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CLIMATIC CHANGES INCREASE GLOBAL DISASTERS OF DENGUE HEMORRHAGIC VIRUS FEVER: IS EGYPT AGAIN AT DENGUE RISK?

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Abstract

Spreading of dengue fever after globalization presents an emerging worldwide threating especially in tropical and subtropical regions. Co-infections of Dengue virus (DENV), Zika, virus (ZIKV) and Chikkungunya virus (CHIKV) are *Aedes* mosquito-borne diseases reported in some countries. Climate change is likely to increase global outbreaks incidence of *Aedes*-borne arboviruses has been more frequent and more intense in the recent years. Unfortunately, current evidence suggests that climatic changes can be partially driving recent mosquito-borne diseases outbreaks worldwide. Besides, the global climatic change already made the conditions more suitable for risk spreading of certain zoonotic vector-borne diseases to non-endemic countries. The areas with risk of dengue are changing.

Key words: Global climate change, Vector-borne diseases, Epidemic and pandemic outbreaks

Introduction

Records of dengue-like illness date back more than 200 years; its viral etiology was established in the 1940s (Ashburn and Craig, 2004). Major changes in dengue virus infections epidemiology began after the 2nd World War and geographic expansion of transmission has continued to date given estimates of 390 million infections worldwide each year and <2.5 billion individuals at risk for infection, and remain important arthropod-borne viruses from a medical and economic perspective (Bhatt *et al,* 2013). Rocklöv and Dubrow (2020) in Sweden reported that climate change is affecting vector-borne disease transmission and spread, and its impacts are likely to worsen, there must intensify efforts to prevent and control vector-borne diseases (VBDs). Mojahed *et al.* (2022) in Iran reported that climate change especially in rising temperature is one of the world's greatest concerns affected pathogen-vector and host relation as lice, fleas, mites, ticks, and mosquitos are the prime public health importance in transmission of zoonotic diseases. WHO (1017) identified the major global VBDS as malaria, dengue, chikungunya, yellow fever, Zika, lymphatic filariasis, (schistosomiasis), onchocerciasis, Chagas disease, leishmaniasis and Japanese encephalitis Other regions include African trypanosomes, Lyme disease, tick-borne encephalitis & WNF, in tropical and subtropical low- & middle-income countries bear highest VBDS burden.

Classification: Dengue viruses are members of genus *Flavivirus*, family Flaviviridae, (Wilder-Smith and Schwartz, 2005). Dengue virus complex has at least 4 anti-genic related, but distinct viruses, designated dengue virus types 1 through 4. All dengue viruses are mosquito-borne human pathogens that exclusively cause acute infection.

Transmission cycle: Epidemic and endemic transmission of dengue viruses were maintained via a human-mosquito-human cycle inolving mosquitoes of the genus *Aedes* or *Stegomyia* (Kuno, 1995). Susceptible humans become infected after an infected female *Aedes* mosquito takes a human blood meal. Viremia in humans begins toward the end of

a four- to six-day incubation period and persists until around the time fever abates that was typically three to seven days (Gubler, 1998). Dengue virus's transmission between mosquitoes and nonhuman primates has been reported in Asia and Africa, but without evidence as an important reservoir for transmission to humans (Wang *et al,* 2000)

An uninfected *Aedes* mosquito may acquire the virus from an infected human if they feed during this time and the human viremia is of sufficient titer to support mosquito infection. The incubation period within the mosquito is 8 to 12 days; after this period, it is capable of transmitting the virus to humans. Once infected, mosquitoes carry the virus for their lifespan and remain infective (Vaughn *et al,* 1997).

Mosquito vectors: *Aedes* (*Stegomyia) aegypti* mosquitoes, the main vector of dengue virus transmission have many characteristics that make them ideal for virus dissemination (Halstead, 1984). *Ae. aegypti* typically breed in or close to houses, laying eggs in both man-made and natural water containers. The typical flight distance is relatively short (Harrington *et al,* 2005). *Ae. aegypti* are preferentially daytime feeders, and their feeding episodes often go unnoticed. They are easily interrupted in their feeding and often move on to another host, frequently taking multiple blood meals in a single breeding cycle (Scott *et al,* 2000) Thus, an infected *Ae. aegypti* mosquito may transmit dengue virus to several individuals within the household. For these reasons, family members who are at home during the daytime, typically women and young children are at particularly high risk for infection. *Ae. aegypti* are widely distributed in tropical and subtropical areas from latitude 45ºNorth to 35ºSouth. Yellow fever is also principally transmitted by *Ae. aegypti*; efforts to control urban yellow fevers in the Americas in the 1940s greatly restricted the distribution of mosquitoes in the Western hemisphere, but the mosquitoes have since re-infested nearly all of their former habitats (Henchal and Putnak, 1990).

Ae. albopictus is also a competent vector for dengue virus transmission of under both experimental and natural conditions (Gratz, 2004); they are more tolerant of cold with a wider geographic distribution than *Ae. aegypti* (CDC, 1989). However, they are less likely to transmit since they don't feed on man as frequently as *Ae. aegypti* and thus less efficient dengue virus natural vector. Both vectors are also competent ones for transmission of chikungunya virus with simultaneous outbreaks in some areas (Caron *et al,* 2012).

Also, Chikungunya (chik-un-GUN-yuh) fever virus (CHIKV) develops some symptoms, 3-7 days after an infected *Aedes aegypti* and *Ae. albopictus* bites (Gould *et al,* 2017). The commonest symptoms are fever and joint pain as well as headache, muscle pain, joint swelling (stooped walk), or rash. Most patients feel better within a week, but joint pain can be severe and disabling and may persist for months. Risky people with severe complications include newborns infected around birth time of, older adults (≥65 years), and those with high blood pressure, diabetes, or heart disease. Death from chikungunya fever is rare. Outbreaks have occurred in countries in Africa, Americas, Asia, Europe, and the Caribbean, Indian and Pacific Oceans (CDC, 2022). Also, Zika virus (ZIKV) is transmitted to humans primarily by the bite of an infected *Aedes aegypti* and *Ae. albopictus*. Nonhuman and human primates are likely the main virus reservoirs, and anthroponotic (man-to-vector-to-man), perinatal, in utero, and possible sexual and transfusion transmission occurs during outbreaks and RNA was identified in asymptomatic blood donors (CDC, 2019). Symptoms may include fever, red eyes, joint pain, headache, and a maculopapular rash for more generally seven days. It didn't cause any reported deaths during the initial infection. Mother-to-child transmission during pregnancy can cause microcephaly and other brain malformations in some babies and Guillain-Barré syndrome in adults (Silva *et al,* 2020). Waggoner *et al*. (2016) in USA reported that

ZIKV, CHIKV and DENV had similar clinical presentations with relatively common co-infections that needed for accurate, multiplex diagnostics for patient care and epidemiologic surveillance. Pessôa *et al.* (2016) in northeast region of Brazil during a febrile outbreak in 2015 reported co-infection of DENV and ZIKV co-infected in two of 77 patients. Chia *et al.* (2017) in Singapore reported 5/163 (3.5%) ZIKV &/or DENV in positive dengue patients. Mercado-Reyes *et al.* (2019) in Columbia found that arbovirus frequency (DENV, CHIKV &/or ZIKV) co-infection was low and CHIKV/ZIKV co-infection was common with seven fatal cases. Farias *et al.* (2023) in Brazil found that epidemiologic profile of dengue cases didn't change with CHIKV and/or ZIKV introduction and females were the most diagnosed cases,and that differences in arboviruses age profile must be considered by public health policies in virus-host interaction studies.

Other *Aedes* mosquitoes have been suspected of dengue virus transmission in the Pacific islands' outbreaks but, without significant in global transmission (Savage *et al,* 1988).

Aedes aegypti: *Ae. aegypti* is a vector with worldwide distribution, especially in tropical and subtropical environments, and is closely associated with urban areas and areas with environmental disturbances (Espinal *et al,* 2019). The incidences of dengue hemorrhagic fever were highest in parts of Asia and South America. *Ae. aegypti* exposure risk increased in urban areas. Many tourist facilities present a lower risk than local residential areas because of air conditioning, less standing water, grounds keeping, elevation, or combinations of these factors.

The dengue fever (DF) and DHF cases reported globally varied from year to year, although the overall trend is one of increasing incidence. Periodic shifts in the suspected ratio of clinically symptomatic to asymptom atic infections seem to occur at various times of several years (WHO, 2014a). The reported dengue activity in specific regions was gathered by passive surveillance without laboratory diagnosis (Undurraga *et al,* 2013).

Southeast Asia: *Ae. aegypti* are present via the region, extending to southern China and the south of the island of Taiwan, and all regional countries were affected by dengue virus infection. Hyperendemic transmission of all dengue serotypes (with the DHF cases) occurred in Thailand, Vietnam, and Indonesia for over 40 years. Epidemic dengue re-emerged in China during the 1980s to 1990s after an absence of several decades and was associated with the first occurrence of DHF in that country (Qiu *et al,* 1993). Over 140 locally acquired dengue cases were detected in Japan in 2014, representing the first transmission in that nation since World War II (Kutsuna *et al,* 2015). More than 80% of cases were associated with visiting a single location in Tokyo, and *Ae. albopictus* is the apparent vector in this outbreak. A review of epidemiologic trends between 1980 & 2010 indicated increasing incidence of dengue infection, with annual average percentage change of 6% in Thailand, 10% in Vietnam, 12% in Indonesia, 18% in Malaysia, and 24% in the Philippines (Wartel *et al,* 2017).

Dengue virus transmission occurs all year round but typically reaches a seasonal peak that varies in timing between countries (for example, between June and November in Thailand, between January and February in Indonesia). More than 200,000 of DHF cases were reported from the region each year from 2012 with the exception of 2011 (177,500 cases); Indonesia and Thailand accounted for the majority of cases in each of these years (WHO, 2014b). A completed dengue vaccine trial in Thailand, Indonesia, Philippines, Malaysia, and Vietnam demonstrated significant reporting differences between national surveillance systems and the trial's active case finding (Nealon *et al,* 2016).

South Asia: *Ae. aegypti* are widely distributed in India, Pakistan, and Sri Lanka. Dengue virus transmission, particularly in India and Sri Lanka, increased substantially over the 1980s and 1990s. Hyperendemic circulation of all four dengue serotypes appears to

be established, and outbreaks of DHF became more common. Over 50,000 cases were reported from India in 2012, more than twice the average over the previous decade. A seroprevalence study among children living in India noted rates of seropositivity between 60 and 80% (Garg *et al,* 2017).

Western Pacific islands: The *Ae. aegypti* were present in most of the region. High incidence rates were reported from 14 island nations for 2009, including American Samoa, Cook Islands, French Polynesia, New Caledonia, and Tonga (WHO, 2014c).

Australia: *Ae. aegypti* mosquitoes are present in the northeastern corner of Australia. Dengue viruses are not endemic to the continent, but periodic introduction of dengue viruses from neighboring islands has led to epidemics in urban areas of north Queensland (Mackenzie *et al,* 1998). In Australia in 2013 to 2014, 212 dengue virus infections were acquired in Australia and 1795 cases were acquired overseas (Knope *et al,* 2016).

Africa & Eastern Mediterranean: *Ae. aegypti* are present in much of sub-Saharan Africa and the Middle East. Data were scant on dengue transmission (Eisenhut *et al,* 1999). However, documented infections in visitors to area indicated that there was ongoing dengue virus transmission (Sharp *et al,* 1995). Several outbreaks were reported from Central Africa, East Africa, and the Middle East during the 1990s and 2000s (CDC, 2000).

A systematic review of records from Middle East and North African countries identified 81 outbreaks reported from 9 countries between 1941 and 2015; *Ae. aegypti* and/or *Ae. albopictus* were present in 15 countries (Humphrey *et al,* 2016).

Europe: *Ae. albopictus* is present across all southern Europe (Schaffner *et al,* 2013). Dengue cases reported from tregion have been acquired during travel to endemic countries. However, local transmission of dengue virus was documented in both southern France and Croatia in 2010, & in 2012, an outbreak of dengue was reported on Madeira Island (Portugal) associated with *Ae. aegypti* presence (Tomasello and Schlagenhauf, 2013). Gwee *et al.* (2021) reported that imported cases in Europe were from Asia (66%), Americas (21.9%), Africa (10.8%) and Oceania (1.1%). They added that dengue outbreaks occurred globally with *Aedes* population expansion due to global warming and globalization, especially in all non-endemic regions.

North America: *Ae. aegypti* are present in most areas of Mexico and in the southeastern United States. *Ae. albopictus* is also present in these areas, but its range extends farther north, nearly to the Great Lakes. Hyperendemic transmission of all four dengue virus serotypes is present throughout *Ae. aegypti* ranged in Mexico (Rigau-Pérez *et al,* 1994). Dengue virus transmission is seasonal, with peak activity in late summer and fall. Over 230,000 cases of dengue infection were reported from Mexico, including more than 18,000 cases of severe dengue and 104 deaths (CDC, 2013). Most dengue virus infections identified in the continental United States and all cases identified in Canada were acquired during travel abroad or to Puerto Rico or the United States Virgin Islands (CDC, 2005).

Limited transmission of dengue virus was within southern Texas has been described since the 1980s (CDC, 1998a). The United States CDC reported a case of DHF in a resident native to Texas who lived in a bordering area with Mexico (CDC, 2007); this prompted a serosurvey of 346 households in the immediate neighborhood, which demonstrated that 38% of the residents had IgG antibodies to dengue. A subsequent surveillance effort in 2013 identified 53 laboratory-positive cases in southern Texas; 49% of infections were acquired locally (Thomas *et al,* 2016). In 2010, dengue fever was reported in 28 residents of Key West, Florida, who had not traveled abroad (CDC, 2010), and a serosurvey of 240 participants living in Key West found that 5 percent had evidence of recent dengue infection. There was an outbreak of dengue in Hawaii between 2015 and 2016 (Effler *et al,* 2017). The Hawaii

Department of Health reported a total of 264 cases were confirmed, with 26 being in travelers and the remainder Hawaiian residents. These were the first cases in Hawaii since 2011 (Johnston *et al,* 2016). Stephenson *et al.* (2021) in USA reported that focal outbreaks of dengue in the state of Florida have increased since 2009, and dengue virus continues to occur in south Florida, but thus far appears to be very limited in scope. They added that the vector competence across all DENV serotypes was greater for mosquitoes from areas with the highest dengue incidence in south FL compared to north FL. Vector competence for low passage DENVs was significantly higher, revealing that the transmission risk was influenced by virus/ vector combinations. These data support the targeted mosquito-plus-pathogen screening approach to more accurately estimate DENV transmission risk.

Central America: *Ae. aegypti* mosquitoes and hyperendemic transmission of all four dengue virus serotypes are present throughout the region. The region experienced a major outbreak in 2013; Nicaragua and Costa Rica reported among the highest numbers of cases of dengue (77,000 and 49,000, respectively) and incidence rates (over 1000cases/ 100,000 population) that year (WHO, 2023) However, all of these countries have had one or more years of heavy dengue activity during the past five years. The Pan American Health Organization (PAHO) reported over 26,000 laboratory-confirmed cases in Central America and Mexico during 2016; underreporting is suspected to be considerable. Torres *et al.* (2017) identified 530 articles, 60 of which met criteria for inclusion. In general, dengue seropositivity across the region was high and increased with age. All four virus serotypes were reported to circulate in the region. These observations varied considerably between and within countries over time, potentially due to climatic factors (temperature, rainfall, and relative humidity) and their effect on mosquito densities and differences in socioeconomic factors.

Caribbean: *Ae. aegypti* are prevalent allover the region. Hyperendemic circulation of dengue virus serotypes 1, 2, & 4 occurred on the larger islands (other than Cuba) for many decades, and dengue virus serotype 3 were present since 1998 (Chadee *et al,* 1998). In Puerto Rico, peak dengue virus transmission usually occurs between October and December; over 21,000 dengue virus cases were reported there in 2010, represented the largest outbreak ever recorded. Dengue fever was in the Dominican Republic (16,000 cases), French Guiana (16,000 cases), Guadeloupe (12,000 cases), Martinique (7000 cases), and St. Martin (3000 cases) all reported major outbreaks in 2013, numbers declined in 2016 to about 3700 laboratory-confirmed cases. Others experienced periodic dengue epidemics French Guiana, Guadeloupe, Martinique, Saint-Martin, and Saint-Barthélemy (PAHO/ WHO, 2018).

South America: *Ae. aegypti* mosquitoes were present allover South American country except Chile, with hyperendemic circulation of all four dengue virus serotypes in the north of the contin-ent since the reintroduction of dengue virus serotype 3 was detected in Brazil and Venezuela during 2000. According to PAHO, Brazil, Argentina, and Colombia reported the largest number of confirmed dengue cases in 2016. Low-level year-round transmission has been observed, but most cases follow an epidemic pattern; in Brazil, peak dengue transmission occurs between February and May (Siqueira *et al,* 2005). Brazil experienced a major outbreak in 2013, with nearly 1.5 million cases nationwide, including almost 7000 severe dengue cases (Fares *et al,* 2015). Colombia (127,000 cases) and Paraguay (144,000 cases) also, reported major dengue outbreaks in 2013. According to PAHO, the Andean and Southern cone of South America account for over 400,000 laboratory-confirmed cases in 2016, of which more than 270,000 laboratory-confirmed cases occurred in Brazil.

Transmission patterns: Dengue virus transmission follows two general (but not mutu-

ally exclusive) patterns, with different implications for disease risk in both the local population and travelers.

Epidemic dengue: Epidemic transmission occurs when the introduction of dengue virus into a region is an isolated event involving a single virus strain. If sufficiently large populations of susceptible hosts and mosquitoes are present, transmission of dengue is explosive, leading to a recognizable epidemic. The incidence of infection among susceptible individuals often reaches 25 to 50% and can be considerably higher. Herd immunity, changes in weather, and mosquito control efforts all contributed to the epidemic termination (McBrid *et al,* 1998).

Prior to World War II, dengue viruses' transmission almost exclusively followed this pattern. Seaports frequently were the point of initial introduction of dengue viruses, and these port cities then acted as distribution points to nearby inland areas (Gubler, 1997). In smaller island nations, certain areas of South America and Africa, and in the areas of Asia where dengue virus transmission has reemerged, epidemic activity is the predominant pattern of dengue virus transmission. The incidence of dengue virus infections in these locations varies considerably from year to year. Intervals of several years or more usually pass between epidemics, allowing the number of susceptible individuals to accumulate so that the next epidemic can be perpetuated.

In the setting of epidemic transmission, adults and children in the local population are affected. Among travelers, the risk for acquisition of dengue virus is high during an epidemic but low at other times. The frequency of dengue hemorrhagic fever (DHF) is usually low, with some exceptions (Kouri *et al,* 1989). The viral serotype and strain and the interval since the previous epidemic seem to influence the risk for DHF.

Hyperendemic dengue virus: This refereed to the continuous circulation of the multiple dengue virus serotypes in the same area. This requires the year-round presence of competent vector mosquitoes and either a large population or steady movement of individuals into the area to maintain a pool of susceptible individuals. Hyperendemic circulation involves the occurrence of multiple epidemics in a smaller geographic scale such as village or school (Endy *et al,* 2002).

Seasonal variation in virus transmission is common, even also varies from year to year, with increased dengue transmission at intervals of three to four years, but this variation is not as dramatic as in areas where transmission predominantly follows the epidemic pattern. A mathematical analysis of data from Thailand suggested that these surges in dengue transmission originate in waves from major urban centers (Cummings *et al,* 2004). Areas with hyperendemic dengue virus transmission contribute to the majority of cases of dengue virus infection globally. In some regions, 5 to 10% of the susceptible population experiences dengue virus infection annually (Burke *et al,* 1988). Urban areas are particularly affected.

In the hyperendemic transmission setting, the prevalence of antibody against dengue virus rises with age (Porter *et al,* 2005). Children are more likely than adults to experience disease, and most adults in the local population are immune to infection. Among travelers, the risk for acquisition is higher than in areas that experience epidemic transmission, but the seasonal variation in risk is somewhat predictable. Hyperendemicity is a major factor contributing to the occurrence of DHF (Endy *et al,* 2002).

Factors influencing transmission: Worldwide incidence of dengue and dengue hemorrhagic fever (DHF) has been increasing in the past several decades, and the geographic distribution of these diseases has expanded. Emergence of DHF as a public health problem has largely been a result of human behaviors including population growth, poor urban planning with overcrowding and poor sanitation, modern transportation, which allows increased movement of humans, mosquitoes, and viruses, and lack of effective

control (Hales *et al,* 1996). Potential effects of global climate change are a major source of the future concern. Incre-ased dengue virus transmission has been associated with El Niño/Southern Oscillation events (CDC, 1998b). Mathematical models predict that increased global temperatures would further expand the range of *Ae. aegypti* and dengue virus (Jetten and Focks, 1997).

The transmission cycle for dengue viruses is dependent upon the interaction between infective mosquitoes and susceptible humans and between susceptible mosquitoes and viremic humans.

Dengue virus transmission is enhanced by factors (Hales *et al,* 2002): 1- Increased vector density, naturally infected man had viremia levels of 6 to 8 log10 RNA copies/ml led to infection of half of *Ae. Aegypti* took a blood meal under laboratory conditions. In many tropical countries, seasonal increases in rainfall contribute to an increased density of mosquitoes. One factor that can be modified is the presence of open water storage containers in or near the home (Nguyet *et al,* 2013). 2- Shorter mosquito incubation, incubation time in the mosquito (known as the extrinsic incubation period) was inversely associated with the ambient temperature. Warmer temperatures increase the length of time that a mosquito remains infective. 3- Increased movement of mosquito vectors and viruses by air, land, and water transportation of mosquitoes or viremic humans facilitate the dissemination of dengue viruses. 4- Increased density of susceptible hosts, as crowded conditions probably increase potential for virus transmission. However, as the prevalence prior infection increases, the fraction of the population that remains susceptible is reduced (Bhamarapravati *et al,* 1987). 5- Increased duration and magnitude of viremia in humans in laboratory have produced low titers of virus in blood, which were not efficiently transmitted to mosquitoes, but not clear whether natural strains of dengue virus differ in the produced viremia titers (Schoepp *et al,* 1991). Hossain *et al.* (2023) in Bangladesh reported that maximum and minimum temperatures, humidity, and wind speed positively impact dengue incidence, but rainfall and sunshine hours have a significantly negative effect.

Other routes of transmission: Given the high titers of infectious dengue virus found in blood and tissues during acute infection, the potential exists for virus transmission by routes other than mosquito vectors.

Nosocomial transmission: Dengue may be transmitted via blood products, needle-stick injury, and mucocutaneous exposure (Chen and Wilson, 2004). Blood donors may be asymptomatic even in the setting of viremia (Stramer *et al,* 2012). One report estimated a dengue transmissibility rate of 37% via blood products (Sabino *et al,* 2016).

Vertical transmission: Vertical transmission of dengue were reported in a few small case series (Sirinavin *et al,* 2004): based on these cases and the known pattern of viremia, this possibility should be considered in cases where illness in the mother occurs within the 10 days before delivery (including onset on the day of delivery). Illness presented in these newborns up to 11 days (median 4 days) after birth.

Pregnancy didn't increase the incidence or severity of dengue (Carroll *et al,* 2007). In Kuala Lumpur of 2958 parturients, 2531 paired maternal-umbilical cord blood samples were tested for dengue-specific IgM to identify infection prevalence and the vertical transmission rate (Tan *et al,* 2008). Sixty-three women (2.5%) had a positive IgM serology. Only one (1.6%, 95% CI 0-9.5%) of the paired umbilical cord samples was seropositive for dengue. None of the maternal and fetal blood samples had evidence of viral RNA by PCR. Breastfeeding was suggested as a route of vertical dengue virus transmission (Barthel *et al,* 2013), but so far no reports of dengue virus sexual transmission.

A new dengue vaccine is approved for use in children aged 9-16 years with laboratory-confirmed previous dengue virus infection and living in areas where dengue is endemic

(occurs frequently or continuously). Endemic areas were in some U.S. territories and freely associated states, but not approved for use in U.S. travelers who visit but not live in a dengue area (CDC, 2021). CDC (2022b) recommended dengue vaccination for children 9 to 16 yea-rs old, but only when they have been previously infected with dengue and living in areas where dengue is common. This previous infection should be confirmed by laboratory testing. This vaccine is different from other vaccines in that it is only recommended for people who have already been infected with dengue virus. Children without previous infection are at increased risk for severe dengue disease and hospitalization if they get dengue after the Dengvaxia vaccination. So, healthcare providers must check for a laboratory-confirmed previous dengue infection before vaccination.

Now in the Sudan on the southern board of Egypt Ahmed *et al.* (2022a) reported that arboviruses are posing a serious global health threat, such as, chikungunya (CHIKV), Crimean-Congo hemorrhagic fever (CCHF), dengue (DENV), yellow fever (YFV), and Zika (ZIKV) virus infections. Other arboviruses, such as Rift Valley fever (RVF), African swine fever, bluetongue, and Marburg (MBGV) and Schmallenberg viruses caused risky economic impacts due to the high morbidity and mortality among domestic cattle, sheep, and goats (Ahmed *et al,* 2020). While others, such as the Shuni virus, Wesselsbron virus, and West Nile virus (WNV), severely affect domestic and wildlife animals (Blahove and Carter, 2021).

Aedes albopictus was a more recent species to Africa that only emerged in area during the recent three decades, and estimated to be present in 197 countries by 2080 (Kraemer *et al,* 2019). Ahmed *et al.* (2022b) in North and South Kordofan, Sennar, and White Nile, identified 30% as *Anopheles gambiae* & *An. stephensi* & 117 ones were *Ae. luteocephalus* (39%), *Ae. aegypti* (32%), *Ae. vexans* (9%), *Ae. vittatus* (9%), *Ae. africanus* (6%), *Ae. metalicus* (3%), & *Ae. albopictus* (3%), as an invasive risky vector of Chikungunya and dengue.

Brady and Hay (2020) reported that the 4 serotypes of DENV cause 390 million yearly infections worldwide, with 240million remaining asymptomatic maintaining the virus transmission. Mustafa and Makhawi (2023) in Sudan reported that an outbreak of dengue fever on November 8, 2022, killed at least five people in North Kordofan State. On 23 Nov 2022, the Sudanese Ministry of Health reported 3326 cases across 8 Sudanese States and 23 patients died from the fever. Sudan is witnessing its worst outbreak of dengue fever in over a decade, especially in North and South Kordofan and Red Sea State are hit hard. Desog *et al.* (2023) detected serotypes- DENV-2, -3 & -4, as the first causes of DENV-4 serotype outbreak.

In Saudi Arabia, Zaki *et al*. (2008) reported that four dengue serotypes (DENV-1,-2 -3 & -4) circulated, with more than one serotype in each DEN outbreak. Al-Tawfiq and Memish (2018) reported that Dengue virus Alkhurma hemorrhagic fever, Chikungunya virus, Crimean-Congo hemorrhagic fever as well as Rift Valley fever do existed. They added that dengue infections were limited to Western and South-western regions, where *Ae. aegypti* existed and the cases majority had mild disease and related to serotypes 1, 2 or 3, but not serotype 4. Hakami *et al.* (2021) reported that the chikungunya virus prevalence was the Southern Region, and that detailed investigation of this viral infection and its vectors should be focused.

In Egypt, Heikal *et al.* (2011) in Aswan reported the re-emergence of *Ae. aegypti*, the vector of Dengue fever, Yellow fever and Chikungunya fever that were encountered in Africa, needs to alert for this public health threat. El Bahnasawy *et al*. (2011) declared that *Ae. aegypti* presence and endemic DF in the neighboring regional countries must be in mind of Egyptian Health Authorities. Shoukry *et al.* (2012) reported that *Ae. aegypti* in Toshka is a critical mark of dengue and other *Aedes* borne-viruses from Sudan.

Saleh (2012) in Aswan district detected the immature and matures stages of *Ae. aegypti*. Ducheyne *et al.* (2018) for the WHO/EMR mapped the distribution and maximum risk of establishment created for *Ae. aegypti* and *Ae. albopictus*. They added this must increase the awareness and preparedness of the different countries for *Aedes* borne diseases. Morsy (2018) reported that the increased air travel and breakdown of vector control measures have also contributed greatly to global burden of dengue and DH fevers. He added that without vectors effectively control or a cost effective vaccine developed, dengue virus can be expected to continue to escalate.

Ghweil *et al.* (2019) reported that dengue virus patients have symptoms ranged from asymptomatic to sever form depending on their primary and secondary immune status, infecting genotype and ages. In prospective cohort study on dengue disease 100 patients (mean age of 40.34±15.74 years) found that all were presented with fever, headache and fatigue. Thirteen of them after 3 months suffered from acute pancreatitis with positive serum dengue virus IgM, antibodies and negative serum dengue virus PCR.

Hussen *et al.* (2020) reported specific dengue virus antibodies in man residing within Asyut and Sohag Governorates with serologi cal evidence in camels. Gaber *et al.* (2022) reported the first serotyping of DENV in an outbreak in Upper Egypt using RT-LAMP assay, which was induced was reinforced the reemergence of *Ae. aegypti*. They added that mosquito-based surveillance of DENV infection is important to elucidate viral activity rate and define serotype diversity to know the virus dynamics.

AbdEl-Wahab *et al*. (2022) mentioned that risk of transfusion transmitted dengue is increasingly recognized, posing a risk to blood safety as well as spreading into non-immune communities. They concluded that dengue awareness programs are urgently needed for effective prevention of transmission. Eassa and Abd El-Wahab (2022) reported that there was a lack of implementation of an integrated vector borne diseases (VBDs) management strategy that integrates chemical, environmental, and biological control as well as health education. This necessitates cross-sectoral coordination and community to improve vector control activities and the use, storage, and disposal of pesticides.

Fang *et al.* (2022) in Egypt reported five common mosquito-borne viruses included dengue virus, Rift Valley fever virus, West Nile virus, Chikungunya virus, and Sindbis virus (MBVs). They added that man, animal and these viruses were retrieved from Web of Science, PubMed, and Bing Scholar, and 33 eligible studies were analyzed. The monophyletic characterization of Egyptian both RVFV and WNV strains found, which spans about half a century, indicated that RVFV and WNV are widely transmitted locally. The sero-positive rates of DENV and WNV in hosts raised in recent years, and spillover events of DENV & WNV to other countries from Egypt have been recorded. They concluded it is must to evaluate local transmission risk, establish an early warning system for MBVs, and develop an alarm for the Public Health Authorities to control the MBVs.

El Bahnasawy *et al.* (2012) reported three immigrant employees with Crimean-Congo hemorrhagic fever cases, one in Almaza Fev er Hospital and two in Gharbia Fever Hospital. They added that *Hyalomma*-vector has a global distribution. El-Kady *et al.* (2022) in Elquseir City, Red Sea Governorate, reported 144 patients with symptoms indicative of DENV, which was the first serotyping of the DENV caused outbreak in 2017. They added that serotype identified was DENV-2, while DENV-1 was the serotype found in 2015 the outbreak in Assiut Governorate. This indicated a comprehensive risk assessment to be done, including an entomological survey, to assess presence & geographical expansion of mosquito vectors. Frank *et al.* (2024) in German reported DENV infections among 36 cases vs. zero to eight in 2017 to 2022. They stayed on the Red Sea Coast (Hurghada), of whom 50% were private residences.

Conclusions

are members of family Fl-aviviridae, genus *Flavivirus*, with four antigenically related, but distinct viruses, which are mosquito-borne human pathogens. Humans become infected after being bitten by an infected female *Aedes* mosquito and viremia begins toward end of a four- to six-day incubation period and persists until fever abates. An uninfected *Aedes* o may acquire the virus after feeding on an infected patient during this viremic period. Once infected, it carries virus for lifespan remain infective to man, and passes infection to its off springs.

Aedes aegypti are daytime humans bite feeders frequently not noticed. They usually interrupted feeding and move on to another host taking multiple blood meals in a single breeding cycle transmiting dengue virus to several individuals within a small area.

Epidemic dengue virus transmission occurs when the introduction of dengue virus into a region is an isolated event involving a single virus strain. If sufficiently large populations of susceptible hosts and mosquitoes are present, transmission is explosive, leading to a identify epidemic. Herd immunity, weather changes, and mosquito control efforts can all contribute to terminate the epidemic.

Hyperendemic transmission is continuous circulation of multiple dengue serotypes in the same area. This requires the year-round presence of competent vector mosquitoes and an ongoing presence of susceptible individuals. Dengue virus transmission is activated by many factors, including higher vector density, greater movement of mosquito vectors, and increased density of susceptible humans.

Aedes species and dengue viruses and perhaps other *Aedes*-borne viral disease are endemic in all continents except Antarctica, although epidemic dengue hemorrhagic fever occurs predominantly in Americas, Asia, Africa and some European countries. Also, may be found in non-endemic areas

Recommendations

There must be local, national and international collaboration to face the climatic changes impact on man, animal and agriculture.

One may quote the French Novelist and Playwright Alexandre Dumas the Three Musketeers, Author "All for one and one for all, united we stand divided we fall"

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