HEALTH PROMOTION

Vaccine Acceptance among travelers directed to areas with risk of dengue: a pilot study

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Keywords

Dengue • Vaccine hesitancy • Travelers • Prevention • Vaccine acceptance

Summary

Introduction. *Dengue is a vector-borne viral disease that causes a million of cases every year (including deaths). A tetravalent live-attenuated virus vaccine is available for this infection. The aim of our work was to study vaccine acceptance, attitudes and behaviors among travelers heading to areas with risk of dengue.*
Methods. *We conducted a cross-sectional study in February-April 2024 at the Travel Medicine Clinic of Rozzano (Italy), focusing on travelers directed to areas with risk of dengue. We collected the following information anonymously: travel destination, reason for travel, date/month of departure, length of stay, and accepted/refused vaccinations.*
Results. *58 travelers were included in our study and they chose 23 countries for their travel with a mean length of stay of 16.98 days. Five (8.62%) refused dengue vaccination because they considered the vaccination not necessary (80%), or for its cost (20%). There was no statistically significant difference between men and women in vaccination acceptance. Age and length of stay did not influence the percentage of refusals.*
Conclusions. *Although the results are limited by the small number of travelers, they highlighted the problem of vaccine hesitancy among travelers, and further efforts are needed to address this phenomenon.*

Introduction

Dengue is a vector-borne viral disease caused by the flavivirus dengue virus (DENV). Approximately 400 million cases and 22,000 dengue-related deaths occur worldwide each year. It has been reported in more than 100 countries in tropical and subtropical regions. A positive-stranded enveloped RNA virus (DENV) is principally transmitted by *Aedes* mosquitoes. It has four antigenically distinct serotypes, DENV-1 to DENV-4, each with different genotypes, three structural proteins and seven non-structural proteins [1].
In February 2023, the Italian Drug Agency (AIFA) authorized the use and marketing of TAK-003 (Qdenga®), a live attenuated tetravalent vaccine for the prevention of Dengue disease caused by all the virus serotypes. The vaccine also received approval from the European Medicines Agency (EMA) in December 2022 [2].
TAK-003 is based on a DENV2 backbone with recombinant strains expressing surface proteins for DENV1, DENV3 and DENV4. By using a backbone of DENV2 instead of yellow fever virus it has the potential to stimulate a broader humoral and cell mediated immunological reaction [3].
TAK-003 is administered as a subcutaneous injection, two doses with 3 months of interval. It is contraindicated in immunocompromised individuals, as well as in pregnant and breastfeeding women. It seems to be well tolerated and no serious adverse events reported [4].
TAK-003 induces antibody responses against all four serotypes of varying levels, highest for DENV2. The neutralizing antibody levels are higher in individuals with previous dengue fever compared to dengue naïve.
In 2024, the Italian Ministry of Health published a document named "Dengue - Global Update" [5] and, in the same year, the Italian Society of Travel Medicine (SIMVIM) formulated a list of indications to facilitate the healthcare workers in using dengue vaccine during their activity [6].
Several studies demonstrated that certain travel-related infections can be prevented through vaccination, however many travelers fail to seek or receive pre-travel vaccines. Several factors seem to contribute to the poor uptake of pre-travel vaccines such as low disease risk perceptions and vaccination costs [7-10], nonetheless, other determinants influencing individual travelers' decisions regarding pre-travel vaccination are largely unknown [11, 12].
Since January 30, 2024 the TAK-003 vaccine has been available in the Travel Medicine Clinic of Rozzano (ASST Melegnano Martesana).
The aim of our work was, therefore, to study vaccine acceptance, attitudes and behaviors among travelers directed to areas with risk of dengue.

Materials and methods

From February to April 2024, we conducted a cross-sectional study at the Travel Medicine Clinic of ASST Melegnano Martesana (Rozzano, Lombardy, Italy).

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We included adult travelers (≥18 years old) heading to areas with risk of Dengue. Travelers could be resident or domiciled in the Lombardy region and booked an appointment for counseling at the Travel Medicine Clinic of Rozzano, using an online reservation system. This system is used in Lombardy and allows travelers book an appointment for a counseling in the city/clinic with the lowest waiting times and the highest number of free slots. So we include in our study all the travelers who had an appointment at the Travel Medicine Clinic of Rozzano in the study period.
During the counseling, a travel medicine specialist gathered information about travelers' past medical history (including any underlying conditions or symptoms), informed them about the travel-connected risks and recommended malaria chemoprophylaxis and vaccinations, if necessary. Vaccinations could be accepted or refused by completing a consent form.

Statistics

Socio-demographic information (country of origin, age, gender) and other information such as travel destination, reason of the travel, date/month of departure, length of stay and the accepted/refused vaccinations were collected in an anonymous database.
From the answers percentages, means and standard deviations were calculated. Shapiro-Wilk test was performed to assess the non-normality of the variables "age" and "length of stay." Mann-Whitney test (for dichotomous variables), the Kruskal-Wallis test (for variables with more than two categories) and odds ratios were calculated to assess the relationship between dengue vaccination refusals and the collected variables. Data were processed using Stata SE, Version 12.1 (StataCorp, College Station, TX). The level of significance was set at $p < 0.05$.
The study was conducted in complete anonymity and approved by the Health Direction of ASST Melegnano Martesana (Vizzolo Predabissi, Milan, Italy).

Exclusion criteria

We excluded from the study travelers directed to areas not at risk for Dengue. The map of the areas with risk was retrieved from the CDC [13].
In accordance with the guidelines, we also excluded travelers who could not receive the vaccination for medical reasons (including women who were pregnant or breastfeeding) [14].
Information about the second dose was not collected due to the limited time span.

Results

From February to April 2024, we enrolled 58 adult travelers (50% female, 50% male). Their mean age was 42.15 years (SD 1.95); 98.27% were Italian. The destinations (and months) chosen from their travels are resumed in Table I.
Participants chose 23 countries for their travels; the most popular destinations were Thailand, Tanzania (including Zanzibar), Indonesia, Vietnam. The mean length of stay was 16.98 days (standard deviation 1.59), and the main reasons for travel were tourism (94.83%), work (3.45%), volunteering (1.72%). Travelers chose to go abroad principally in March, April, July and August.

Tab. I. Travelers' destinations and months chosen to travel.

	Destination	N	%
1	Angola	2	3.45
2	Antilles	1	1.72
3	Benin	1	1.72
4	Bolivia	2	3.45
5	Brazil	4	6.90
6	Cambodia	1	1.72
7	China	1	1.72
8	Colombia	3	5.17
9	Philippines	1	1.72
10	Ghana	1	1.72
11	Indonesia	5	8.62
12	Kenya	3	5.17
13	Madagascar	2	3.45
14	Mexico	2	3.45
15	Peru	2	3.45
16	Seychelles	2	3.45
17	Singapore	1	1.72
18	Sri Lanka	1	1.72
19	South Africa	2	3.45
20	Tanzania	7	12.07
21	Thailand	8	13.79
22	Uganda	1	1.72
23	Vietnam	5	8.62
	Month	**N**	**%**
	February	1	1.72
	March	11	18.97
	April	17	29.31
	May	2	3.45
	June	3	5.17
	July	10	17.24
	August	10	17.24
	September	4	6.90

Approximately 89.66% of our sample also received information about malaria chemoprophylaxis. Five travelers (8.62% of our sample) refused dengue vaccination especially because they considered the vaccination not necessary (80% of them) or for its cost (20% of them; the cost includes the price of the vaccine and the injection according to the regional price list). No one refused due to fear of side effects.
No one declared a past exposure to DenV virus or a past vaccination.
There was no statistically significant difference between men and women in vaccination refusals (p 0.64). Age and length of stay did not influence the percentage of refusal (all $p > 0.05$)
Table II shows the other vaccinations that travelers decided to accept and to refuse.

Tab. II. Vaccinations that travelers decided to accept and to refuse.

Vaccination	Considered sample	Accepted	%	Refused	%
Yellow fever	13	13	100	-	-
Typhoid fever	40	38	95	2	5
Hepatitis A	35	35	100	-	-
Polio	31	31	100	-	-
Diphtheria - pertussis - tetanus	24	24	100	-	
Men ACWY	9	7	77.78	2	22.22

Discussion

Traveling is inseparable from the modern way of life [15]. However, traveling to various places can expose people to infectious hazards. Moreover, other authors affirmed that travelers are potentially at higher risk of a broad range of infectious diseases and play a key role in their global spread [16].

Vaccine-preventable disease (VPD) in travelers are not limited to exotic diseases in developing countries. For example, a previous study demonstrated that non-immune adult US travelers are at significant risk of measles in wealthy, industrialized countries, including Western European countries and Mexico [17].

Vaccines protect the recipients at an individual level but also create a barrier against the transmission of infectious agents within the community. Both vaccines for tropical diseases and vaccines with routine indications can protect their recipients from infectious diseases associated with international travels [18].

Since the beginning of 2024 over two million dengue cases and over 500 dengue-related deaths have been reported globally. Most cases were reported in the WHO PAHO region with a cumulative number of 1 874 021 suspected cases reported until week 8 of 2024 (ending 25 February 2024). According to the PAHO report of 7 March 2024, this is an increase of 249% compared to the same period in 2023 [19].

Dengue is a mosquito-borne viral infection that has spread throughout the tropical world over the past 60 years and now affects over half of the world's population. The geographical range of dengue is expected to expand further due to ongoing global phenomena including climate change and urbanization [20].

In our study five travelers (8.62%) refused dengue vaccination.

Other studies demonstrated that the primary reason for refusing vaccines is a lack of knowledge about the severity of vaccine-preventable diseases [21].

However, vaccine hesitancy among travelers is influenced by the interplay of contextual conditions, individual characteristics, and specific factors related to vaccinations. Vaccine hesitancy is more prevalent in developed countries free of tropical diseases. Poor access to information or dissemination of inaccurate or incomplete data may construct an erroneous knowledge of immunobiological products. In this context, exaggerated accusations of the side effects and disparagement of the effectiveness of vaccines find fertile ground, especially among individuals with a lower educational level [22]. In our study, instead, no one refused for fear of side effects.

Lopes et al. observed that extreme cultural or religious motives may fuel reactions towards immunizations. Personality traits, political ideologies, idiosyncrasies, and the duration of travel are individual features that can affect the acceptance of the recommended vaccinations [22]. In our study, instead, age and length of stay did not influence the percentage of refusals.

Furthermore, the same authors affirmed that difficulties in the accessibility of the necessary services and products, including incompatibility of working hours, long distance, excessive waiting time, and high cost, may foster indifference towards vaccines, while past failures of immunization programs might shake travelers' confidence in vaccinations [22]. In our study, 80% of travelers who refused dengue vaccination considered the vaccination not necessary, 20% refused for its cost.

Similar evidence has been reported by Adongo et al. who observed that travelers' rejections of vaccinations are multidimensional constructs. Common reasons for the refusal of the recommended vaccines include doubts about their necessity, concerns about their safety, and cost issues. Ignorance of the risks of tropical infectious disease, as well as a lower level of education, fuels the omission of travel vaccinations. Other secondary dissuading factors may include mistrust against pharmaceutical companies and health authorities, anticipated pain from the injection, uncertainty about previously received vaccinations, lack of available time, and negligence for seeking appropriate pre-travel advice. Sometimes, the refusal of vaccines may be due to the belief that the recommended guidance limits personal autonomy and violates the sense of freedom that is often inextricably related to the procedure of traveling and the identity of travelers [23].

In our study there was no statistically significant difference between men and women in vaccination refusals. This is an unexpected result as women tend to refuse vaccination more than men [24, 25].

Among the other vaccinations that, in our study, have been proposed to travelers, meningococcal vaccine (ACWY) was the most refused (22.22%). This result is similar to what observed in other studies (but focused on pediatric population): in these studies parents considered this vaccination unnecessary. The explanation given by the opposing parents was the fear of side effects, poor information received and doubts about the actual efficacy of the vaccine [26, 27].

Limits

Our study has several limits. First, the limited time span: in fact it was impossible to collect information about the second dose acceptance. According to the vaccine schedule, the second injection is given 3 months after the first injection and our study was performed in February, march, and April so no one was eligible to receive the second dose.
The second limit was the number of enrolled patients: 58 travelers is a limited sample and it could not be representative of the entire population. Therefore, we encourage other authors to integrate our evidences with their findings.

Conclusions

Although the results are limited by the small number of participants, they highlight the problem of vaccine hesitancy among travelers. Despite the existing evidence of the value of vaccines in protecting public health, vaccine hesitancy represents a growing phenomenon. Achieving a wider vaccine acceptance could limit the spread of infectious diseases, and further efforts are needed to limit the phenomenon of vaccine hesitancy.

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Conflicts of interest statement

We declare no conflict of interest.

Authors' contributions

GT: had the idea of the article, analyzed data and wrote the article; IW: collected data and helped to conceptualize the ideas; AN: supervised the work and helped to conceptualize the ideas.

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