

Short Communication

Adherence to malaria prophylaxis among travelers from a middle-income country

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Abstract

Introduction: Malaria is the main cause of death by infection among travelers and is preventable through a combination of chemoprophylaxis and personal protective measures. **Methods:** Travelers were interviewed by phone 28–90 days after returning, to assess adherence to pre-travel advice for malaria prevention. **Results:** A total 57 travelers were included. Adherence to chemoprophylaxis was significantly higher among participants prescribed mefloquine (n=18; 75%) than doxycycline (n=14; 45%). Adherence to mosquito repellent and bed net use was 65% and 67%, respectively. **Conclusions:** Adherence to malaria prophylaxis was lower than expected. Further studies testing innovative approaches to motivate travelers' compliance are required.

Keywords: Travel medicine. Malaria. Prophylaxis. Mefloquine. Doxycycline.

An estimated 125 million travelers visit malaria-endemic areas every year, with 25,000 possibly acquiring the disease. Of these, 10,000 are reported and 150 are fatal¹. The individual risk of acquiring malaria is influenced by host immune status, travel duration and destination, season, and use of preventive measures².

Malaria prevention relies on a combination of chemoprophylaxis and personal protective measures, such as insect repellent, insecticide-treated bed nets, and sleeping in air-conditioned rooms³. Chemoprophylactic drugs include chloroquine, doxycycline, mefloquine, primaquine, and atovaquone/proguanil. The choice relies on drug availability in the country, the traveler's destination, medical history, and budget.

To our knowledge, there are no data on adherence to malaria preventive measures among travelers departing from middle-income countries like Brazil. Given that malaria and other mosquito-borne diseases are endemic in the country, travelers may have greater awareness about risks in similar settings, which could influence adherence to preventive recommendations.

Our study objective was to assess compliance of Brazilian travelers to malaria-prevention strategies, specifically regarding use of repellents, bed nets, and malaria chemoprophylaxis, as well as factors associated with non-adherence.

Travelers who consulted the Travel Medicine Center of the Federal University of Rio de Janeiro (*Cives*) from April 2014 to November 2015 were invited to participate. Chemoprophylaxis prescriptions were tailored to travelers' characteristics and planned trip. Doxycycline is the only malaria chemoprophylactic drug marketed in Brazil, making it the only choice for many centers. Mefloquine was provided by the Pharmaceutical Laboratory of the Brazilian Army for this study and offered without cost to travelers. Travelers who used atovaquone/proguanil bought it abroad before reaching malaria risk areas.

Returning travelers were contacted by phone 28–90 days after returning. Data collected included age, sex, marital status, travel route, and trip motivation and duration. Travelers were asked about their compliance with use of repellent, bed nets, and malaria chemoprophylaxis. Travelers who used malaria chemoprophylaxis were asked about the occurrence of adverse events.

Adherence to malaria chemoprophylaxis was categorized as complete (no doses missed), missed <50% of doses, missed ≥50% doses, stopped medication on return, and no doses taken. Similarly, adherence to repellents and bed nets was graded as

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always adhered, adhered >50% of the time, adhered 25%–50% of the time, and <25% of the time.

Categorical data variables are described as absolute counts and percentages. Quantitative variables are summarized as median and interquartile range (IQR). The distribution of categorical variables was compared using chi-square and Fisher's exact tests. The Mann–Whitney test was used for quantitative variables. For all analyses, significance was set at 0.05.

Among 85 travelers successfully contacted, 57 had visited malaria risk areas; these were included in the analyses. Median time between travel return and the interview was 48 days (IQR: 31–57 days).

Table 1 presents the general characteristics of included participants. Business was the main reason for travel. Pre-travel consultation occurred a median 24 days before travel, and median trip duration was 21 days. The most visited continent was Africa, especially sub-Saharan countries (68% of trips), followed by South America (25%) (**Table 2**). Domestic travel within Brazil (mainly the Amazon region) ranked second (15%) among all travel destinations.

Most patients were prescribed doxycycline (n=31, 54%) or mefloquine (n=24, 42%). Atovaquone/proguanil was used by only two (4%) participants.

Complete adherence to chemoprophylaxis was reported by 34 (60%) travelers; 1 (2%) traveler missed <50% of doses, 12 (21%) missed ≥50%, 7 (12%) discontinued upon return, and 3 (5%) decided not to take any medication after pre-travel consultation. Complete adherence was significantly more frequent among travelers prescribed mefloquine (n=18; 75%) than those prescribed doxycycline (n=14; 45%; p=0.024). Among 54 travelers that started chemoprophylaxis, 10 (18%) reported adverse events. There was a non-significant trend toward higher incidence of adverse events among participants treated with mefloquine (n=6, 26%) than those treated with doxycycline (n=4; 14%; p=0.3). Adverse events associated with mefloquine were nightmares and vivid dreams (n=3), anxiety, depressed mood, and nausea (n=1 each). Adverse events reported with doxycycline were nausea (n=1), headache (n=1), and candidiasis (n=2). There was no association between adherence and occurrence of side effects (p=0.4).

Full adherence to mosquito repellent was observed in 37 (65%) travelers. Bed nets were recommended to 33 travelers, with full adherence in 22 (67%). We found no significant association between complete adherence to malaria chemoprophylaxis and full compliance with repellent or bed net use (p=1.00).

Table 3 presents analysis results for factors associated with reported adherence to preventive measures. Adherence to malaria chemoprophylaxis was higher among travelers who stayed at hotels (p<0.01). Married travelers were more adherent to repellents (n=27; 79%; p=0.01) and bed nets (n=19; 83%; p=0.006). We also found a borderline significant association between traveling for leisure and lower adherence to bed net use (p=0.05). No other significant associations were found between

TABLE 1: General characteristics of travelers in this study.

Characteristics	n (%)
Travelers	57 (100)
Age (years)	40 (32–47)*
Female sex	31 (54)
Marital status	
Married	34 (60)
Single	23 (40)
Main motivation for consultation	
Malaria prevention	21 (37)
Others' suggestion	13 (23)
Vaccination	9 (16)
Diseases in general	7 (12)
Altitude illness prevention	2 (3)
Other	5 (9)
Reason for travel	
Leisure	17 (30)
Business	24 (42)
Religious (missionaries)	15 (26)
Visiting friends and relatives	1 (2)
Accommodation	
Hotel	28 (49)
Local residence	20 (35)
Hostel	1 (2)
Other	8 (14)
Travel insurance	49 (86)
Time between consultation and departure (days)	24 (12–41)*
Trip duration (days)	21 (13–32)*

* Median (interquartile range).

the studied covariates and adherence to preventive measures.

To offer better travel counseling, it is important to assess adherence, reasons for non-compliance, and the influence on risk of travel-related illnesses. Full adherence to preventive recommendations is an ideal but difficult goal that depends on aspects related both to the traveler and physician. In this study, we present data on adherence to preventive interventions used to avoid malaria infection among travelers departing from Rio de Janeiro, Brazil. As reported elsewhere, sub-Saharan Africa was the most frequent travel destination⁴. However, our center commonly advises travelers planning domestic trips within Brazil, mainly to the Amazon region, where malaria and yellow fever are major concerns. Malaria chemoprophylaxis

TABLE 2: Travel destinations of participants.

Destination	n (% total)
Sub-Saharan Africa	39 (68)
Guinea-Bissau	17 (22)
South Africa	9 (12)
Tanzania	6 (8)
Senegal	4 (5)
Other	17 (22)
South America	14 (25)
Brazil (Amazon)	9 (12)
Brazil (other)	2 (3)
Other	4 (5)
Southeast Asia and Pacific Islands	4 (7)
Indonesia	3 (4)
Myanmar	2 (3)
Vietnam	1 (1)
Cambodia	1 (1)
Malaysia	1 (1)
Other	1 (1)

*Median (interquartile range).

is not usually recommended by the Brazilian Health Ministry⁵ for travelers to the Amazon because *Plasmodium vivax* is the predominant etiologic agent in the region, and drugs frequently used for chemoprophylaxis do not act on the hypnozoites. Nonetheless, the risk of exposure to *P. falciparum* infection is unpredictable in some areas. Therefore, chemoprophylaxis may be indicated for travelers to areas with difficult access to medical assistance, trip duration longer than the incubation period of disease, or those presenting any health condition that could increase the risk of severe malaria^{5,6}.

Although the studied population lived in an endemic area for mosquito-borne infections and thus should be aware of the importance of preventing these diseases, compliance with the preventive recommendations was lower than expected. In fact, adherence to malaria chemoprophylaxis tended to be lower than adherence reported among travelers departing from high-income countries^{4,7}. This may be partly related to differences in the definition of complete adherence, which in our study was travelers reporting having taken a full course of the prescribed drug. Alternatively, our results might be influenced by the fact that doxycycline, the most frequently prescribed drug in this study, was associated with significantly lower compliance than mefloquine. This finding is in line with recommendations for the use of mefloquine as the first choice for chemoprophylaxis, after excluding any possible contraindications, in places where doxycycline is the only other alternative⁸.

The lower adherence to doxycycline found in this study was apparently not related to a higher frequency of adverse events. In line with other reports⁹, we found no significant difference in the frequency of such events between patients treated with doxycycline and mefloquine. Others have reported that doxycycline is associated with more adverse effects that interfere with daily life than mefloquine⁸. This might explain the lower adherence to doxycycline, despite the absence of a significant difference in the frequency of adverse events in our study. Additionally, the lack of association between the rate of side effects and non-adherence could be, in many cases, a consequence of travelers' beliefs and intentions. This should be considered during pre-travel consultation, to improve adherence¹⁰.

Reported adherence to mosquito repellent use varies widely in the literature, ranging from 40% to 91%^{5,7,11}. In some reports, the probability of adhering to repellents was higher among travelers who were compliant with chemoprophylaxis¹². This association was not supported by our results. Insecticide-treated bed nets have been shown to reduce the malaria risk among residents of endemic areas¹³, and studies among travelers report adherence between 32% to 50%^{14,15}. The intermediate level of compliance with bite-avoidance measures in this study suggests that travelers already living in an area endemic for mosquito-borne infections are not more likely to adhere to repellent use, possibly because it is more difficult for these travelers to perceive risk in an environment that they find familiar.

TABLE 3: Analysis of factors associated with adherence to different preventive recommendations.

Variable	Chemoprophylaxis		p	Repellent		p	Bed net		p
	Adherent n (%)	Non-adherent n (%)		Adherent n (%)	Non-adherent n (%)		Adherent n (%)	Non-adherent n (%)	
Sex			0.6				0.3		0.3
Male	17 (65)	9 (35)		19 (73)	7 (27)		12 (80)	3 (20)	
Female	17 (55)	14 (45)		18 (58)	13 (42)		10 (56)	8 (44)	
Age (years)*	43 (36-49)	43 (39-49)	0.8	43(37-48)	39 (38-56)	0.5	44 (39-49)	40 (35-44)	0.2
Marital status			1.0			0.01			0.006
Single	14 (61)	9 (39)		10 (44)	13 (56)		3 (30)	7 (70)	
Married	20 (59)	14 (41)		27 (79)	7 (21)		19 (83)	4 (17)	
Motivation for consultation			0.6			0.2			0.2
Malaria prevention	14 (67)	7 (33)		11 (52)	10 (48)		6 (50)	6 (50)	
Other	20 (56)	16 (44)		26 (72)	10 (28)		16 (76)	5 (24)	
Reason for travel			0.8			0.1			0.05
Business	13 (54)	11 (46)		14 (58)	10 (42)		8 (73)	3 (27)	
Missionary	9 (60)	6 (40)		13 (87)	2 (13)		12 (80)	3 (20)	
Leisure	11 (65)	6 (35)		10 (59)	7 (41)		2 (29)	5 (71)	
Destination			0.2			0.4			0.6
Sub-Saharan Africa	26 (67)	13 (33)		27 (69)	12 (31)		20 (69)	9 (31)	
Other	8 (44)	10 (56)		10 (56)	8 (44)		2 (50)	2 (50)	
Accommodation			0.01			0.6			0.7
Hotel	18 (82)	4 (18)		13 (59)	9 (41)		6 (60)	4 (40)	
Other	16 (46)	19 (54)		24 (69)	11 (31)		16 (70)	7 (30)	
Time between consultation and trip (days)*	23 (18-41)	30 (19-36)	0.7	26 (19-34)	30 (20-56)	0.7	23 (16-37)	30 (20-37)	0.4
Trip duration (days)*	20 (17-31)	19 (10-33)	0.8	19 (11-33)	21 (19-25)	0.7	19 (10-33)	21 (19-25)	0.9

*Median (interquartile range).

Identification of predictors of low adherence to preventive measures may help to improve pre-travel counseling, to further raise awareness about the risk of malaria acquisition among travelers perceived to be at high risk for non-adherence. Our results suggest that travelers who are single, not staying in hotels, and traveling for leisure have increased risk of failing to comply with malaria preventive measures.

This study has limitations such as its small sample and the fact that assessment of self-reported adherence may have overestimated the actual frequency. We also cannot rule out the possible influence of interannual variations in the characteristics of traveler groups. The large proportion of travelers belonging to a missionary group traveling to Guinea-Bissau might have introduced biases related to behavioral and cultural aspects.

The suboptimal adherence to preventive measures observed in this and similar studies underlines the importance of further research assessing the predictors of non-compliance and testing innovative approaches to motivate traveler adherence to preventive recommendations.

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Ethics Approval

The study has been approved by the ethics committee of the Federal University of Rio de Janeiro (approval number CAAE: 40828115.4.0000.5257), and all participants signed the consent form.

Conflict of Interest

The authors declare that there is no conflict of interest.

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