Dengue Fever in Makkah, Kingdom of Saudi Arabia, 2008-2012

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ABSTRACT

PURPOSE Dengue fever is a reportable condition in the Kingdom of Saudi Arabia (KSA). Case-based information is collected by the Vector-Borne Disease Unit (VBDU) in the Ministry of Health (MOH). However, these case records have not been analyzed statistically beyond producing aggregated reports by year. Therefore, we analyzed dengue fever data collected by the VBDU from 2008 to 2012 to inform policymakers about the distribution and trends in Makkah city, especially because it hosts the Hajj, a yearly mass gathering.

METHODS Using reported data from the VBDU, we calculated incidence rates and trends by nationality, age, and gender from 2008 –2012.

RESULTS In 2008, the incidence rate of dengue fever was 6.2 per 100,000 (95%CI=5-7.5). This rate increased approximately 20-fold in 2009 to 110.6 (95%CI=105.4-115.9). The incidence rate then declined in 2010 to 62.95 (95%CI=58.1-66). In 2011 it declined further to 56.5 (95%CI=52.8-60.3) and in 2012 to 37.6 (95%CI=34.6-40.8). We observed significant increases in dengue fever incidence among males throughout the study period, as well as among those 25-44 years of age.

CONCLUSION Dengue fever is endemic in Makkah city. There was an outbreak in 2009. We recommend improving the surveillance system to include the types of dengue fever (dengue hemorrhagic fever and dengue shock syndrome) plus outcomes (i.e., full recovery, recovery with complication, death). We also recommend using the revised WHO 2009 classification system. Additionally, dengue information should be available to the public to increase awareness. Finally, vector control efforts should be enhanced.

Keywords: Dengue fever; trend; incidence; Case-based information; Saudi Arabia; Hajj

Running title: Dengue fever in Saudi Arabia

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INTRODUCTION

Dengue fever is a serious disease with many complications. It is a vector-born disease that is transmitted from person to person by mosquitos. According to the Centers for Disease Control and Prevention (CDC), there are two species of mosquitos that transmit dengue fever, but the primary vector of dengue is *Aedes aegypti.*[1]This species, whose food source is human blood, lives mainly inside buildings in dark areas like closets and bathrooms. However, it can also be found in outdoor areas with standing water like construction sites and gardens.[2] Dengue

fever has a wide range of presentations from mild to severe. On the mild side, it entails a low, self-limited fever, but severe cases can entail life-threating hemorrhagic shock. The incubation period of the dengue fever virus in humans ranges from three to 14 days. [3]

This disease has a major impact on the health and economy of any population. In 2000, the estimated number of disability-adjusted life years (DALYs) lost to dengue was about 528 worldwide.[3] The number of cases reported yearly to WHO ranged from 0.4 to 1.3 million between1996and2005.[4]In one prospective study in Thailand, the yearly burden of dengue infection during a 5-year period was 465.3 DALYs per million, with non-hospitalized infected people with dengue illness at 44 DALYS per million.[5]In the Americas, studies on the cost of dengue infection[6] indicate that the general cost of a non-fatal outpatientcase averaged around $514, and the cost of anon-fatal hospitalized case around$1,491. Generally, a hospitalized caseof dengue infection costs three times what an outpatientcase costs. If both types of care are considered together, the average cost of a dengue infection is $828.

Dengue fever is treated by administering intravenous fluids and blood transfusions in severe cases. The treatment of dengue fever is only supportive, and there is no licensed vaccine or medication yet.[7] According to the World Health Organization (WHO), the incidence of this disease has increased around the globe. The number of people who are at risk of acquiring dengue is more than 2.5 billion, which is more than 40% of the world's population.[8] According to the WHO, dengue fever can be classified into dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS).[8] Most DF cases are self-limited, but DHF and DSS cases are life-threating if not treated. The mortality rate from complications of dengue fever is 20% when untreated. However, it is less than 1% if recognized early and treated. [9]

Dengue fever is prevalent in tropical and subtropical areas. According to the CDC, there are about 100 million cases of DF, with 100,000 cases of DHF needing hospitalization every year. The disease accounts for 22,000 losses of life each year in more than 100 countries, many of those children. [2]

Many factors are associated with the transmission of this disease, including climate change, population growth, urbanization, travel, and poor vector control. All of these factors are present in Makkah city, Saudi Arabia.

This study aimed at describing reported cases of dengue fever investigated by the Vector-Borne Disease Unit (VBDU) from 2008 to 2012 as well to identify risk factors (e.g., age, outdoor exposure) and endemic channel.

METHODS

Dengue fever is a notifiable disease in KSA; weekly and yearly aggregates (2008-2009) of dengue fever cases by gender, nationality, age and work were reported to VBDU department in Makkah. Makkah is a city in the western region (called Hejaz) and is the capital of Makkah province. It is located in a narrow valley at a height of 277 m (909 ft.) above the sea, 75 km from Jeddah city. Its population is around 2 million according to the 2012 census. It is the third largest city in Saudi Arabia after Riyadh and Jeddah. It is the holiest city for all Muslims worldwide, and most Muslims wish to visit Makkah at least once in their lives. More than 15 million Muslims visit Makkah annually to perform Hajj and Omrah.

Since 2008, the dengue fever registry has been maintained electronically. Population data (i.e., nationality, age, gender) were obtained from the KSA Ministry of Economy and Planning, Central Department of Statistics and Information, which draws statistical information from censuses, field surveys, and statistical studies, in addition to extracting data from administrative records.[10]

Case Definition

The MOH has a case definition for both suspected cases and confirmed cases. This definition has not been changed since 2004. For suspected cases, they have the following definition:

1. DF: Sudden high fever for five days, frontal headache, joins and muscle spasm with vomiting.
2. DHF: fever, platelets <100000, positive tourniquet test and hematocrit < 20%
3. DSS: same as above plus shock.

Confirmed cases are only diagnosed through laboratories by tissue culture, IgM, or PCR methods. [11]

The reporting and control of dengue fever in Makkah each operate on different levels. The Vector Control Department receives notification about dengue fever cases from all hospitals in Makkah via a special form, gives a unique code for each case, and records the cases in their database. It follows the progress of specimen transfers from the hospital to the regional lab, and it receives the results from regional labs (IgM, IgG, Ns1, and PCR) and records them in their database. Then it sends the results back to hospitals as well as sending a vector exploration team to investigate each individual case and implement preventive measures. After this, the

Department records the results from the vector exploration team into the database. It archives all the notification cases and disseminates the data to Makkah Municipality, the MOH in Riyadh, hospitals and local schools.

The vector exploration teams identify the contacts for each case and follow them for the incubation duration, trying to locate their residence for the previous two weeks to identify the source of the infection and discover any unreported cases. The teams also educate the contacts about the disease: their symptoms and signs, and how to prevent the spread of the disease. At the houses of cases, they take a sample of the mosquitos. If there any positive results for Aedes Aegypti, the Makkah municipality will be notified to spray the house once a day for three days. The exploration teams also spray the rooms inside the case house, identify the types of mosquitos there, and perform sensitivity tests for different pesticides.

Hospitals are responsible for undertaking their own set of procedures concerning dengue fever. Any suspected case is assessed by the public health doctor on the hospital staff. T he public health doctor, along with the treating doctor, fills out a special form and uses a unique code from the Vector Control Department. The form is then sent to the Vector Control Department in Makkah. The patient is isolated in a mosquito-free room to prevent the spread of the infection. The hospital takes 5mlbloodto be sent to the regional lab. The results are then sent to the Vector Control Department by fax, and they notify the hospital.

This secondary data analysis (without any personal identifiers) did not meet the definition of Human Subjects Research, so it did not require Institutional Review Board approval.

Statistical Analyses

We used secondary data and incidence rates calculated per100, 000 persons. Rates were analyzed over a 5-year period (2008 – 2012) using Poisson regression and classified as increasing, decreasing, or stable as determined by positive, negative or non-significant coefficients. Significance was determined at a 5% level using two-sided P values. Rates were compared using rate ration and 95% confidence intervals.

RESULTS

The incidence rate for dengue fever was lower in 2008 than in any of the other years that were studied (Table 1).The highest incidence rate occurred in 2009. This indicates that there was an outbreak of dengue fever in 2009. After 2009, the incidence rate started to gradually decrease again, and continued to do so from 2010 to 2012. The dengue fever incidence rate trends from 2008 to 2012 were as follows: it was low in 2008, then it increased significantly in 2009, and after that, it started to decrease gradually from 2010 to 2012 (Figure 1).

TABLE 1: Dengue Fever Incidence Rate per 100,000 Population and Number of Cases, Kingdom of Saudi Arabia, Makkah, 2008 – 2012

Year	Rate (n)	95% CI
2008	**6.2 (95)**	5-7.5
2009	**110.6 (1697)**	105.4-115.9
2010	**62(951)**	58.1-66
2011	**56.5 (867)**	52.8-60.3
2012	**37.6(577)**	34.6-40.8

CI = confidence interval

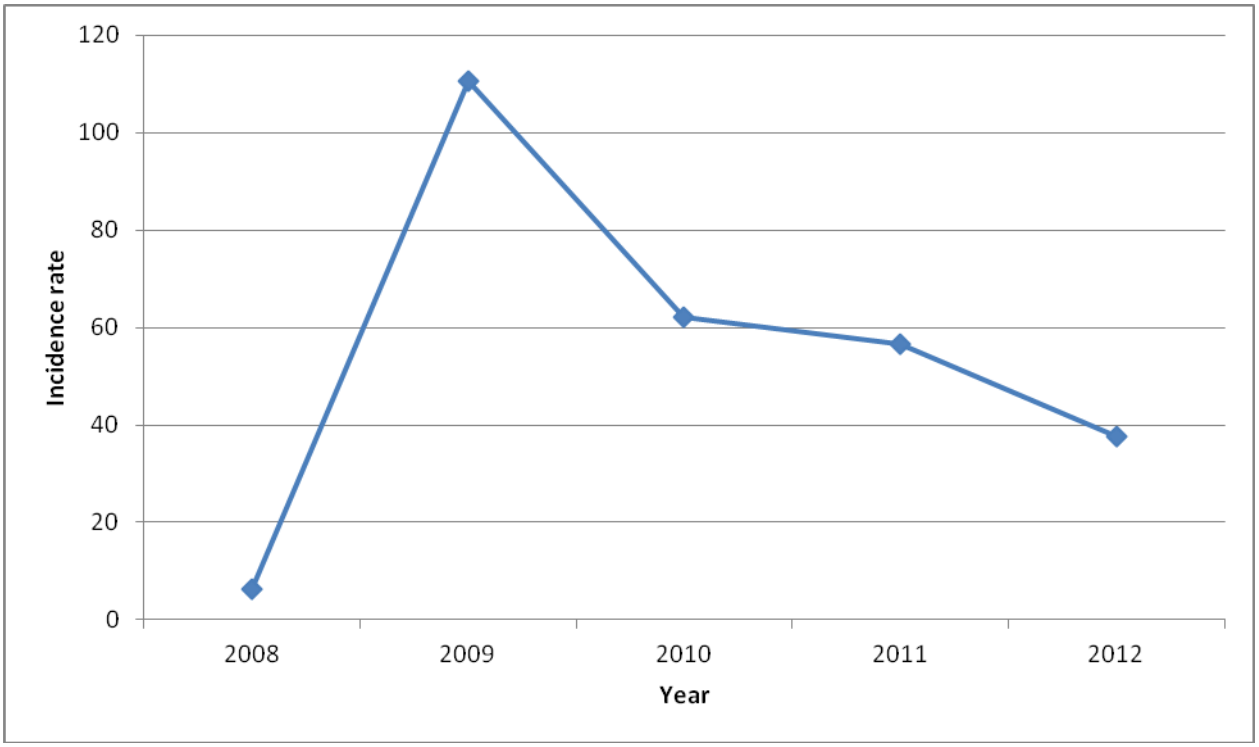


FIGURE 1: Dengue Fever Incidence Rate Trends, Kingdom of Saudi Arabia, Makkah, 2008 – 2012.

The number of dengue fever cases started to rise in January, peaking between April and May (Figure 2). There were more cases during spring, while the number of cases during summer and early winter (from January to December) was low.

Breaking down dengue fever rates by gender, males had an almost two-fold greater incidence rate in the KSA from 2008 to 2012 (Table 2 and Figure 3), assuming the population under surveillance included equal numbers of males and females. So, males were at significant risk of acquiring the dengue fever infection compared to females.

More cases of dengue fever occurred among Saudisthan non-Saudis in the KSA from 2008 to 2012. More than 70% of all cases were among Saudis, and this is a significant percentage (Table 3) (Figure 4).

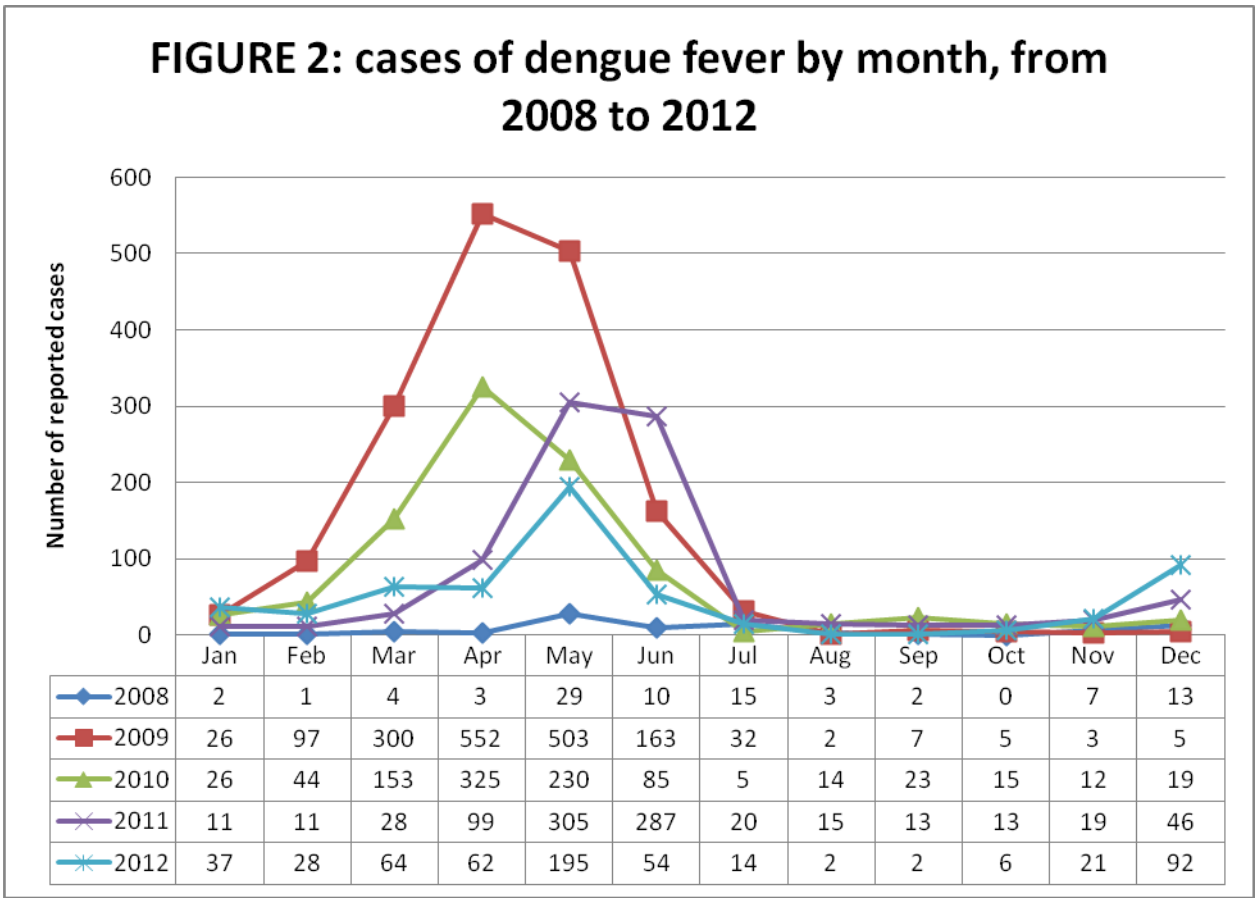


TABLE 2: Dengue Fever Incidence Rate per 100,000 Population and Number of Cases among Gender, Kingdom of Saudi Arabia, Makkah, 2008 – 2012

Year	Male		Female	
	Rate (n)	95% CI	Rate (n)	95% CI
2008	*7.9(68)*	6.1-9.9	4(27)	2.7-5.8
2009	*148.3(1278)*	140.3-156.7	62.3(419)	56.5-68.4
2010	*79.9(663)*	71.2-83	42.8(288)	38.1-48
2011	*69.2(596)*	63.8-74.9	40.3(271)	35.7-45.3
2012	*50.2(433)*	45.7-55.1	21.4(144)	18.1-25.1

CI = confidence interval.

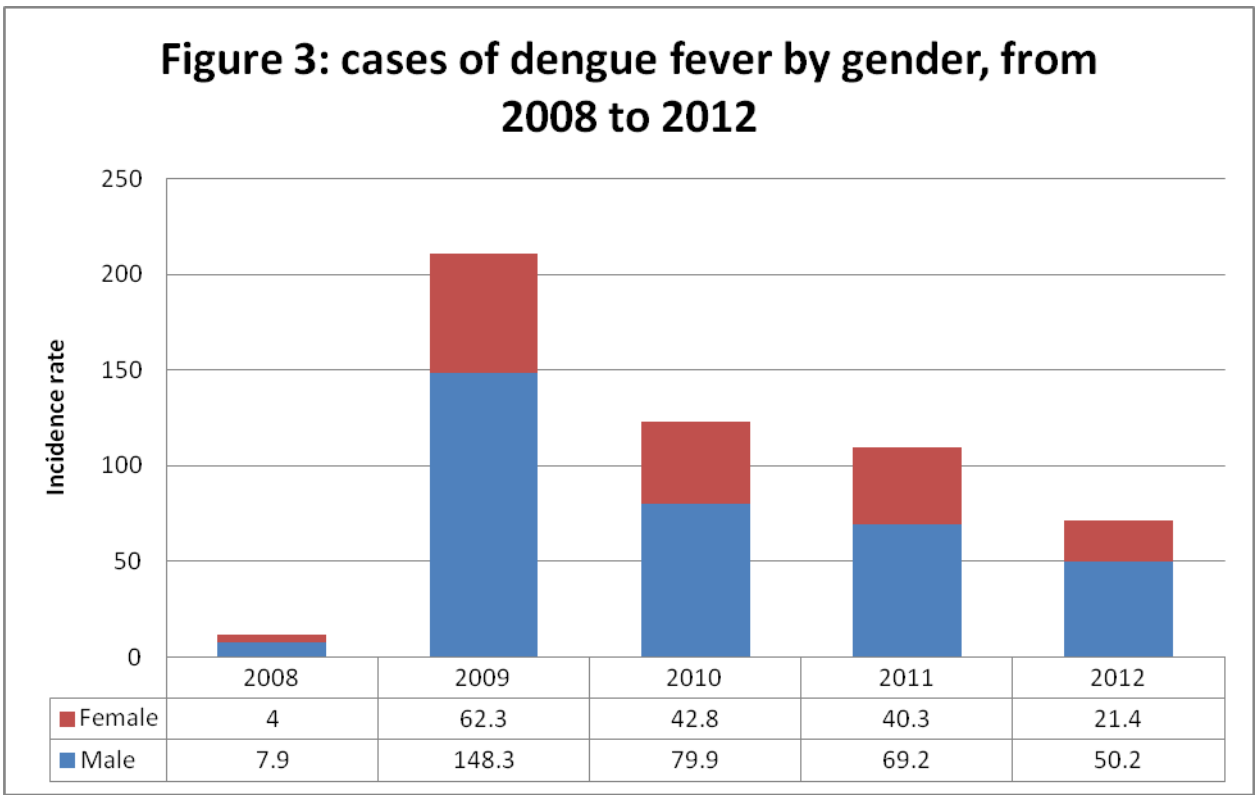


FIGURE 3: Dengue Fever Incidence Rate per 100,000 Population and Number of Cases among Gender, Kingdom of Saudi Arabia, Makkah, 2008 – 2012.

TABLE 3: Dengue Fever Incidence Rate per 100,000 Population and Number of Cases among Nationality, Kingdom of Saudi Arabia,Makkah, 2008 – 2012

Year	Saudi		Non-Saudi	
	Rate (n)	95% CI	Rate (n)	95% CI
2008	*8.9(73)*	7-11.1	3.1(22)	2-4.6
2009	*146.8(1205)*	138.7-155.3	68.9(492)	63-75.2
2010	*87.6(719)*	81.4-94.2	32.5(232)	28.5-36.9
2011	*64.9(533)*	59.6-70.6	46.8(334)	42-52
2012	*43.4(356)*	39.1-48.1	31(221)	27.1-35.2

CI = confidence interval

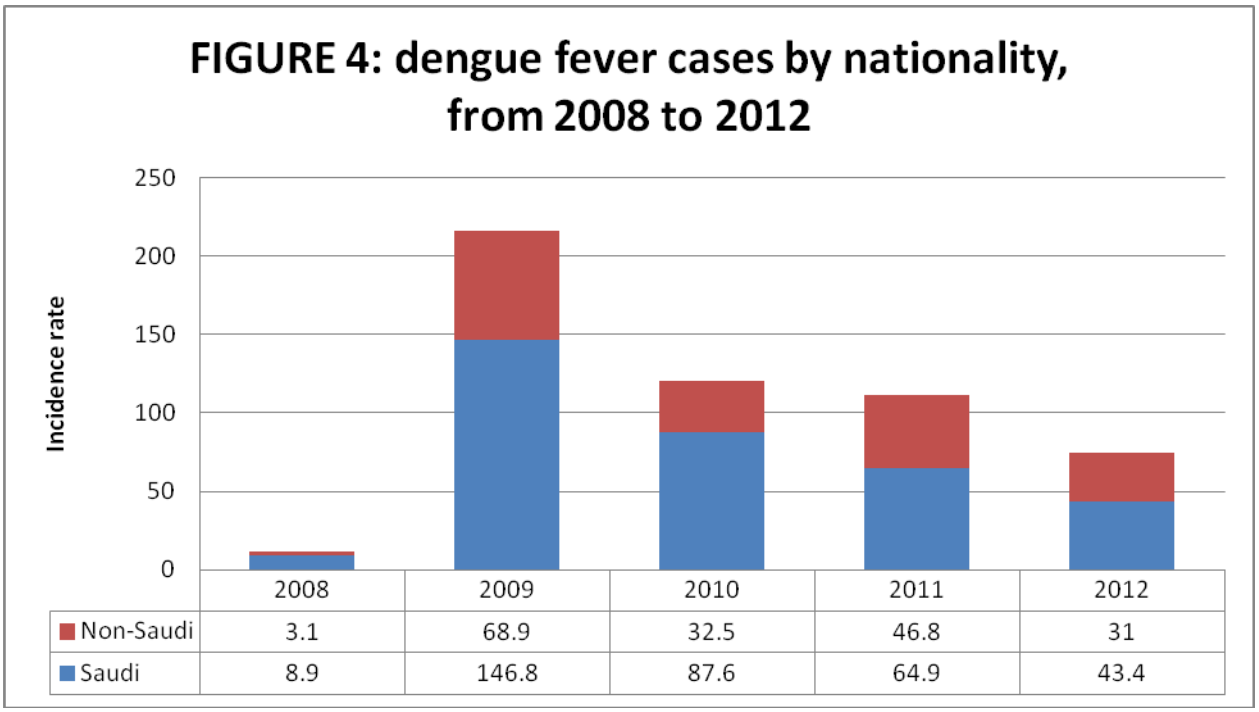


FIGURE 4: Dengue Fever Incidence Rate per 100,000 Population and Number of Cases among Nationality, Kingdom of Saudi Arabia,Makkah, 2008 – 2012.

Regarding the affected age groups, there was an increase in the number of cases among those between the ages of 25and44 compared to other age group; that group hadalmost 50% of all cases. On the other hand, there were very few cases among those who were less than one year old. The number of cases started to decrease in those older than 45 years (Figure 5).

*Aedes aegypti*has a population density that varies throughout the year and from one year to another (Figure 6). In 2008, its population density peaked in January. In 2009, its density peaked in June. In 2010, it peaked in March. In 2011, it peaked in October, and in 2012, April.

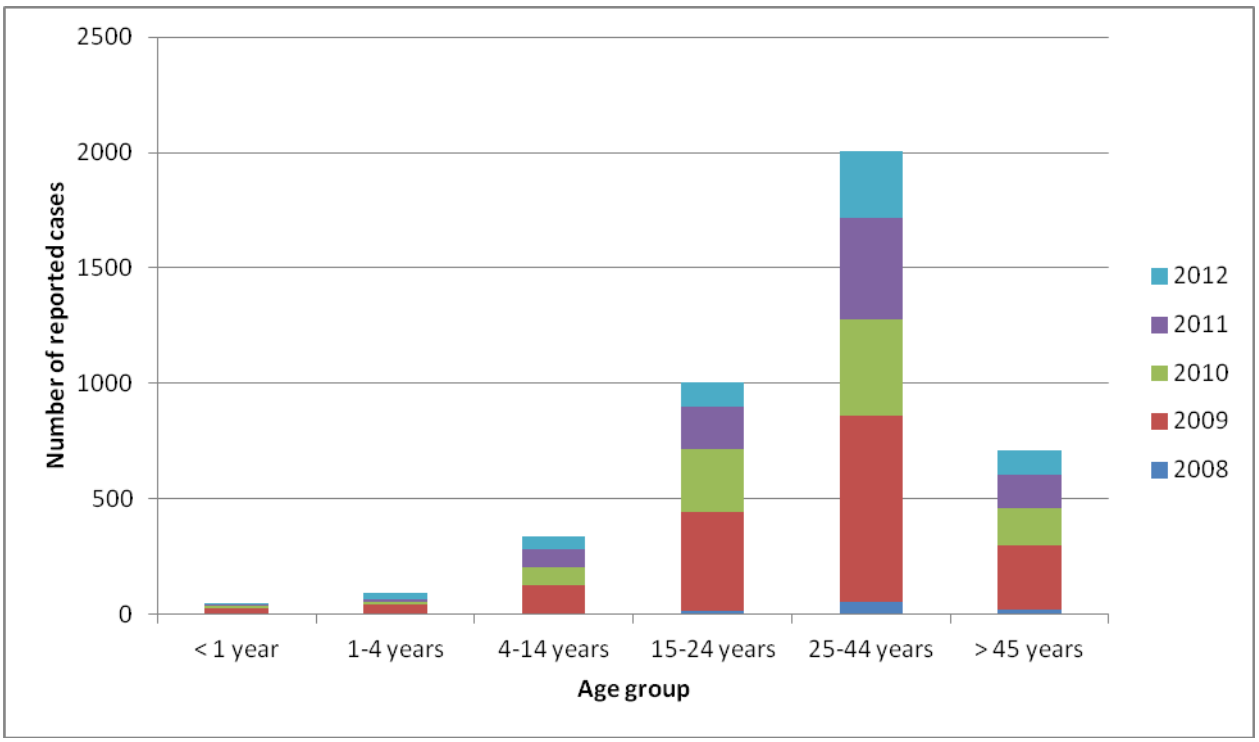
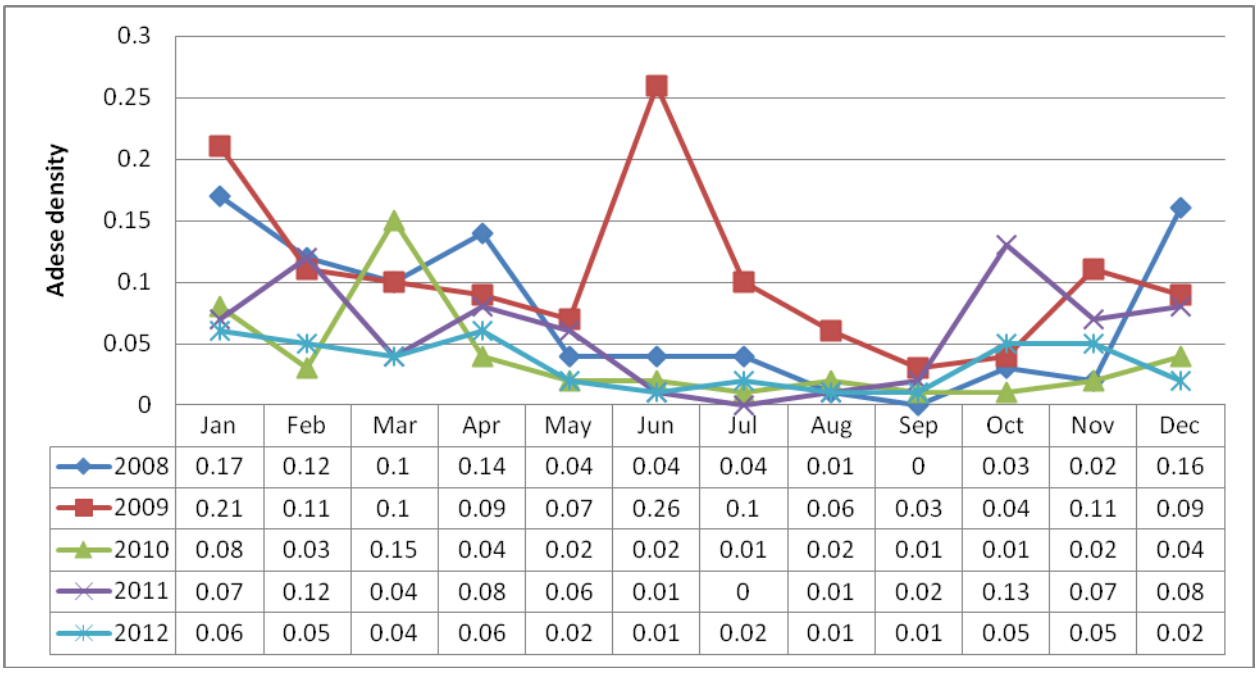


FIGURE 5: Number of Reported Cases of Dengue Fever by Age Group, Kingdom of Saudi Arabia, Makkah, 2008 – 2012.



	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
2008	0.17	0.12	0.1	0.14	0.04	0.04	0.04	0.01	0	0.03	0.02	0.16
2009	0.21	0.11	0.1	0.09	0.07	0.26	0.1	0.06	0.03	0.04	0.11	0.09
2010	0.08	0.03	0.15	0.04	0.02	0.02	0.01	0.02	0.01	0.01	0.02	0.04
2011	0.07	0.12	0.04	0.08	0.06	0.01	0	0.01	0.02	0.13	0.07	0.08
2012	0.06	0.05	0.04	0.06	0.02	0.01	0.02	0.01	0.01	0.05	0.05	0.02

FIGURE 6: Aedes Density Each Month, Kingdom of Saudi Arabia, Makkah, 2008 – 2012.

DISCUSSION

The incidence rate of dengue fever in Makkah is high. Although it started to decrease after 2009, it is still high. That makes Makkah an endemic city for dengue fever. The incidence rate in 2008 was 6.2(CI 95%5-7.5), considered high, though it was the lowest rate found from 2008 to 2012. An outbreak occurred in 2009 and the incidence spiked at110.6per 100,000 persons (95%CI=105.4-115.9); this was mainly due to an increase in *Aedes aegypti* activity during that year.

Increased mosquito activity was associated with huge construction projects that took place in Makkah when the government started to expand the city by adding large buildings. The open water containers at these construction sites provide a good environment for *Aedes aegypti* growth.[12] As a result; the MOH increased its support of the VBDU by funding the recruitment of more health educators to provide door-to-door education. Moreover, communication between different government branches started to become more frequent. As a consequence, the incidence of dengue fever decreased gradually in the subsequent years. In 2010, it dropped to 62 (95%CI=58.1-66), in 2011, it was 56.5 (95%CI=52.8-60.3), and by 2012, it had fallen to 37.6 (95%CI=34.6-40.8). However, the incidence was still high, and more work needed to be done to reduce the incidence further. Also of note was that the incidence of dengue increased during late spring and early winter, even though evidence shows that high temperatures increase *Aedes aegypti* activity. [13, 14] So, this area needs further research.

The incidence rate of dengue fever is almost twofold among men compared to women (Table 2) (assuming the population under the surveillance included approximately equal numbers of males and females). This is due to fact that men are mainly the ones who work outdoors, and

women, in addition to spending more time indoors, wear clothes that cover them for religious reasons.

We also found also that Saudis experienced almost twice the risk of getting dengue fever than on-Saudis (Table 3). This is due to the availability of treatment for Saudis as compared to non-Saudis. Health care in Saudi Arabia is free for Saudis. As a result, Saudis seek medical advice more often than non-Saudis, who must pay. In addition, the nature of the disease is self-limited, and most non-Saudis choose to wait it out rather than paying for a minor illness.

The number of dengue fever cases is high among the 24-44 age group; this case number started to decrease after the age of 44 years. The higher number of cases among those between 24-44 years old is to be expected because of their being outdoors more often than other age groups. Few cases occur among those < 1 year old.

There are limitations to our study. First, data entry for dengue fever cases at the VBDU doesn't follow a classification system. According to their protocol, they followed the old WHO classification scheme (1997),[15] but they do not use it in practice. So, they will label any case with a lab confirmation as dengue fever regardless of its severity. As a result, in the analysis, we didn't know the number of cases classified as DH or DSS.

Moreover, the surveillance data did not include the follow-up result for the patient. We need to know how many patients recovered without complications, how many patients recovered with complications, and how many patients died from this disease.

Another limitation was that our incidence rate was based on a KSA census that was taken in 2010, which is not as accurate as the yearly census. In addition, the national census doesn't provide the number of people by age group in Makkah city.

In conclusion, Dengue fever is endemic in Makkah city, with many outbreaks that can be missed easily, and it continues to be a significant health problem. As a result, we recommend using the newer WHO dengue case classifications, revised in 2009[16] as well as identifying the type of dengue infection (DF, DH, and DSS) instead of reporting cases only as dengue fever from lab confirmations and initiating a consultation with the WHO regarding dengue activity needs under the International Health Regulations. [17] Finally, ensuring that the VBDU follow the strategic approach to vector control promoted by the WHO,called Integrated Vector Management (IVM). [18]

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