

[ORIGINAL ARTICLE]

Typhoid Vaccination among Japanese Travelers to South Asia and the Factors Associated with Compliance

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Abstract:

Objective In 2010, candid advice concerning the low rate of typhoid vaccination among Japanese travelers was received from Nepal. Recently, progressive Japanese travel clinics have encouraged Japanese travelers to be vaccinated against typhoid fever in conjunction with officially approved vaccines, such as hepatitis A vaccine. We herein report the status of typhoid vaccinations for Japanese travelers to the most endemic area (South Asia) and describe the factors associated with compliance.

Methods In the travel clinic at Kurume University Hospital, we used the following criteria to retrospectively extract the records of new pre-travel Japanese clients between January 2011 and March 2015: hepatitis A vaccine administered, traveling to South Asian countries, and ≥ 2 years of age. We first summarized the participants and then divided them into typhoid-vaccinated and typhoid non-vaccinated groups for a comparative analysis.

Results This study included 160 clients. A majority (70.0%) of these clients traveled for business. The duration of trips was long (≥ 1 month) (75.0%), and India was a popular destination (90.6%). A comparative study between the vaccinated group (n=122) and the non-vaccinated group (n=38) revealed that the two factors most positively associated with typhoid vaccination were business trips [adjusted odds ratio (aOR) 3.59, 95% confidence interval (CI) 1.42-9.06] and coverage by a company/organization payment plan (aOR 7.14, 95% CI 2.67-20.3).

Conclusion The trend toward typhoid vaccination among Japanese travelers to South Asia with pre-travel consultation is correlated with business trips and coverage by a company/organization payment plan. If problems concerning the cost of vaccines were resolved, more travelers would request typhoid vaccination.

Key words: Japanese travelers, pre-travel consultation, typhoid vaccine, Typhim Vi[®], typhoid fever, hepatitis A

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Introduction

Typhoid fever is endemic in developing countries, particularly in South Asia, and the risk of acquiring typhoid fever among travelers to South Asia is greater than in travelers to other areas (1, 2). More than 16 million Japanese travel abroad annually, and travel to tropical areas (e.g., South Asia) endemic for hepatitis A and typhoid fever (3, 4), has increased (5). Recently, 20-65 typhoid cases per year have

been reported to Japanese national surveillance, and most cases were imported (6, 7). Furthermore, some Japanese long-term travelers acquire typhoid fever and must be treated abroad (8). Those cases fall outside the data collected by Japanese national surveillance unless they visit healthcare facilities in Japan. Therefore, typhoid vaccines are recommended for Japanese travelers to South Asia, regardless of trip duration (9).

A report by the Nepal International Clinic described that 95% of their Japanese patients had not been vaccinated

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against either hepatitis A or typhoid fever (10). Ten years later, another report by the same clinic favorably described that Japanese authorities had begun to encourage hepatitis A vaccinations for travelers to endemic areas (8). They warned, however, that the status of typhoid vaccination remained insufficient (8). While hepatitis A vaccines, which are the core vaccines for travelers to developing countries, were administered to 54.8% of Japanese long-term travelers to South Asia (11), the prevalence of typhoid vaccination among the same population was estimated to be as low as 23.4% (11). The main reason for this discrepancy can be attributed to the official disapproval of such typhoid vaccines in Japan.

Some travel clinics in Japan have recently introduced typhoid vaccines (9). The introduction of typhoid vaccine in Japan is an urgent matter. Our travel clinic initiated pre-travel consultations beginning in 2007, and began to import typhoid polysaccharide vaccine in 2011. Our clinical question was, "What are the factors that influence hepatitis A-vaccinated travelers to request the optional typhoid vaccination before visiting endemic countries?"

We analyzed the clinical characteristics of pre-travel clients with hepatitis A vaccinations who planned to travel to South Asia (endemic area for hepatitis A and typhoid fever), and examined the factors that contributed to compliance with typhoid vaccination. This survey of the current status of typhoid vaccination in Japan will clarify the status of typhoid vaccination in Japan.

Materials and Methods

This research involved a single-center study that was conducted by the Department of Infection Control and Prevention, which manages a travel clinic in Kurume University Hospital, a tertiary-care medical center. On the first day of consultation, our doctors explain the risks of particular destination countries and recommended vaccines using the Japanese vaccine guideline for overseas tourists 2010 (Japanese Society of Travel and Health) and Tropimed[®] [ASTRAL SA, Geneva, Switzerland (<http://www.tropimed.com/en/index.html>)]. Our explanation is not confined to the vaccines that clients request, and the first consultation requires 45 minutes per client. We use AIMMUGEN[®] (KAKETSUKEN, Kumamoto, Japan) and HAVRIX[®] (GlaxoSmithKline Biologicals, Rixensart, Belgium) as hepatitis A vaccines, and Typhim Vi[®] (Sanofi Pasteur, Lyon, France) as typhoid vaccine. The safety of this imported typhoid polysaccharide vaccine has been confirmed among the Japanese population in previous studies (12, 13). The Kurume University Research Ethics Committee has approved the use of these imported vaccines (HAVRIX[®] and Typhim Vi[®]).

Between January 2011 and March 2015, there were 1,003 new pre-travel Japanese clients (without other travel clinic's consultation) who visited our clinics. For the present study, we included participants who met all of the following criteria: hepatitis A vaccine administered, traveling to South

Asian countries, and ≥ 2 years of age.

Among 1,003 pre-travel Japanese clients, 160 were chosen to participate in this study, according to the criteria. We retrospectively reviewed their medical records and classified their factors as follows: age, sex, typhoid vaccine administered or not, purpose of travel [business, leisure, accompanying family members, education, volunteer work, visiting friends and relatives (VFRs)], destination country, interval between the first consultation and the intended departure time (<1 month and ≥ 1 month), scheduled duration of travel (<1 month and ≥ 1 month), and payment for vaccines (cost was covered by a company/organization payment plan or not). If a company/organization paid a portion of the cost, the participants were categorized as follows: "company/organization pays." We summarized the characteristics of the clients and performed a comparative study: a typhoid-vaccinated group was compared with an unvaccinated group.

All statistical analyses were performed using EZR software (Saitama Medical Center, Jichi Medical University), which is a graphical user interface for R (The R Foundation for Statistical Computing, version 3.2.3) (14). Categorical data were tested using Fisher's exact test, and continuous data were tested using Student's *t*-test. Multiple logistic regression analyses were performed with adjustment for age and sex for each of the factors showing *p* values of <0.10 in the univariate analyses.

The Kurume University Research Ethics Committee approved this study (Research No. 15214).

Results

A summarized clinical profile of the participants appears in Table 1. Most of our clients traveled for business (70.0%). The duration of most trips was long (≥ 1 month) (51.3%), and India was the most popular destination (90.6%). Typhoid vaccine was administered to 122 clients (75.8%).

A univariate comparison between the vaccinated group (*n* =122) and the non-vaccinated group (*n*=38) among travelers going to South Asia is shown in Table 2. In this analysis, there were statistically significant differences in the proportions of sex, the purposes of travel (business, accompanying family members, education, volunteer work), the scheduled duration of travel, and the existence of a company/organization payment plan.

Multiple logistic regression analyses adjusting for age and sex between the vaccinated group and the non-vaccinated group among travelers to South Asia were also performed. We evaluated each of the factors that showed *p* <0.10 in the univariate analysis. The results are presented in Table 3. Factors positively associated with the administration of typhoid vaccine were business trips [adjusted odds ratio (aOR) =3.59, 95% confidence interval (CI) 1.42-9.06] and the existence of a company/organization payment plan (aOR=7.14, 95% CI 2.67-20.3).

Table 1. The Characteristics of the Participants (n=160).

	(%)		(%)	
Age, mean±SD (year)	38.1±14.9		Scheduled duration of travel	
Sex (male)	136	(84.5)	<1 month	34 (21.3)
Typhoid vaccine administration			≥1 month	120 (75.0)
Yes	122	(75.8)	(Unknown)	6 (3.8)
Purpose of travel			Cost of vaccines	
Business	112	(70.0)	Company/organization pays	87 (51.9)
Leisure	25	(15.6)	Clients pay	42 (26.3)
Accompanying family members	10	(6.3)	(Unknown)	31 (19.4)
Education	7	(4.4)	Destination country	
Volunteer	6	(3.8)	India	145 (90.6)
VFRs	5	(3.1)	Pakistan	3 (1.9)
Interval between consultation and departure			Nepal	5 (3.1)
<1 month	74	(46.3)	Butan	3 (1.9)
≥1 month	82	(51.3)	Sri Lanka	3 (1.9)
(Unknown)	4	(2.5)	Bangladesh	2 (1.3)

SD: standard deviation, VFRs: visiting friends and relatives

Table 2. The Comparison between a Typhoid-vaccinated Group and Typhoid Non-vaccinated Group among Travelers Visiting to South Asia.

	Typhoid vaccinated group (n=122)	(%)#	Typhoid non-vaccinated group (n=38)	(%)#	p value
Age, mean±SD (year)	38.9±14.8	-	35.6±14.9	-	0.242 ¹⁾
Sex (male)	109	(89.3)	27	(71.1)	0.009 ²⁾
Purpose of travel					
Business	95	(77.9)	17	(44.7)	<0.001 ²⁾
Leisure	17	(13.9)	8	(21.1)	0.311 ²⁾
Accompanying family members	5	(4.1)	5	(13.2)	0.058 ²⁾
Education	3	(2.5)	4	(10.5)	0.055 ²⁾
Volunteer	2	(1.6)	4	(10.5)	0.029 ²⁾
VFRs	5	(4.1)	0	(0)	0.340 ²⁾
Interval between consultation and departure					
≥1 month	62	(52.5)	20	(52.6)	1.000 ²⁾
Scheduled duration of travel					
≥1 month	96	(82.1)	24	(64.9)	0.040 ²⁾
Payment for vaccines					
Company/organization	78	(77.2)	9	(32.1)	<0.001 ²⁾

¹⁾ Student's t-test, ²⁾ Fisher's exact test, # calculated after excluding missing values.

SD: standard deviation, VFRs: visiting friends and relatives

Discussion

The risks of acquiring typhoid fever are known to vary depending on a client's travel destination. In the USA, the results of national surveillance data have shown that approximately half of USA typhoid patients have traveled to India, followed by other South Asian countries (Pakistan and Bangladesh) (2). Other surveillance studies have also established a high risk for travel to India and South Asian countries (1, 15). Our study indicated that most clients traveling to South Asia (75.8%) tended to be vaccinated with typhoid

vaccine. This was a result of the countermeasures for the infection risk in the most endemic areas.

The present study also demonstrated that business trips and the existence of a company/organization payment plan were important factors for ensuring compliance with typhoid vaccination (Table 3). Only nine participants who traveled for business purposes had not received a typhoid vaccination, despite the fact that their company/organization had a payment plan. In Japan, travel medicine doctors must personally import typhoid vaccines. This has led to negative consequences such as a high cost and insufficient compensation schemes. For example, many students who travel for

Table 3. Multiple Logistic Regression of Administration of the Typhoid Vaccination on Each Explanatory Variable among Travelers Who Went to South Asia after Adjusting for Age and Sex.

	aOR	95% CI	p value
Purpose of travel			
Business	3.59	1.42-9.06	0.007
Accompanying family members	0.58	0.13-2.62	0.468
Education	0.28	0.05-1.44	0.125
Volunteer	0.30	0.04-1.91	0.215
Scheduled duration of travel			
≥1 month	2.43	0.99-5.90	0.05
Payment for vaccines			
Company/organization	7.14	2.67-20.3	<0.001

aOR: adjusted odds ratio, CI: confidence interval

education/volunteer/leisure are unable to pay for vaccination, but most business travelers are able to pay for typhoid vaccine, which is considered optional in contrast to the vaccines approved officially in Japan. Similar results were seen in our previous report concerning hepatitis B vaccination among Japanese travelers (16).

Our study had several limitations. First, this study was conducted in a single institution and not generalized to other hospitals or areas. Second, this was a retrospective study, and some data were not available (Table 1). Third, we were unable to consider some human factors (e.g., the existence of vigorous occupational health practitioners in the clients' companies, and the differences in our travel medicine doctors' recommendations). These factors might have influenced the clients' decisions to be vaccinated. Fourth, we did not interview our clients regarding negative sentiments that might promote the avoidance of imported vaccines. Health injuries caused by vaccination from imported vaccines are not covered by the Japanese relief system for injury to health. Only the importing agency's original relief system covers the health injuries due to vaccination. Some of our clients may have been worried about the use of imported vaccines and therefore chose not to be vaccinated. Resolving these limitations will require prospective multi-center studies in Japan.

In conclusion, the designation of a business trip and the existence of a company/organization payment plan that would cover the cost of vaccines were positive factors for typhoid vaccination among travelers to South Asia, which is the most endemic area. Typhoid vaccine administration (in addition to hepatitis A vaccination) among Japanese travelers to endemic areas has been encouraged, and most of our clients to South Asia comply with vaccination. Therefore, In order to promote the prevalence of typhoid vaccination, travel medicine doctors should continue to emphasize the

importance of typhoid vaccination for all Japanese companies and organizations.

The authors state that they have no Conflict of Interest (COI).

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