incidence rate which was comparable to those in medium-risk Asian countries, with the majority of cases being due to *P. vivax*.

Discussion

Using different methodologies, studies have been conducted to establish malaria incidence rates among travelers of various nationalities. Two longitudinal studies were published targeting returning travelers with questionnaires administered in-flight[7] or at the airport,[8] with a follow-up questionnaire mailed later. The advantage of this approach is that it captures detailed information on malaria infections, *e.g.*, the purpose and duration of travel and chemoprophylaxis use. These data can be used to determine malaria risk in travelers, adjusting for the duration of exposure and the use of chemoprophylaxis. The volume of target population, however, is limited, and malaria incidence may be partially based on reports of malaria infection diagnosed abroad — the accuracy of which is uncertain.

In other studies, malaria risk was assessed using cases of malaria reported to national surveillance bodies, with denominator data derived from various sources. Some denominators were derived from home countries of the

Table 1 Malaria incidence rates among Japanese travelers by destination country (no. of malaria cases per 100,000 travelers) (April 1999—December 2005)

Region	Subregion	Country	No. of travelers	All species		*P. falciparum*		*P. vivax*		*P. ovale*		*P. malariae*	
				No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
Asia	Southeast Asia	Laos	127,900	3	2.3	2	1.6	1	0.8	0	0.0	0	0.0
		Cambodia	537,200	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0
		Thailand	7,865,300	14	0.2	4	0.1	10	0.1	0	0.0	0	0.0
		Myanmar	140,500	11	7.8	3	2.1	7	5.0	0	0.0	1	0.7
		Malaysia	2,278,400	1	0.0	1	0.0	0	0.0	0	0.0	0	0.0
		Singapore	4,676,100	1	0.0	1	0.0	0	0.0	0	0.0	0	0.0
		Philippines	2,487,500	7	0.3	3	0.1	4	0.2	0	0.0	0	0.0
		Indonesia	3,927,100	70	1.8	14	0.4	54	1.4	2	0.1	0	0.0
	South Asia	India	576,000	32	5.6	5	0.9	27	4.7	0	0.0	0	0.0
		Pakistan	79,700	3	3.8	0	0.0	3	3.8	0	0.0	0	0.0
		Nepal	191,600	2	1.0	0	0.0	2	1.0	0	0.0	0	0.0
		Sri Lanka	99,300	1	1.0	1	1.0	0	0.0	0	0.0	0	0.0
Africa	East Africa	Ethiopia	11,200	5	44.6	2	17.9	3	26.8	0	0.0	0	0.0
		Kenya	112,700	9	8.0	6	5.3	1	0.9	1	0.9	1	0.9
		Uganda	5600	9	160.7	8	142.9	0	0.0	1	17.9	0	0.0
		Tanzania	40,000	13	32.5	10	25.0	0	0.0	2	5.0	1	2.5
		Madagascar	20,900	5	23.9	5	23.9	0	0.0	0	0.0	0	0.0
	West Africa	Nigeria	60,900	32	52.5	28	46.0	1	1.6	3	4.9	0	0.0
		Ghana	19,200	27	140.6	26	135.4	1	5.2	0	0.0	0	0.0
		Mali	12,800	15	117.2	13	101.6	2	15.6	0	0.0	0	0.0
	Central Africa	Central African Republic	400	1	250.0	0	0.0	1	250.0	0	0.0	0	0.0
		Chad	400	1	250.0	1	250.0	0	0.0	0	0.0	0	0.0
		Zambia	18,100	2	11.0	1	5.5	1	5.5	0	0.0	0	0.0
	Southern Africa	South Africa	165,200	4	2.4	4	2.4	0	0.0	0	0.0	0	0.0
Oceania		Papua New Guinea	26,000	37	142.3	10	38.5	26	100.0	1	3.8	0	0.0
Latin America		Brazil	338,800	10	3.0	1	0.3	9	2.7	0	0.0	0	0.0

travelers,[9,10] while others were from recipient countries with data provided by the UNWTO,[11,12] as with our study. The British[13,14] and Swedish[15] studies estimated travel volume to a specific country/area using passenger surveys conducted at international airports and telephone interviews, respectively. These approaches benefited from larger sample sizes (numerator and denominator data) and greater diagnostic accuracy of malaria, as the infections were confirmed after returning home. However, illnesses that occurred abroad are not captured, and the effect of length of stay may not be evaluated due to lack of data. Furthermore, the incidence rates could be greatly influenced by chemoprophylaxis use in high-risk groups, and this could not be assessed in these studies.

Although differences in study methodologies make it difficult to compare results across the various studies, relative infection risks between destination countries or areas could be derived from individual studies. This information is invaluable when making malaria chemoprophylaxis recommendations for travelers. This is particularly true for Japanese travelers as no country-specific data have previously been acquired to assess the risk of malaria for these travelers.

Our results support previous findings which showed that travelers visiting sub-Saharan countries are at high risk for malaria,[7–13,15] especially if travel is to West Africa,[7,10,12,13] with most infections due to *P. falciparum*. It is also noted that our country-specific rates were generally lower than those obtained for Western travelers; rates in Japanese travelers to Nigeria and Ghana were several to 10-fold less than those of British,[13] Italian,[10] and Danish[11] travelers. Recently, however, Steffen et al.[16] showed the 10-fold decreased malaria incidence rate among travelers to Tropical Africa (200 per 100,000 per month of stay) than previously reported, some of whom were on chemoprophylaxis. Our current results are rather comparable to those new data. The low incidence rate in Kenya was unexpected and far lower than that of British travelers (8.0 per 100,000 compared with 149 per 100,000)[13] or Danish travelers (245.9 per 100,000),[11] although it was similar to the rate reported among Italian travelers (9.0 per 100,000).[10] This may be because Japanese travelers tend to visit safari parks which may pose a lower risk than visits to coastal areas such as Mombassa. In fact, visits to game parks in Kenya were found to be 4.7-fold lower risk than visits to the coast and 14.3-fold lower risk than to Lake Victoria.[8]

In line with the Australian (723.5 per 100,000)[9] and US (only bars but not exact figures were shown)[12] studies, we demonstrated a high incidence rate among travelers to Papua New Guinea (142.3 per 100,000) — comparable to those in sub-Saharan Africa. The British study also showed a very high rate in Oceania (4100 per 100,000), with most cases occurring after visits to Papua New Guinea.[13] In addition, the Australian study reported even a greater risk in the Solomon Islands than Papua New Guinea.[9] In our study, however, we could not accurately assess the risk in the Solomon Islands as denominator data were only available for three of the study years. Based on these data, an estimated 1600 travelers visited this country during the study period and six malaria cases (two *P. falciparum*, four *P. vivax* infections) were reported, giving an incidence rate of 375.0 per 100,000 travelers. We found that 70% of malaria cases acquired in Papua New Guinea were due to *P. vivax*, with 27% due to *P. falciparum*. Even if considering the lower proportion of *P. falciparum* infections, chemoprophylaxis may be recommended for travelers to this region of Oceania, as long as it is recommended for travel to sub-Saharan Africa.

Travel to countries in Asia or Brazil posed a much lower risk of malaria, with the majority of cases being due to *P. vivax*. Limited prescribing of malaria chemoprophylaxis for travelers to the Indian Subcontinent[17] and Latin America[18] has been proposed by European groups, because of the low incidence of malaria and low risk of travelers acquiring *P. falciparum* infection. Our study results provide support for this recommendation. Although previous studies have shown that among Asian countries, the risk of malaria is high in India and the Indian Subcontinent,[9,10,12,13,15] our study showed the highest risk in Myanmar, which may have not been previously documented. Similar to previous studies,[9,11,12] the risk of malaria in Thailand was lower than in Indonesia, both being Asian countries attracting an enormous number of tourists worldwide.

Our study results are subject to limitations in data interpretation. Malaria cases that developed and were cured before returning home were not captured, the length of stay in the malaria-endemic countries or the extent of chemoprophylaxis use was not known, each of which might have had some influences on the results. Nevertheless, such data on the incidence of malaria in travelers are invaluable in helping to define the risk and chemoprophylaxis recommendations. These data need to be constantly updated and at the same time, such studies should clearly outline limitations in data interpretation that are inherent in various methodologies.

Conflict of interests

We declare that we have no conflicts of interest.

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