

Recent Outbreaks of Dengue Fever in the WHO Eastern Mediterranean Region: A Narrative Mini-review

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Abstract:

Dengue Fever (DF) is the most important, rapidly spreading, emerging/re-emerging, arboviral disease that threatens a global human health and economic development. Dengue viral infection is transmitted to human by infected female *Aedes* mosquito vector, significantly *Aedes aegypti*. This article reviewed the recent status of dengue fever outbreaks indicated in the World Health Organization (WHO) Eastern Mediterranean Region (EMR) in the last five years (2016-2020), based on reports of WHO, and other available data. Recent DF outbreaks were in Sudan (2017, 2019), Yemen (2016, 2018, 2019), Oman (2018), and Pakistan (2017, 2018, 2019, 2020). The two species, *Aedes aegypti* and *Aedes albopictus* were geographically distributed and mapped by country-level according to the published reports. There are several factors contributing to the emergence and rapid transmission of dengue in the region, include rapid prevalence of the main dengue vector, host vulnerability, favorable environmental conditions (temperatures, precipitation and humidity), and unplanned expanding urbanization. In addition to the movement of traveler's people during an outbreak responsible for introducing DF to new locations. Early detection of diseases and effective mosquito vector control is an essential strategy for preventing the transmission of diseases outbreaks.

Keywords: Dengue fever, recent outbreaks, *Aedes aegypti*, WHO Eastern Mediterranean Region.

الفاشيات الأخيرة لحمى الضنك في إقليم شرق المتوسط لمنظمة الصحة العالمية: مراجعة سردية مصغرة

ملخص البحث

حمى الضنك dengue هي أكثر الأمراض الفيروسية التي ينقلها البعوض انتشاراً في العالم، مما يهدد الصحة العامة والتنمية الاقتصادية. تشير تقديرات منظمة الصحة العالمية الحديثه بأن حالات حمى الضنك حول العالم تصل لأكثر من 390 مليون حالة سنوياً. تنتقل العدوى الفيروسية لحمى الضنك إلى الإنسان عن طريق لدغات أنثى بعوض الزاعجة المصابة بالفيروس وخاصة الزاعجة المصرية (*Aedes aegypti*)، وهناك نوع آخر من البعوض الناقل الثانوي (*albopictus Aedes*) يتسبب أيضاً في نقل المرض، كما ينقل هذا النوع من البعوض داء الشيكونغونيا والحمى الصفراء والعدوى بفيروس زيكا. تتمثل الأعراض الرئيسية لحمى الضنك والشبيهة بالإنفلونزا في الإرتفاع الحاد في درجة الحرارة والصداع الشديد، الغثيان والتقيؤ، والآلام المبرحة في العضلات والمفاصل؛ وتتفاقم أحياناً لتصبح مرضاً مميتاً يعرف بحمى الضنك النزفي.

أصبح هذا المرض سريع الانتشار في كل أقاليم منظمة الصحة العالمية في السنوات الأخيرة، من بينهم إقليم منظمة الصحة العالمية لشرق المتوسط والذي يتألف من ٢٢ دولة (إحدى وعشرين دولة عضوا ودولة فلسطين). واجهت الدول العديد من حالات تفشي الأمراض المعدية الناشئة حديثاً/ أو التي عاودت الظهور على مدار العقد الماضي، من بينهم ٨ دول في المنطقة (جيبوتي ومصر وعمان وباكستان والمملكة العربية السعودية والصومال والسودان واليمن) مستوطنة بحمى الضنك ذات الكثافة العالية من بعوض الزاعجة.

استعرض هذا البحث الفاشيات الأخيرة لحمى الضنك في إقليم شرق المتوسط لمنظمة الصحة العالمية خلال السنوات الخمس الماضية في الفترة (٢٠١٦-٢٠٢٠) بناءً على تقارير منظمة الصحة العالمية وغيرها من البيانات المتاحة. وايضا خريطة

التوزيع الجغرافي للنوعين *Ae. albopictus* و *Ae. aegypti* في المنطقة وفقاً للتقارير المنشورة. لوحظ ظهور/عودة ظهور فيروس حمى الضنك وانتشاره السريع في السودان عامي (٢٠١٧ ، ٢٠١٩)، اليمن (٢٠١٦ ، ٢٠١٨ ، ٢٠١٩)، عُمان (٢٠١٨) ، وباكستان (٢٠١٧ ، ٢٠١٨ ، ٢٠١٩ ، ٢٠٢٠) مما أدى إلى ظهور حالات حمى الضنك وتشي المرض في مناطق مختلفة. وقد أسهمت عوامل عديدة في ظهور حمى الضنك وسرعة انتقالها في المنطقة منها: الانتشار السريع للبعوض الناقل للمرض، والقابلية لانتشار الأنماط الفيروسيه الأربعة (DENI-4)، وزيادة الكثافة السكانية البشرية والتوسع الحضري العشوائي (مما أدى الى خلق بيئات مواتية لتوالد البعوض الناقل للمرض)، والمتغيرات البيئية الملائمة (مثل درجات الحرارة، الأمطار، والرطوبة)؛ هذا بالإضافة إلى حركة الأشخاص المسافرين عبر المدن الموبوءه بالمرض والذي يعتبر المسؤول عن إدخال حمى الضنك إلى مناطق جديدة.

وبما أنه لا يوجد لقاح فعال لحمى الضنك، فإن الوضع الوبائي لحمى الضنك في المناطق التي يتوطن فيها المرض ضروري لإيلاء المزيد من الإهتمام للتخفيف من خطر ظهور أمراض جديدة. يعد الكشف المبكر للأمراض وعلاجها ومكافحه البعوض الناقل للمرض استراتيجية أساسية للتخفيف أو لمنع انتقال الأمراض المعدية. هذا بالإضافة إلى الحاجة لفهم أفضل للوضع الوبائي لحمى الضنك، وبذل الجهود للحد من مشكلة نقص الإبلاغ عن الحالات، ومواصلة رصد ناقلات الأمراض، وكذلك تعزيز القدرات المخبرية لتحديد مسببات الأمراض الجديدة، والوقاية والسيطرة بشكل جيد.

Introduction

Dengue Fever (DF) is the most important, rapidly spreading, emerging/re-emerging, mosquito-borne viral infection that threats of a global human health and economic development. Dengue fever is transmitted to human by infected bites of female *Aedes* mosquito, significantly the species *Aedes aegypti* (the primary

vector transmitting the dengue virus in urban areas) (WHO 2016, Souza-Neto *et al.* 2019) and *Aedes albopictus* (secondary vector in peri-urban and rural environments) (Gratz 2004, Diallo *et al.* 2005, Benedict *et al.* 2007, Simmons *et al.* 2012, Kraemer *et al.* 2015, Semenza *et al.* 2014, Dhar-Chowdhury *et al.* 2016). The two species also can transmit other viruses causing chikungunya, yellow fever, and Zika fever (WHO 2016). This is due to their prevalence, diversity and productive ability and potential as vectors of various diseases and recurrent infection (Njabo *et al.* 2013). Human beings are the virus' principal host and amplifier; infected humans serve as a virus vector for uninfected mosquitoes.

Dengue fever is caused by one of 4 major serotypes of virus (DENV-1 to 4) (genus *Flavivirus*, family *Flaviviridae*), that can cause mild flu-like illness to more severe and potentially fatal humans disease (hemorrhagic fever/shock syndrome) (Endy *et al.* 2010). The most present symptoms of dengue include acute fever and one or more of the following: “Flu-like” syndrome, intense headaches, nausea and vomiting, and acute muscle pains, joint pain, or bone pain (WHO 2014).

Currently, DENV infection is classified as one of the world's emerging infectious diseases (Bhatt *et al.* 2013). According to WHO estimation, there are approximately 390 million cases of dengue infections annually, nearly half the world's population at risk of dengue infection in 128 endemic countries (Beatty *et al.* 2011, Brady *et al.* 2012).

Outbreaks of Dengue fever in the WHO Eastern Mediterranean Region (EMR)

The Eastern Mediterranean region as defined by the World Health Organization consists of 22 countries (Figure 1); Afghanistan, Pakistan, Iran, Kuwait, Iraq, Jordan, Syrian Arab Republic, Lebanon, Occupied Palestine Territory, Saudi Arabia, Bahrain, Qatar, United Arab Emirates, Oman, Yemen, Somalia, Djibouti, Sudan, Egypt, Libya, Tunisia, and Morocco.

Eastern Mediterranean countries have faced numerous outbreaks of newly emerging or re-emerging infectious diseases over the past decade with the potential to trigger a global health emergency (WHO 2016). Many countries in EMR are particularly vulnerable to infectious disease epidemics, as they are experiencing various environmental and social stresses. At least 8 of the 22 countries namely (Djibouti, Egypt, Oman, Pakistan, Saudi Arabia, Somalia, Sudan and Yemen) in the region are endemic for dengue with a high density of *Aedes spp.* (WHO 2016). While outbreaks of suspected dengue were detected in Egypt during 2015, Sudan and Yemen during 2012–2015, Oman during 2014, 2015, and Pakistan during 2011, 2014, as imported cases only. On one hand, both Djibouti and Somalia have reported sporadic cases, which are evidence of the presence of endemic vectors in these countries with the risk of local transmission. All of the four serotypes of DENV have been circulated during the outbreak. Recently, outbreaks of suspected dengue fever were published by WHO

(2020) in the last five year (2016-2020) in Sudan, Egypt, Pakistan, Yemen, and Oman (Figure 1).

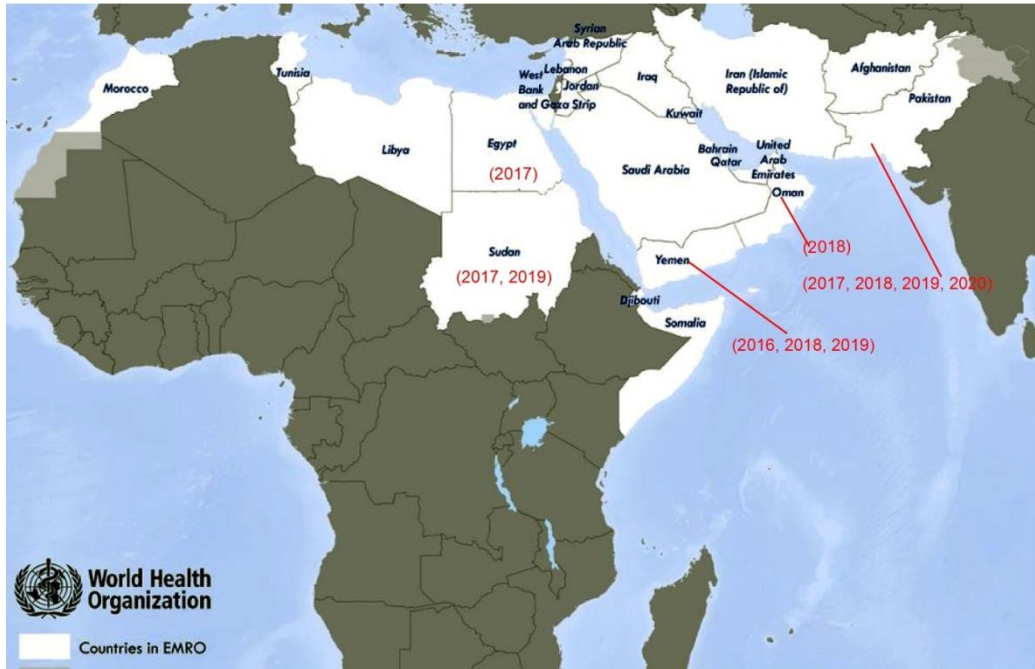


Fig 1. Outbreaks of dengue fever in the WHO Eastern Mediterranean Region during 2016-2020

DENV may be resurging in EMR (Hotez *et al.* 2012, WHO 2014). Up to this time, despite rapid global spread of *Aedes* mosquito, the epidemiology of DENV in the EMR and North Africa remains largely uncharacteristic. Humphrey *et al.* (2016) promoted the understanding of the epidemiology of DENV through a systematic review of human propagation and incidence studies and infection rates in *Aedes* mosquitoes.

Yemen

Dengue fever is endemic in Yemen, with outbreaks repeated incidence in many Governorates over the last ten years. In 2016, Yemen recorded a total of 9,818 suspected cases mostly from ten Governorates (Al Hudaydah, Abyan, Aden, Lahj, Shabwa, Al-Mukala, Taiz, Sayoun, Hajja and Al-Mahara). During 2018, the number of cases gradually raised, a total of 27902 suspected cases including 46 deaths were reported. Recent heavy rainfall, disruption of water supply and storage (containers), inadequate safe drinking water, sanitation conditions, and population movements may have led to mosquito prevalence in the affected areas, contributing to a rapid rise in dengue cases. Owing to the presence of *Ae. aegypti* and slow vector control strategies mostly attributed to security situations in the country.

Oman

The first imported dengue fever cases reported during 2001. Since 2001, the numbers of travel-related dengue fever cases were presented in the country regularly. A previous study confirmed 64 imported cases over a 15 year periods (Al-Abri *et al.*, 2015), and until the beginning of 2018, Oman was considered free of DENV. Dengue fever outbreaks re-emerged at the end of 2018; reporting 67 cases of which 30 dengue fever cases were in travelers returning from dengue-endemic countries. The circulating dengue serotype is DEN-2. Although, *Ae. aegypti*, is well established in south of Oman but no local transmission of dengue fever was previously reported from the country.

Pakistan

The recent outbreak of 2017 in Peshawar district (Khyber Pakhtoonkhwa province), a total number of 25872 confirmed cases of dengue with 69 associated deaths were reported. The majority of cases were from the provincial capital city Peshwar; 23 809 laboratory-confirmed cases and 64 deaths. In 2018, 3,204 cases were appeared. Dengue virus serotype (DENV-2) was detected as the causative strain of this outbreak. In 2019, dengue fever re-emerged with increasing cases across country with progressive cases of 53,600 with 95 deaths. Most affected cities were Islamabad and Rawalpindi (39% of total cases) and Karachi (29% of total cases). In 2020, 416 confirmed DF cases have emerged during the post-monsoon months.

Sudan

Sudan has faced a number of dengue fever outbreaks in the past. The dengue epidemics have been documented in different parts of Sudan (Sohaier *et al.* 2014), in 2017, the first dengue fever case was reported in Kassala city, East Darfur. Then cases increased to reach 90 cases with two deaths across 6 states; Khartoum, Kassala, West Darfur, East Darfur, South Kordofan, and Red Sea states. At the end of 2017, a total of 179 suspected cases and three associated deaths were reported (WHO 2017). The most affected area with more than 89% of the reported case load is Kassala state. In August 2019, the number of reported

dengue cases, spiked up to reach 4236 cases and 13 associated with death.

Egypt

Currently, number of studies reviewed the re-emergence of *Ae. aegypti* vector, but did not promote more evidence on its occurrence in Egypt (Heikal *et al* 2011, Shoukry *et al* 2012). In October 2017, Egypt's Ministry of Health in Upper Egypt confirmed about 101 dengue cases incidence in Qena Governorate (Abdelkader 2018). The first record of *Ae. aegypti* and the re-emergence of dengue outbreak with more than 680 cases were reported in city of Qusair (Red Sea Governorate) (Abozeid *et al.* 2018).

Distribution of *Aedes aegypti* and *Aedes albopictus* in the WHO EMR

Published reports on the distribution of the species *Ae. aegypti* and *Ae. albopictus* are recorded and mapped by country (Humphrey *et al.* 2016) (Fig. 2). The mosquito vectors, *Ae. aegypti* was reported in 10 EMR countries. While, *Ae. albopictus* was reported in countries, including Palestine, and Syria. No published reports on the occurrence of *Ae. aegypti* or *Ae. albopictus* (or DENV outbreaks) were identified from Libya, Morocco, Tunisia, Iraq, Iran, Jordan, UAE, Qatar, Bahrain, and Kuwait.

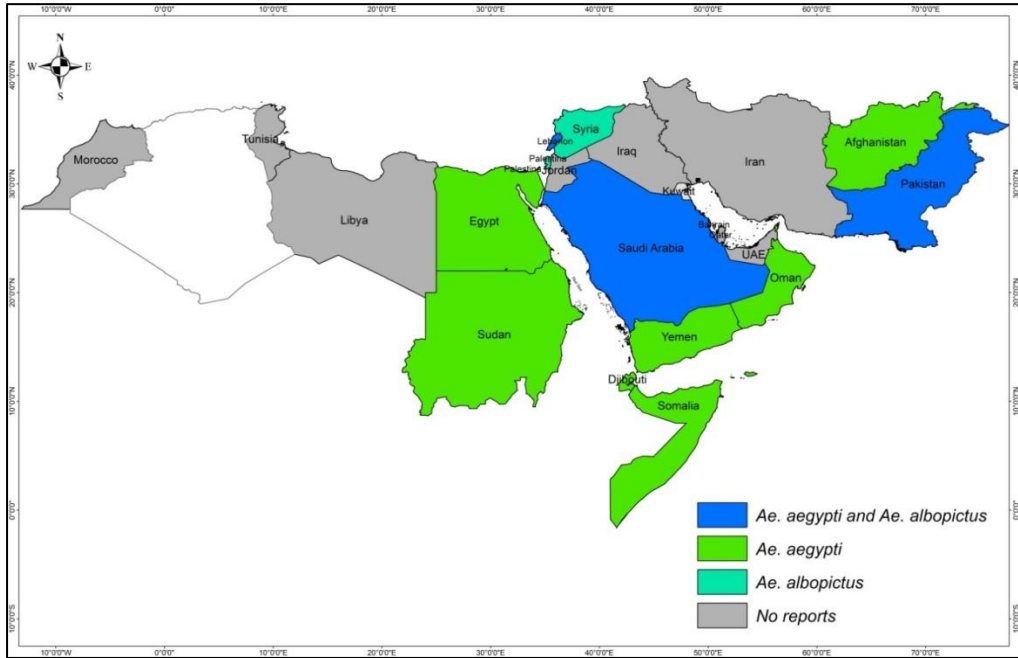


Fig 2. Distribution of *Aedes aegypti* and *Aedes albopictus* in the WHO EMR (modified from Humphrey *et al.* 2016).

Factors associated with dengue fever outbreaks

Even though the vector of disease is known to be occurrence in the affected areas, other factors are played a major part in this upsurge of dengue fever include start of monsoon season with dense rains, which is favoring the breeding of the mosquito and amplifying the virus transmission. The factors that contribute to the breeding sites are also inadequate water and sanitation, water supply and storage (containers), and high population growth, which increase interaction between vectors and humans (Wilson and Chen 2015).

WHO listed dengue fever as a potential threat among 10 diseases for 2019 and current outbreaks in many countries confirms this observation. Dengue epidemics tend to have seasonal patterns,

with transmission often peaking during and after rainy seasons, which is favoring the breeding of the mosquito and amplifying the virus transmission. There are several factors contributing to the emergence and rapid transmission of dengue in the region, include poor socioeconomic conditions, rapid prevalence of mosquito vector population, susceptibility to circulating serotypes, increase human population density (that increase contacts between vectors and humans and increased biting and pathogen transmission rates), favorable environmental variables (temperatures, precipitation and humidity), and unplanned expanding urbanization (creates favorable environments for increased vector density and create urban heat islands that induce transmission) (Juliano and Lounibos 2005, Wilcox and Gubler 2005, Were 2012, Bhatt *et al.* 2013, Wilson and Chen 2015). All of which affect the breeding and feeding patterns of mosquito populations, as well as the dengue virus incubation period, lack of proactive control interventions and staff is some of the other challenges.

Increased human transportation to cities from rural areas with endemic pathogens is a common route of urban mosquito-vectorized disease outbreaks across developing countries (Yasuoka and Levins 2007, Myers and Patz 2009), as they can carry new dengue strains into areas where mosquitoes can transmit infection (WHO 2014).

Recommended actions

WHO efforts in mitigating dengue fever outbreaks are focus on supporting countries' efforts regarding surveillance, case

management, and technical policy and guideline formulation (WHO 2020). The main method to control or mitigate the transmission of dengue virus is to fight a mosquito vector of disease. Careful clinical detection of dengue cases can significantly reduce death rates from acute dengue. In order to effectively control mosquitoes over the long term, it is essential to use several integral management techniques including;

- 1- Environmental control: Elimination of breeding sites through draining the water where mosquitoes breed, and destruction of vector populations.
- 2- Sanitation: Removing artificial man-made habitats; and cleaning of domestic water storage containers on a weekly basis.
- 3- Chemical control: Applying appropriate insecticides as space spraying during outbreaks throughout all locations and regular monitoring of mosquito resistance.
- 4- Mechanical control: Personal household protection such as window screens, long-sleeved clothes, insecticide treated materials, coils and vaporizers; improving community participation and mobilization for sustained vector control.

Conclusions

During the last five years, an emergence/re-emergence and rapid expansion of dengue virus has been observed in Sudan, Egypt, Pakistan, Yemen, and Oman, which led to the appearance of dengue fever cases, and multiple outbreaks in different areas. The

factors contributing the emergence and rapid transmission of dengue in the region have been identified including; environmental conditions, rapid population growth, travelers through cities endemic to disease. As mosquitos' prevalence in addition to evidence of emerging diseases, the epidemiological situation of dengue fever in areas where the disease is endemic is necessary to take more attention to alleviate the area at risk of new diseases emergence, as environmental factors are subject to continual changes. Early detection of diseases and treatment is an essential strategy for preventing the transmission of infectious diseases. In addition, the need to better understand the epidemiological situation of dengue fever in areas that are endemic, and make efforts to reduce the problem of under-reporting, continued monitoring vector of disease as well as strengthen laboratory capabilities to identify new pathogens, prevention and control, and manage vector well.

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