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Dengue infection in patients with febrile illness and its relationship to climate factors: A case study in the city of Jeddah, Saudi Arabia, for the period 2010–2014

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ABSTRACT

Dengue is an important global arboviral disease with expanding geographical range. It is a major public health concern in Western Saudi Arabia since its first detection in the city of Jeddah in 1994. In this retrospective study, we examined dengue incidence among febrile patients suspected for acute dengue infection at King Abdulaziz University Hospital, Jeddah from 2010 to 2014 and we tried to determine the effect of climate factors on dengue incidence in the city. Acute dengue incidence rates among clinically suspected patients showed annual variation with a range from 29.3% to 57%. Male gender and 11–30 years age range were found to be risk factors for dengue infection in Jeddah. While dengue infections can be detected throughout the year, most cases occurred between March and July with peaks in May and June. Seasonality of dengue was found to be significantly associated with the decrease in relative humidity and increase in temperature within the range of ~25 °C to ~33 °C but not extremely hot temperatures. Moreover, we found that rainfall during winter (November to February) has a significant lag effect on dengue infection among febrile patients in the city. Jeddah is the second largest city in Saudi Arabia and a major hub for pilgrims because of its close proximity to the holy sites in the Kingdom. The observed high rates of acute dengue infections clearly show the endemicity of dengue in Jeddah. The observed higher incidence rates at young age are expected to cause an increase in severe dengue cases in the future especially that multiple dengue serotypes are co-circulating in the city. Furthermore, the significant association between the different climate factors and dengue and their impact on the disease seasonality should help in the effort to implement effective control and management measures to reduce dengue burden in the Kingdom.

1. Introduction

Dengue is a serious global public health arboviral infection. It is suggested that dengue incidence has increased by more than 30 folds in the past 50 years (Kyle and Harris, 2008; Ratnam et al., 2013; Mallhi et al., 2015; Banu et al., 2014). Currently, it is estimated to cause 50–100 million cases with more than 22,000 deaths annually. There are ~2.5 billion people at risk of dengue infection living in more than 100 endemic countries in tropical and subtropical regions including countries in South-East Asia, South Asia, Western Pacific, the Americas, Europe and Africa (Banu et al., 2014; Guzman and Isturiz, 2010; Garg et al., 2011; Racloz et al., 2012; Pem-Novosel et al., 2015; Medlock et al., 2015). Dengue virus (DENV) is a flavivirus with 4 antigenically and genetically divergent serotypes (1–4) which can cause disease ranging from asymptomatic to severe infection. Usually, sequential infection with heterologous serotypes can result in severe and fatal outcomes (Anoop et al., 2010; Figueiredo et al., 2011).

Jeddah is a coastal city on the Red Sea in the western region of Saudi Arabia and has a tropical arid climate with very low annual average rainfall (~51.2 mm, Almazroui et al., 2012a). The rainfall amount in Jeddah varies significantly between wet (November-April; 47.8 mm) and dry (June-September; 0.5 mm) seasons (Almazroui et al.,

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2012b). The annual average temperature of this city is ~28.7 °C, however, it varies from season to season and ranges from 24.22 °C to 32.44 °C per season (Almazroui, 2011). Jeddah as well as other Saudi cities including Jazan, and the holy cities of Makkah and Al-Madinah are considered endemic for dengue. While dengue surveillance studies are very limited in Saudi Arabia, prevalence of DENV infection among clinically suspected patients has been shown to range from 31.7–56.9% (Khan et al., 2008; Al-Azraqi et al., 2013; Ayyub et al., 2006; Alhaeli et al., 2016). All DENV (1–4) serotypes have been reported to be circulating in these cities (Ayyub et al., 2006; Alhaeli et al., 2016; Fakeeh and Zaki, 2001; Zaki et al., 2008; Ahmed, 2010; El-Badry et al., 2014; Azhar et al., 2015; Ashshi, 2017; El-Kafrawy et al., 2016). In addition, Jeddah is a major port of entry to Saudi Arabia and millions of pilgrims from all over the world visit this city on their way to perform Hajj or Umrah pilgrimages because of its close-proximity to the holy cities of Makkah and Al-Madinah. Visitors from dengue endemic countries have been suggested as a potential source for DENV importation into Saudi Arabia (El-Kafrawy et al., 2016 Alshehri, 2013). Furthermore, the high prevalence of *Aedes aegypti* in Jeddah throughout the year could increase the risk of autochthonous transmission of DENV (Alshehri, 2013; Alikhan et al., 2014).

Several demographic, economic, social and environmental factors have been proposed to impact vector-borne diseases. Climatic factors in particular such as rainfall, temperature and humidity have been shown to be directly or indirectly associated with *Aedes aegypti* dynamics and ultimately the incidence of dengue infections (Banu et al., 2014; Pandey et al., 2012; Lee et al., 2013; Morin et al., 2013; Ribeiro et al., 2006). Several studies have suggested that increase in rainfall and temperature could increase vector-breeding sites, enhance breeding and virus maturation; thereby increasing dengue transmission (Ribeiro et al., 2006; Brunkard et al., 2008; Yang et al., 2009). Similarly, the direct impact of relative humidity on mosquitoes has been proposed (Banu et al., 2014; Pandey et al., 2012). However, the effect of climate on dengue infection varies from one region to another (Morin et al., 2013), highlighting the importance of investigating these factors and their relationship to dengue infection in endemic regions. Therefore, the main goal of this study was to determine the incidence rate of dengue infection among febrile patients and its relationship to climate factors in the city of Jeddah. Such study should help in our understanding of the impact of climate factors on dengue seasonality and may provide useful information to decision makers to implement effective control and preventative measures when needed.

2. Materials and methods

2.1. Study design

In this retrospective study, King Abdulaziz University Hospital (KAUH) records for all patients presented with febrile illness and investigated for DENV infection at the Special Infectious Agents Unit, King Fahd Medical Research Center, King Abdulaziz University, Jeddah, Saudi Arabia between January 2010 and December 2014 were reviewed. KAUH is one of the major hospitals in the city of Jeddah with 1002 bed capacity (http://hospital.kau.edu.sa). All patients' data were anonymized before the study. Patient demographic information and laboratory results were analyzed. Data from all patients tested for DENV infection were included in this study including age, gender and DENV laboratory results (RT-PCR, IgM and IgG). Study was approved by the Unit of Biomedical Ethics Research Committee at the Faculty of Medicine, King Abdulaziz University.

2.2. Laboratory tests

Samples from patients with febrile illness were routinely tested for anti-DENV IgM and IgG by ELISA and DENV RNA by real-time RT-PCR. Serum samples were screened for anti-DENV IgM and IgG antibodies (Abs) using DENV IgM and IgG capture ELISA kits (Panbio, Australia) according to the manufacturer's instructions. Viral RNA was extracted from samples using QIAamp viral RNA mini kit (Qiagen, Germany) and tested for DENV RNA by real time RT-PCR as previously described (El-Kafrawy et al., 2016; Drosten et al., 2002). Classification of recent acute primary or secondary infections and previous cases was based on detection of viral RNA, IgM and IgG Abs as shown in Table 1. Secondary infections in all presented data include both confirmed and probable acute cases.

Table 1
Classification of primary, secondary and previous dengue virus (DENV) infections.

DENV RNA[a]	IgM	IgG	DENV infections status
Detected	+/−	−	Recent acute primary infection
ND	+	−	Recent acute primary infection
Detected	+	+	Recent acute secondary infection
ND	+	+	Probable recent acute secondary infection
ND	−	+	Previous infection
ND	−	−	Never infected

[a] ND: not detected.

2.3. Meteorological data

Climate factors including rainfall, temperature and humidity from 2010 to 2014 in Jeddah were collected from the records of the Department of Meteorology, Faculty of Meteorology, King Abdulaziz University, Jeddah, Saudi Arabia. Rainfall was measured in millimeters (mm) as the accumulative monthly amount of rainfall. Temperature (TEM), measured in degrees Celsius (°C), is expressed as the mean (TEM-mean) of monthly temperature calculated from the average daily air temperature at 2 m. Relative humidity (RHU) is expressed as percentage of the mean (RHU-mean) of monthly relative humidity calculated from the average daily records. Relationship and correlation between the different climatic factors (rainfall, temperature and relative humidity) and dengue cases were analyzed using Spearman's rank correlation coefficient in IBM SPSS Statistics for Macintosh, Version 22.0.

3. Results

3.1. Demographic findings

During the 5-year period of this study there were a total of 1132 patients with febrile illness who were investigated for dengue infection at KAUH (Table 2). The annual incidence rate of acute dengue infections among these patients ranged from 29.3% in 2014 to 57% in 2010 (Table 2) with overall rate of 44% (See Tables S1–S3 for more details). The highest number of cases was in 2013 (158 cases) and lowest number was in 2012 (42 cases) as shown in Table 2. As expected, primary infections were more common than re-infections although secondary cases increased during 2010 and 2013 epidemic years (Fig. 1). There was a total of 684 males and 448 females with suspected dengue

Table 2
Incidence of recent dengue virus (DENV) infections in patients with febrile illness.

Year	Total no. of suspected cases	No. of recent infections (%)		
		Primary	Secondary	Total
2010	270	100 (37.0)	54 (20.0)	154 (57.0)
2011	205	63 (30.7)	20 (9.8)	83 (40.5)
2012	142	37 (26.1)	5 (3.5)	42 (29.6)
2013	303	118 (38.9)	40 (13.2)	158 (52.1)
2014	212	47 (22.2)	15 (7.1)	62 (29.3)
Total	1132	365 (32.2)	134 (11.8)	499 (44.0)