Study of Dengue Virus Infection in Kuwait

by

Alexander Pacsa, Abu S Mustafa* and Umesh C Chaturvedi

Department of Microbiology, Faculty of Medicine, Kuwait University,
PO Box 24923, Safat 13110, Kuwait

Abstract

Kuwait has a workforce of more than one million non-Kuwaitis coming from countries where vector-borne diseases like dengue fever are endemic. This study was aimed at investigating the magnitude of the dengue problem by determining the prevalence of dengue virus-specific antibodies and diagnosing suspected dengue fever cases in Kuwait. The antibody prevalence was determined by testing 909 serum samples from persons of various nationalities resident in Kuwait. In addition, laboratory diagnosis of the dengue virus infection was attempted on samples from 210 patients with the clinical presentation of dengue-like illness. Overall, 48% (436/909) donors had dengue virus-specific IgG antibodies. However, in Kuwaitis the seroprevalence was only 14% (59/425), which was significantly lower than in any group of the non-Kuwaiti residents, (p<0.001). Among the IgG-positive donors, the antibodies were most frequently detected against DEN-1 (55%), followed by DEN-2 (35%) and DEN-3 (10%). None of the 436 positive samples showed IgG antibodies to DEN-4. Moreover, among the 210 clinically suspected patients, IgM detection and RT-PCR confirmed dengue illness was found in 2 patients. Both of these patients were infected with DEN-2 and had visited dengue-endemic areas in the recent past. There was no evidence of the transmission of dengue infection within Kuwait as all of the 47 subjects who had never left Kuwait were found negative for dengue virus antibodies. The absence of Aedes aegypti in Kuwait and the poor vectorial capacity of Aedes caspius appear to be responsible for the absence of local transmission of dengue virus.

Keywords: Dengue fever, DEN-1, DEN-2, DEN-3, Aedes caspius, Kuwait.

Introduction

Dengue virus belongs to the flaviviridae family and has four antigenetically but distinct serotypes (DEN-1, DEN-2, DEN-3 and DEN-4). Infection with any of these viruses is usually asymptomatic or produces a mild, self-limiting disease, dengue fever (DF). However, in a small percentage of cases, the infection may result in a life-threatening syndrome, the so-called dengue haemorrhagic fever (DHF)(1,2). The disease is reported in over 100 tropical and subtropical countries with about 2.5 billion people at
risk of infection with dengue virus, leading to approximately 100 million cases of DF, 500,000 cases of DHF and 25,000 deaths per year\(^3\).

Kuwait is a small country with a typical desert climate located between latitudes 28°35' and 30°05' north of the Equator. The country has about 2.2 million people, out of which about 70% are non-Kuwaitis belonging to the expatriate workforce coming from countries where the dengue disease is endemic. Moreover, a large number of Kuwaiti nationals go on vacation to dengue hyperendemic areas during the peak season of dengue virus activity there. Therefore, there are ample opportunities of the virus infestation into the country by both expatriates as well as Kuwaiti nationals, as observed in other countries\(^4,5,6,7\).

In view of the large-scale movement of the expatriate population and that of Kuwaiti nationals, there was a need to assess the potential of the dengue virus importation and the risk of establishment of dengue in Kuwait.

**Materials and methods**

**Study population**

The study was carried out between 1997 and 1999. Serum samples from age- and sex-matched donors were obtained from Kuwaiti nationals (n=425), individuals born and living in Kuwait permanently (Bedouins, n=47), and expatriates from South Asia (India, Pakistan, Sri Lanka, Bangladesh, n=266), south-east Asia (Philippines, n=31) and Middle East (Syria, Egypt and Lebanon, n=140). In addition, sera were obtained from a group of 210 patients admitted to the Infectious Diseases Hospital, Kuwait. The patients were selected on the basis of clinical presentations compatible with dengue-like illness and also with febrile illness of unknown origin. All of them had recently come back after visiting dengue-endemic countries. Blood samples were collected from the patients on days 5-6 of the illness. The sera were frozen at -80°C until tested.

**IgG ELISA and blot tests**

IgG ELISA was performed by using dengue virus (DEN 1-4) – specific antigens, control antigen and appropriate serum controls obtained from the Centers for Disease Control (CDC) Atlanta, USA. The ELISA procedure described by Gentry et al.\(^8\) was followed.

IgG blot test was performed by using commercial kits (Genlab Diagnostics, Singapore) according to the manufacturer's recommendations.

In order to validate the serological survey, all the samples (n=909) were tested by both ELISA-IgG and dot blot-IgG tests. Sera being positive in both tests were considered as "true" positive for the presence of dengue-IgG antibodies.

**IgM capture ELISA**

The test was done using plates coated with anti-human IgM antibodies according to the instructions of the manufacturer (PanBio, Australia).

**RT-PCR**

The serum samples positive for dengue virus-specific IgM antibodies were screened for
the presence of dengue virus (DEN 1-4) – specific RNA by an RT-PCR described previously\(^8\).

**Results**

**Prevalence of dengue virus antibodies in people resident in Kuwait**

The findings (Figure) showed that maximum seropositivity was seen in subjects originating from south-east Asia (56.6%), followed by South Asia (37%), Middle East (25%) and Kuwait (14%). The 47 serum samples collected from Kuwaiti Bedouins, who were born in Kuwait and had never left the country, were negative for dengue IgG antibodies.

The seroprevalence in the Kuwaitis was significantly lower (P<0.001) than in any group of expatriates. The serological data were further analysed to determine the serotypes of dengue viruses infecting the population in Kuwait. Among the 436 subjects found positive for dengue virus IgG, the most prevalent antibody was against DEN-1 (55%), followed by DEN-2 (35%) and DEN-3 (15%). None of the sera was positive for IgG antibodies against DEN-4.

**Laboratory diagnosis of dengue virus infection in clinically suspected patients**

The sera of 210 patients who had dengue-like illness were tested first for the presence of dengue virus-specific IgM antibodies. The capture IgM ELISA showed that 19 (9%) of them had dengue-specific IgM, thus suggesting recent infection with dengue virus. Among these 19 patients, 12 were Kuwaitis and 7 non-Kuwaitis. All of them had visited dengue endemic areas for 1 to 9 weeks and the time gap between the return to Kuwait and the onset of illness was from 2 to 10 days. The presence of dengue virus RNA was studied in the sera of all the 19 patients by RT-PCR using consensus primers, followed by semi-nested PCR with type-specific primers. RT-PCR was found positive for dengue virus in 2 patients and, in both of them, the semi-nested PCR identified the amplified products as DEN-2. One of these patients was a 30-year-old male Kuwaiti who had visited the Philippines for 5 weeks. He developed the clinical symptoms 7 days after his return and was sick for 10 days. The other patient was a 23-year-old Indian who had visited his country for 3 weeks and had developed the clinical symptoms 2 days after his return to Kuwait and was sick for 7 days.

**Discussion**

This study was carried out to determine the magnitude of the threat of dengue to
Kuwait. The results of this study showed that the expatriates who come from dengue-endemic areas have a higher percentage of antibodies to the virus than the Kuwaitis. Although a fraction of the Kuwaiti nationals (14%) also had antibodies to the dengue viruses, the residents of Kuwait who had never left the country did not have antibodies against the dengue viruses. The magnitude of the seroprevalence of dengue in Kuwaitis found in this study was similar to what had been reported by Al-Nakib et al.\(^\text{10}\).

These results also suggest that despite the large number of the workforce coming to Kuwait from dengue-endemic areas, the virus is not transmitted within Kuwait. It may be explained by (i) the absence of \textit{Aedes aegypti}, the classical vector of dengue\(^\text{11}\), and (ii) \textit{Aedes caspius} may not be a vector\(^\text{12}\). However, a recent surveillance study in Saudi Arabia had revealed that in the Jeddah area, there were 665 confirmed cases of dengue infection\(^\text{13}\). This was explained by the expansion of the city, which had resulted in a tremendous increase in the number of fresh water containers being used there. These proved to be the breeding sites for \textit{Aedes aegypti}\(^\text{13}\). Since there is continuous expansion of residential areas in Kuwait city, the risk of the introduction of the dengue virus into the country is real. Therefore, there is no scope for complacency. \textit{Aedes aegypti} is well entrenched in Saudi Arabia and Oman in the region. Local health authorities need to be vigilant against the introduction of this species into the country to prevent dengue endemicity.

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**References**


