Study of Dengue Fever among Israeli Travellers to Thailand

by

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Abstract

During 1995-2002, there were 149 cases among Israeli travellers, of which 110 (74%) were acquired in Thailand. The locations included Ko-Phangan (62%), Ko-Samui (20%), Ko-Tao (3%) and Ko-Phi Phi in Phuket area (15%). During the years of normal transmission in Thailand the cases were seen in the rainy season (July-November), but during the outbreak years (1998 and 2002) maximum cases occurred during the dry season (December-June). It is important for local health authorities to treat this source of information as a “sentinel source” for the detection of this emerging infectious disease.

Keywords: DF, travellers, Thailand, Israel.

Introduction

Dengue fever (DF) has been one of the most important resurgent tropical diseases in the past 20 years, with an expanding geographical distribution of both the virus and the mosquito vector, increased frequency of epidemics, and the emergence of dengue haemorrhagic fever in new areas[1]. It is estimated that about 100 million cases of dengue fever and 250,000 cases of dengue haemorrhagic fever (DHF) occur annually[2]. The 1980s and 1990s saw a dramatic geographical expansion of epidemic DHF from south-east Asia to the South Pacific Islands, the Caribbean and the American region[3]. South-east Asia and the Indian subcontinent, regions where dengue fever predominates, are popular tourist destinations. It is not surprising then, that DF may affect international travellers to these regions. These regions are popular sites for Israeli travellers with an estimation of more than 100,000 travellers annually.

The purpose of this paper is to address aspects of dengue fever among Israeli travellers who acquired DF in Thailand.

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Materials and methods

Patients seen at the Center for Geographic Medicine at Sheba Medical Center, Tel Hashomer, with a history of acute febrile illness were diagnosed as having dengue fever if they had a positive anti-dengue IgM test. Only IgM seropositive cases were included. The serology test was performed using a commercial enzyme-linked immunosorbent assay kit (PanBio, Queensland, Australia). This test was introduced in 1994, and the Sheba Medical Center remains the only place in Israel where it is routinely available.

During 1998, an Israeli physician was placed in Bangkok by a health insurance company. Cases diagnosed in Thailand during this year included Israeli travellers who had subscribed to this firm. The service was based on prior subscription, and subscribers were eligible for free access to consultation provided by the Israeli physician on location. The availability of this free medical service encouraged subscribers to seek medical care, and it is unlikely that ill subscribers would not have called the service that was available at all hours of the day. These patients were also included in this study. The serology test for dengue IgM and IgG was performed by the physician at local hospitals using the PanBio enzyme-linked immunosorbent assay kit.

Results

During the years 1995 through December 2002, 149 cases of dengue fever were diagnosed in travellers to Asia. Among them the majority (71%) acquired DF in Thailand; the rest of the cases did so in India, Laos, and Myanmar (Table 1).

Data regarding the disease pattern in travellers to Thailand are given in Figure 1. There was a peak during 1998, when altogether 52 Israelis were diagnosed as having acquired DF in Thailand. In 29 of these cases, DF was confirmed in Israel and in the other 23 cases, DF was confirmed by an Israeli physician who treated Israeli travellers in Bangkok. Another peak emerged during the year 2002 in which we confirmed 29 DF cases.

Table 1: Distribution of Israeli dengue cases according to country of acquisition

<table>
<thead>
<tr>
<th>Country of acquisition</th>
<th>Number of patients No=149</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thailand</td>
<td>110</td>
</tr>
<tr>
<td>India</td>
<td>28</td>
</tr>
<tr>
<td>Myanmar (Burma)</td>
<td>3</td>
</tr>
<tr>
<td>Laos</td>
<td>2</td>
</tr>
<tr>
<td>Unknown</td>
<td>6</td>
</tr>
</tbody>
</table>
**Seasonality**

Over the years, most cases were seen during the rainy season (July-November). Only during the years with high activity of the dengue virus did we see a high incidence during the dry season (December-June). As can be seen in Table 2, every 3-4 years there is a higher frequency of cases in the dry season. In 1995, there was an even distribution between the dry and rainy seasons (although the numbers were quite small). During 1998, 60% of the cases occurred in the dry season. This year (2002), we have seen 19 cases from Thailand from January to June (another case was acquired in Laos), and only 9 cases during the rainy season (68% vs. 32%, respectively). As can be seen in Table 2, in the other years we had a frequency of 2 out of 47 cases (4%) during the dry season.

**Table 2**: Distribution of dengue fever cases among Israeli travellers according to seasons

<table>
<thead>
<tr>
<th>Year</th>
<th>Dry season (Dec-Jul)</th>
<th>Rainy season (Jul-Nov)</th>
<th>Total Asia</th>
<th>THA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td>5</td>
<td>6</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>1996</td>
<td>1</td>
<td>9</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>1997</td>
<td>0</td>
<td>18</td>
<td>18</td>
<td>4</td>
</tr>
<tr>
<td>1998</td>
<td>36</td>
<td>24</td>
<td>60</td>
<td>52</td>
</tr>
<tr>
<td>1999</td>
<td>1</td>
<td>8</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>2000</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>2001</td>
<td>0</td>
<td>10</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>2002</td>
<td>20</td>
<td>9</td>
<td>29</td>
<td>28</td>
</tr>
</tbody>
</table>

**Location**

Almost all cases of DF were acquired on the islands of southern Thailand. The most common place was the gulf of Thailand where 85% of the cases had acquired infection in Ko-Phangan 62%, in Ko-Samui 20% and in Ko Tao 3%. The rest of the cases (15%) were acquired in Ko-Phi Phi in the Phuket area (Figure 2).

**Figure 2**: The Gulf of Thailand

**Discussion**

Changes in the global epidemiology of dengue fever have been observed in recent years in both North and South America as well as in the Pacific region and in south-east Asia\(^2,3\). This may be due to climatic changes and to the failure to control the mosquito vector\(^1,5,6\). In parallel, there has been a tremendous increase in the number of travellers worldwide, including to tropical areas. These parallel changes increase the likelihood of travellers being infected with the dengue virus.

Diagnosis of DF is a challenge in industrialized countries, since most physicians are less familiar with dengue fever
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and its diagnosis. Moreover, diagnostic means for DF are lacking in many institutions. In addition, because of the short incubation period, most of the infected travellers will go through the sickness while in the endemic area. Thus, cases diagnosed in industrialized countries are probably only the tip of the iceberg.

The diagnosis of dengue virus infection is often based on commercially available ELISA test for serological assays. However, cross-reactivity exists between various flaviviruses such as Japanese encephalitis (JE) virus, yellow fever (YF) virus and the dengue virus. In endemic areas such as in south-east Asia it may be a challenge to differentiate between DF and JE when both circulate in the region\(^7\). However, JE is a very rare disease among travellers being a rural infection, and does therefore not constitute a real diagnostic challenge in travellers. But a substantial percentage of travellers to the tropics receive JE and YF vaccination prior to travelling, and the question arises whether these vaccines can interfere with dengue virus serology tests. Our previous study revealed that the IgG test yielded 11-17% and 15-44% positives in healthy travellers vaccinated against JE and YF, respectively. The dengue IgM was not found to cross-react with the vaccines\(^8\). This limits the ELISA-based IgG test for dengue diagnosis for use as an epidemiological tool to measure seroconversion rates among pre-vaccinated travellers after their stay in endemic areas. Thus, only symptomatic patients who returned from an endemic area with positive dengue IgM antibodies were included in our dengue studies.

Despite the strict criteria we used, DF appears to be a rather common disease among Israeli travellers to south-east Asia\(^4,9,10\). Thailand, which is an attractive tourist destination, is a major site for acquiring DF, mainly in the Gulf of Thailand\(^4,9\). The current study shows the same pattern, where 62% of the cases of the 2002 outbreak were acquired in Ko-Phangan. The high number of cases from Ko-Phangan does not necessarily imply that there is a increased dengue virus activity in this island, since it can be due to the increased number of travellers to this attractive island. Unfortunately, we do not have a breakdown of the number of travellers to destinations within Thailand for a comparison of the attack rate. However, the itinerary of Israelis usually includes Bangkok area and the northern part of Thailand as well. Thus, the high number of cases from Ko-Phangan is highly suggestive for increased dengue activity.

The increase in dengue activity among our traveller population occurs in waves. During an outbreak, the change is not only an increase in the number of dengue cases during the regular dengue season, but rather a change in seasonality. We usually see dengue patients around the rainy season (July-November). However, during an outbreak there is a striking increase in dengue activity during the dry season (December-June) (Table 2). During the 1998 outbreak, the attack rate of cohort of 5,030 Israeli travellers to Thailand was 5.0/1000 (95% CI =2.6-8.4/1000) in the dry season, and of 1.7/1000 (95% CI = 0.5-4.3/1000) in the rainy season\(^9\).
Data collected from travellers can indicate changes in the local epidemiology of infectious diseases, thus serving as a sentinel for emerging infectious diseases.

Regarding DF, travellers heralded the outbreaks of DF that occurred in 1998 and of the current year of 2002 (Figure 1). The Center of Diseases Control and Prevention (CDC, Atlanta) and the International Society of Travel Medicine (ISTM) keep a database – GeoSentinel – that collects data of morbidity among returning travellers from a network of 25 travel and tropical clinics around the world(11). The information gathered by this kind of network may benefit both travellers and the host countries as well.

In a well-designed study which was published 15 years ago, dengue fever was not mentioned as one of the hazards to the traveler(12). The current data, our previous reports(4,9,10), and reports by other authors(13,14), indicate that dengue fever is a definite risk throughout the year for travellers. The attack rate is similar to the estimated rates for other frequent diseases of travellers such as hepatitis A without vaccine or malaria with no prophylaxis. This calls urgently for an efficacious and safe vaccine against this disease.

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References

