Review Article
Published: 27 Jun, 2020

SF Internal Medicine

Aedes - One Mosquito Species, A Few Serious Diseases

Ralapanawa U[1] and Kularatne S[2]*

[1]*Professor in Medicine and Consultant Physician, Department of Medicine, University of Peradeniya, Sri Lanka*

[2]*Senior Professor of Medicine and Consultant Physician, Department of Medicine, University of Peradeniya, Sri Lanka*

Abstract

Background: Aedes mosquitoes have a high vectorial capacity for the dengue virus, chikungunya virus, Zika virus and yellow fever virus akin to their wide spread, behavior, habitats and adoptability.

Methods: A PubMed search was performed on all articles with the key word "Dengue, Zika, Chikungunya and Yellow fever, Aedes" in the title and "management" in the abstract. The search was then restricted to articles published in the English language within the last decades.

Results: Dengue is the most prevalent human arboviral infection causing approximately 100 million annual infections with more than half of the world's population at risk. Chikungunya, a less dreaded alpha viral infection has caused over 2.5 million infections during the past decade. It has spread to America recently and emerging in Europe, generating challenges to the world health systems as it spreads to new areas, infecting native populations and causing large outbreaks. The disease burden of yellow fever has been significantly reduced by large-scale vaccination programs in the twentieth century, but current occurrence of 51,000-380,000 severe cases per year in Africa reflect the difficulty in controlling the disease. Recent outbreak of Zika in Brazil and its perinatal complication caused panic world over.

Conclusion: Considering the disease burden of all these arboviral infection and their unique vector affinity, global mapping of distribution of Aedes mosquitoes is important to understand population at risk and to develop preventive strategies.

Keywords: Aedes; Chikungunya; Dengue; Yellow fever; Zika

Abbreviations

DENV: Dengue Virus; CHIKV: Chikungunya Virus; ZIKV: Zika Virus; YFV: Yellow Fever Virus; DF: Dengue Fever; HI: House Index; CI: Container Index; BI: Breateau Index; PI: Pupa Index; DHF: Dengue Haemorrhagic Fever; DSS: Dengue Shock Syndrome; NS1: Non Structural Protein 1; ELISA: Enzyme-Linked Immuno Sorbent Assay

Introduction

Vector-borne diseases account for more than 17% of all infectious diseases, causing more than one million deaths annually. Aedes is a genus of mosquitoes that are originally found in tropical and subtropical zones, but now found in all continents except Antarctica. Members of the Aedes genus are known vectors for numerous viral infections. The two most prominent species among them are *Aedes aegypti* and *Aedes albopictus* which transmit the viruses of dengue fever, yellow fever, Chikungunya and the Zika. The objective of this review is to highlight the Aedes as a unique mosquito genes which has peculiar biology to become leading vector of most dreaded viral infections in the globe and to discuss them under one theme to bring attention and curiosity.

Materials and Methods

A PubMed search was performed on all articles with the key word "Dengue, Zika, Chikungunya, Yellow fever and West Nile fever, Aedes" in the title and "management" in the abstract. The initial search yielded 1965 articles based on these criteria. The search was then restricted to articles published in the English language within the last decades. Endnote X3 software was used to filter articles. All abstracts were read independently by the two authors, and key articles were identified based on a consensus among the authors. The search was then confined to last decade to select more recent evidence. However, related or cited papers of importance before this period were also included. The epidemiological data and guidelines of management were downloaded from the websites of local and international agencies, including the World Health Organization guidelines.

OPEN ACCESS

**Correspondence:*
Udaya Ralapanawa, Professor in Medicine and Consultant Physician, Department of Medicine, University of Peradeniya, Sri Lanka.
E-mail: udayapralapanawa@yahoo.com

Received Date: *17 May 2020*
Accepted Date: *23 Jun 2020*
Published Date: *27 Jun 2020*

Citation: *Ralapanawa U, Kularatne S. Aedes - One Mosquito Species, A Few Serious Diseases. SF Intern Med. 2020; 1(1): 1002.*

Figure 1: *Aedes aegypti*. Courtesy of https://commons.wikimedia.org/wiki/File:Aedes_aegypti.jpg (Permission is granted to copy, distribute and/or modify this document under the terms of the GNU Free Documentation License, Version 1.2 only as published by the Free Software Foundation; with no Invariant Sections, no Front-Cover Texts, and no Back-Cover Texts. A copy of the license is included in the section entitled GNU Free Documentation License).

Results and Discussion

Vector-Aedes

Aedes aegypti is a predominantly urban vector, utilizing the abundance of artificial containers as larval sites and feeding almost exclusively on humans (Figure 1). *Aedes albopictus* can more often be found in peri-urban and rural environments, feeding readily on a variety of mammalian (including humans) and avian species [1,2].

Global distribution

Aedes aegypti most likely originated in Africa from an ancestral sylvian form; since then, the mosquito has been transported globally throughout the tropical, subtropical, and parts of the temperate world, through global trade and shipping activities [2,3]. *Aedes albopictus* originated in Asia. Like *Aedes aegypti*, *Aedes albopictus* has spread globally throughout the tropical, subtropical, and temperate world, primarily through international trade in used tires. *Aedes albopictus* has adapted to survive in a broader temperature range and at cooler temperatures, which enables them to persist in more temperate climates. Live in close proximity to people, but less so than *Aedes aegypti* [3,4]. In the tropics increased urbanization, the reliance on water storage due to inadequate water supplies, and poor rubbish and waste removal increased populations of *Aedes aegypti*. Large tropical mega cities such as Bangkok, Rio de Janeiro and Delhi have extensive slums with large populations of *Aedes aegypti* and dengue epidemics 'The mosquito *Aedes aegypti* enjoys greater geographical distribution than at any time in the past and is established in virtually all tropical countries [5] (Figure 2).

Aedes and human diseases

Aedes mosquitoes have a high vectorial capacity (effectiveness of virus transmission in nature) for the Dengue Virus (DENV), Chikungunya Virus (CHIKV), Zika Virus (ZIKV) and Yellow Fever virus (YFV) through their behavior and preferred habitats [5]. Dengue is the most prevalent human arboviral infection causing approximately 100 million apparent annual infections with almost half of the world's population at risk. Dengue transmission now occurs in over 120 countries, mostly in the tropics and sub-tropics [2,3]. Chikungunya, another arthropod-borne virus, has caused over 2.5 million infections over the past decade and has more recently been spreading in the Americas and emerging in Europe, posing new challenges to health systems as it spreads into new areas, infecting naïve populations and consequently causing large outbreaks [1,2].

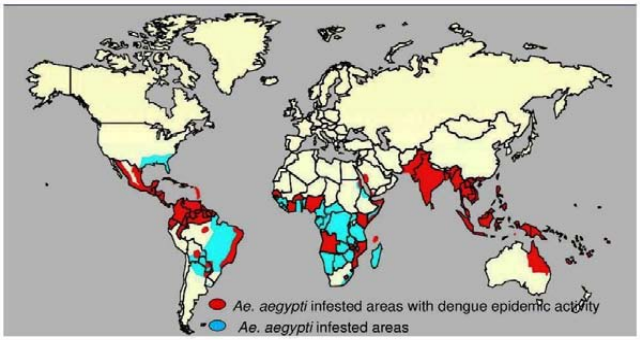

Figure 2: Global distribution of *Aedes aegypti* mosquitoes. The colour shows the probability of finding the mosquito, with red being more likely, blue being less likely. Courtesy of https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4493616/figure/fig1/ (This is an open-access article, free of all copyright, and may be freely reproduced, distributed, transmitted, modified, built upon, or otherwise used by anyone for any lawful purpose. The work is made available under the Creative Commons CC0 public domain dedication).

The disease burden of yellow fever was significantly reduced due to large-scale vaccination programs in the twentieth century but current estimates of 51,000-380,000 severe cases in Africa per year point to the continuing difficulty in fully controlling this virus [6]. Zika virus, transmitted by mosquitoes, has spread rapidly recently in the Americas particularly in Brazil, and it is likely to spread further in the presence of the Aedes mosquitoes [7,8]. As a result, there is growing interest in describing the global geographic distribution of both vector species to better understand the risk of the transmission of these viruses.

Dengue

Introduction

Dengue Fever (DF) is a globally important arboviral infection transmitted by mosquitoes of the Aedes genus (primarily *Aedes aegypti*, but also *Aedes albopictus*) [9]. It affects a large proportion of the population in tropical and sub-tropical countries causing high morbidity and mortality [10-12]. The global burden of dengue is large, an estimated 50 million infections per year occur across approximately 100 countries [13]. DF is caused by four antigenic ally distinct dengue virus serotypes: DENV-1, DENV-2, DENV-3, and DENV-4. All four have the capacity to cause severe disease. They are RNA viruses that belong to the Flaviviridae family [9].

Clinical manifestation

DENV infections may be asymptomatic or lead to a range of clinical presentations, even could be fatal [14]. After an incubation period of 3 to 7 days, symptoms start suddenly and follow three phases to name initial febrile phase, a critical phase, and recovery phase [13]. The initial febrile phase is typically characterized by high temperature (≥38.5°C) accompanied by headache, vomiting, myalgia, and joint pain, sometimes with a transient macular rash [13]. A biphasic or "saddleback" fever curve is not the norm [9]. Laboratory findings include mild-to-moderate thrombocytopenia and leukopenia, often with a moderate elevation of hepatic aminotransferase levels. This phase lasts for 3 to 7 days, followed by spontaneous recovery in majority without developing complications [9,13]. In the critical phase, a small percentage of patients a systemic vascular leak syndrome becomes evident around 4th to 6th day of illness when fever seem settling with the evidence of rising hematocrit, hypoproteinemia, pleural effusions, and ascites [13-16]. Extravasation occurs through endothelial gaps, without necrosis or inflammation of the capillary

endothelium [9,15]. The degree of plasma leakage varies. The leak usually starts slowly, increases gradually, slows down and then ceases altogether at the end of the critical phase [17]. If the pulse pressure narrows to 20 mm Hg or less, accompanied by signs of peripheral vascular collapse, dengue shock syndrome is diagnosed when urgent, but careful, resuscitation is required [13,16]. During the evolution from the febrile to the critical phase, between days 4 and 7 of the illness, it is imperative for the clinician to be aware of warning signs that clinically significant vascular leakage may be developing in the patient [13,18]. These signs include persistent vomiting, increasingly severe abdominal pain, tender hepatomegaly, a high or increasing hematocrit level that is concomitant with a rapid decline in the platelet count, serosal effusions, mucosal bleeding, and lethargy or restlessness [13]. Hemorrhagic manifestations are anticipated during this critical period. In children, clinically significant bleeding occurs only rarely, usually in connection with extreme and prolonged shock. However, major skin bleeding, mucosal bleeding (gastrointestinal or vaginal), or both may occur in adults with no apparent precipitating factors and only minor plasma leakage [13,19]. Moderate to-severe thrombocytopenia is common, with platelet counts under 20×109 per liter often observed during the critical phase, followed by rapid rise during the recovery phase. Infrequently, other severe manifestations, including liver failure, myocarditis, and encephalopathy occur often with minimal associated plasma leakage [13]. The altered vascular permeability is transitory. If the patient survives the 24-48 hour critical phase, a gradual re-absorption of extravascular compartment fluid takes place in the next 48-72 hours of recovery phase and is concurrent with rapid improvement in the patient's symptoms [13,17]. The return of appetite is a good sign of recovery from the illness. Bradycardia is also seen in this period. If present, a confluent petechial rash with erythema and islands of pallor (usually known as a recovery rash) are characteristic of dengue infections. During the convalescent stage, many patients also complain of itching, especially on the palms and soles [15]. Watch for symptoms and signs of fluid overload such as periorbital oedema, cough, wheeze and tachypnoea, rise of both systolic and diastolic blood pressures with widening of pulse pressure, basal crepitations and rhonchi. Urine output is usually high during this phase [18,19]. Shock (dengue shock syndrome) and hemorrhage (dengue hemorrhagic fever) occur in less than 5% of all cases of dengue [20].

Diagnosis

A full blood count should be ordered initially in all patients with symptoms. Typically, leucopenia and thrombocytopenia occur as early as the second day of fever. The haematocrit may also rise about 10% in patients with dengue fever owing to dehydration and is very important determinant in monitoring Dengue Haemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS). The results of liver function tests are usually increased, particularly for alanine and aspartate aminotransferases [9]. Laboratory diagnosis of dengue is confirmed directly by detection of viral components in serum or indirectly by serologic means [13]. During the febrile phase, detection of viral nucleic acid in serum by means of Reverse-Transcriptase-Polymerase-Chain Reaction (RT-PCR) assay or detection of the virus expressed soluble Nonstructural Protein 1 (NS1) through Enzyme-Linked Immuno Sorbent Assay (ELISA) or the lateral-flow rapid test is sufficient for a confirmatory diagnosis [13]. Serologic diagnosis of dengue relies on the detection of high levels of serum IgM. IgM seroconversion between paired samples is considered a confirmatory finding, where as detection of IgM in a single sample obtained from a patient with a clinical syndrome that is consistent with dengue is widely used to establish a presumptive diagnosis [13].

Management

During this febrile phase of illness, liberal administration of oral fluid and treatment with antipyretics like paracetamol is recommended as required [10]. Patients who have approached the critical phase should be admitted for in-ward management. These include patients with warning signs, those with co-existing conditions that may make dengue or its management more complicated (such as pregnancy, infancy, old age, obesity, diabetes mellitus, hypertension, heart failure, renal failure, chronic haemolytic diseases such as sickle cell disease and autoimmune diseases), and those with certain social circumstances (such as living alone, or living far from a health facility without reliable means of transport). Rapid fluid replacement in patients with warning signs is the key to prevent progression to shock state [9,10,13,17,18]. If the patient has dengue with warning signs or signs of dehydration, judicious volume replacement by intravenous fluid therapy from this early stage may modify the course and the severity of the disease. Fluid quota in adults for critical phase is based on the maximum lean mass of 50kg. This fluid quota is calculated by using formula M+ 5%. The entire fluid quota is given over 48 hours (the duration of the critical phase). For patients presenting in shock the quota may be given over 24 hours [9,10,13,17,18,20].

Vaccine

The first dengue vaccine, Dengvaxia (CYD-TDV), was first registered in Mexico in December, 2015. CYD-TDV is a live recombinant tetravalent dengue vaccine that has been evaluated as a 3- dose series on a 0/6/12 month schedule in Phase III clinical studies. It has been registered for use in individuals 9-45 years of age living in endemic areas [21].

Chikungunya

Introduction

Chikungunya fever is an acute febrile illness associated with severe, often debilitating polyarthralgiasis, primarily transmitted to humans through the bites of infected mosquitoes, predominantly *Aedes aegypti* and *Aedes albopictus* [22-26]. It was first described during an outbreak in southern Tanzania in 1952. It is an RNA virus that belongs to the alphavirus genus of the family Togaviridae [27]. Chikungunya occurs in Africa, Asia and the Indian subcontinent. In recent decades, there have been outbreaks of the disease in countries that have never recorded cases before [28].

Signs and symptoms

CHIKV causes a febrile illness in the majority of people with an incubation period of 3-12 days from the mosquito bite [29]. Viremia persists for up to 5 days from the clinical onset. Commonest presenting features are fever (92%) usually associated with arthralgia (87%), backache (67%) and headache (62%). Migratory polyarthritis with effusions may be seen in around 70% cases, but resolves in the majority. Ankles, wrists and small joints of the hand were the worst affected [29]. The fever varies from low grade to high grade, lasting for 24 to 48 hours. Fever rises abruptly in some, reaching 39-40°C, with shaking chills and rigor and usually subsides with use of antipyretics. No diurnal variation was observed for the fever [30]. Transient maculapapular rash is seen in up to 50% patients. The maculopapular eruption persisted for more than 2 days in approx [29]. Stomatitis was observed in 25% and oral ulcers in 15% of patients. Nasal blotchy erythema followed by photo sensitive hyper pigmentation

(20%) have been observed [29]. Persistent arthralgic forms had been described, where a retrospective study has shown complete resolution in 87.9%, 3.7% had episodic stiffness and pain, 2.8% had persistent stiffness without pain and 5.6% had persistent painful restriction of joint movements. Enthesopathy and tendinitis of tendoachilles was observed in up to 53% of those who had musculoskeletal involvement. Neurological, emotional and dermatologic sequelae are also described [29]. Various neurologic sequelae can occur with persistent Chikungunya fever. Peripheral neuropathy with a predominant sensory component is the most common [29].

Diagnosis

The confirmation of Chikungunya fever is through isolation of virus, detection of viral RNA by RT-PCR, detection of virus specific IgM antibody in single serum sample and demonstration of four-fold increase in IgG values in samples collected at least three weeks apart [29,31]. Leucopenia with lymphocyte predominance is the usual observation. Thrombocytopenia is not severe. A small proportion of patients have tested positive for rheumatoid factor during and after clinical episode [29].

Management

There is no specific treatment for chikungunya. The illness is usually self-limiting and will resolve with time. Supportive care with rest is indicated during the acute joint symptoms. Movement and mild exercise tend to improve stiffness and morning arthralgia, but heavy exercise may exacerbate rheumatic symptoms. In unresolved arthritis refractory to NSAIDs, chloroquine phosphate (250 mg/day for several weeks) has given good results [31]. Since an immunologic etiology is suspected in chronic cases, a short course of steroids may be useful [29].

Vaccine

Vaccine for commercial purpose is not available and is under trial [32].

Zika

Introduction

ZIKV is a flavivirus, in the family Flaviviridae [33]. The virus was identified in the late 1940s in Africa [34]. ZIKV is a single stranded RNA virus with two major lineages: Asian and African. In Africa, ZIKV is thought to have been largely maintained in a cycle involving transmission between non-human primates (such as monkeys and apes) and mosquitoes, with humans as occasional unintentional hosts. In areas outside Africa, however, humans have probably become the main host [34]. Substantial evidence now indicates that Zika virus can be transmitted from the mother to the fetus during pregnancy. Also peripartum transmission, sexual transmission has been reported [33]. Recently, a large increase was observed in the circulation of ZIKV worldwide, which initially was endemic only in Africa and Asia. Cases have been reported in countries of Europe, Oceania, and the Americas, particularly in Latin America where it is rapidly spreading to new areas [35].

Signs and symptoms

Common symptoms are macular or papular rash (90% of patients), fever (65%), arthritis or arthralgia (65%), nonpurulent conjunctivitis (55%), myalgia (48%), headache (45%), retro-orbital pain (39%), oedema (19%), and vomiting (10%) [33]. Severe neurologic sequelae have also been described in adults, including meningitis, meningoencephalitis, and Guillain-Barre syndrome [36,37]. In addition current epidemiological data suggest spatial and temporal links with the Zika virus epidemic and congenital microcephaly [34,38-43].

Diagnosis

The mainstays of the routine diagnosis of ZIKV infection are the detection of viral nucleic acid by RT-PCR and the detection of IgM antibodies by IgM-capture enzyme-linked immunosorbent assay (MAC-ELISA) [33,40,44]. After the acute phase, diagnosis by antibody detection in serum samples is compromised by considerable cross reactivity with antibodies to other flavi viruses; false positive results can be seen with past dengue infection or previous yellow fever vaccination [34].

Management

No ZIKV vaccine or antiviral treatment exists; thus, prevention and control measures center on avoiding mosquito bites, reducing sexual transmission, and controlling the mosquito vector [33,34]. Potentially effective methods of prevention that are focused on reducing infections among pregnant women include avoiding unnecessary travel to areas of ongoing ZIKV transmission, avoiding unprotected sexual contact with partners who are at risk for ZIKV infection is advocated [33].

Vaccine

There is currently no vaccine against ZIKV [31].

Yellow Fever

Introduction

Yellow Fever (YF) is a vector-borne acute viral haemorrhagic disease, affecting humans and non-human primates in tropical areas of Africa and Central and South America [45,46]. The causative agent of YF is an arthropod-borne virus from Flavi virus genus of the family Flaviviridae. The virus possesses a single-stranded, RNA genome [47,48]. Despite landmark achievements made in the understanding of the epidemiology of YF disease and the availability of a safe and efficacious vaccine, YF remains a major public health problem in both Africa and America where the disease affects annually an estimated 200,000 persons causing an estimated 30,000 deaths [47,48].

Signs and symptoms

Incubation period of the disease is 3 to 6 days [46]. Once contracted, many people do not experience symptoms, but when these do occur, the most common are fever, muscle pain with prominent backache, headache, loss of appetite, and nausea or vomiting. In most cases, symptoms disappear after 3 to 4 days [46,49-52]. A small percentage of patients, however, enter a second, more toxic phase within 24 hours of recovering from initial symptoms. High fever returns and several body systems are affected, usually the liver and the kidneys. In this phase people are likely to develop jaundice, dark urine and abdominal pain with vomiting. Bleeding can occur from the mouth, nose, eyes or stomach. Half of the patients who enter the toxic phase die within 7-10 days [45,46,53].

Diagnosis

Specific diagnosis depends on histopathologic studies, isolation of the virus, demonstration of viral antigen or a specific antibody response [47,54].

Management

In the absence of specific therapy, treatment of YF is chiefly supportive [52].

Vaccine

While eradication of yellow fever is not feasible due to the sylvatic reservoir, a high level of control is achievable owing to the availability of an efficacious and safe vaccine that confers long lasting immunity from a single dose [45]. Two live attenuated vaccines have been used for the prevention or control of YF epidemics [47]. A YF vaccine, the French Neurotropic Vaccine (FNV) was developed in 1930. Severe post-vaccinal reactions were developed by vaccines, including systemic symptoms in approximately 20%, meningeal signs in 3-4%, and post-vaccinal encephalitis in 0.5-1.3% [47,48]. The manufacture of the French neurotropic vaccine was discontinued in 1980. The second vaccine, the 17 D vaccine, is a safe and efficacious live attenuated vaccine prepared from infected chicken embryo. About 95% of vaccines develop measurable antibody within 10 days of primary vaccination. For international certification, immunization is valid for 10 years, but immunity may be lifelong [55]. Adverse reactions to the 17 D vaccine are mild but there have been reports of rare but serious events following YF vaccination. These events include life-threatening allergic reaction, disease affecting the nervous system, and disease affecting certain internal organs [48,53,56-58].

Single Vector Control-Effective Way to Control Several Diseases

Some of the factors responsible for the resurgence of mosquito borne diseases include: collapse of health care delivery systems, poor or inadequate disease surveillance, inappropriate disease control measures, urban poverty with overcrowding and massive population movements, poor environmental management and indiscriminate deforestation [47]. In addition to address those issues, development of strategies to control Aedes vector and development of effective vaccines against viruses will play a key role controlling the Aedes vector borne diseases. Mosquito control programme generally comprises 3 major components: Vector control and surveillance; community participation and enforcement [59]. During vector surveillance larval surveys and adult surveys basic sampling unit is the house or premise. During larval surveys House Index (HI), Container Index (CI), Breateau Index (BI) and Pupa Index (PI) are calculated to monitor Aedes infection level in that area. For adult mosquito survey landing/biting collection, resting collection and oviposition traps are used to collect data [60-62]. The major environmental management methods used for control of Aedes mosquito are environmental modification (Long lasting physical transformation of vector habitats like improved water supply, mosquito proofing of overhead tanks, cisterns or underground reservoirs), environmental manipulation (temporary changes to vector habitats that involve the management of "essential" and "non-essential" containers and management of or removal of "natural" breeding sites) and changes in human habitations (efforts are made to reduce man-virus contact by mosquito proofing of houses with screens on doors/windows) [59,63-65]. Protective clothing and repellents are common means of personal protection against mosquitoes and other biting insects. Household insecticide products, namely, mosquito coils, pyrethrum space spray and aerosols have been used extensively for personal protection against mosquitoes. Biological Control methods are used to control Aedes are Larvivorous fish (are recommended for control of *Aedes aegypti* in large large water containers) and Endotoxin-producing bacteria, Bacillus thuringiensis serotype H-14 (Bt H-14) [60,62,63]. Chemical control measures (larvicides) are recommended in permanent big water containers where water has to be conserved or stored because of scarcity of water or irregular and unreliable water supply. Methods recommended for the control of adult *Aedes aegypti* mosquitoes are Pyrethrum spray and Malathion fogging or Ultra Low Volume (ULV) spray [62]. Therefore, the key to control the Aedes vector borne disease is the adoption of a comprehensive approach by way of regular vector surveillance and integrated management of the Aedes mosquitoes through biological and chemical control that are safe, cost effective; and environmental management, legislations as well as action at household and community levels [62].

Conclusions

Considering the disease burden of all these arboviral infection and their unique vector affinity, global mapping of distribution of Aedes mosquitoes is important to understand population at risk and to develop preventive strategies.

Acknowledgments

We express our gratitude to all who encourage us to write this review article.

References

1. Kraemer MU, Sinka ME, Duda KA, Mylne A, Shearer FM, Brady OJ, et al. The global compendium of Aedes aegypti and Ae. albopictus occurrence. Scientific data. 2015.
2. Kraemer MU, Sinka ME, Duda KA, Mylne AQ, Shearer FM, Barker CM, et al. The global distribution of the arbovirus vectors Aedes aegypti and Aedes albopictus. Elife. 2015; 4: e08347.
3. Powell JR, Tabachnick WJ. History of domestication and spread of Aedes aegypti-A Review. Memorias do Instituto Oswaldo Cruz. 2013; 108: 11-17.
4. Centers for Disease Control and Prevention. Surveillance and control of Aedes aegypti and Aedes albopictus in the United States. 2016; 7: 2016.
5. Ritchie SA. 24 Dengue Vector Bionomics: Why Aedes aegypti is Such a Good Vector. Dengue and Dengue Hemorrhagic Fever. 2014.
6. Tomori O. Yellow fever in Africa: public health impact and prospects for control in the 21st century. Biomedica. 2002; 2: 178-210.
7. Basarab M, Bowman C, Aarons EJ, Cropley I. Zika virus. BMJ. 2016; 26: 352.
8. WHO, Rift Valley fever, Updated October 2016.
9. Kularatne SAM. Dengue fever. BMJ. 2015; 351: h4661.
10. Ralapanawa DMPUK. Kularatne SAM. Current Management of Dengue in Adults: a Review. The International Medical Journal of Malaysia. 2015; 14: 29-42.
11. Kularatne SA, Weerakoon KG, Munasinghe R, Ralapanawa UK, Pathirage M. Trends of fluid requirement in dengue fever and dengue haemorrhagic fever: a single centre experience in Sri Lanka. BMC Research Notes. 2015; 8: 1.
12. Rigau-Pérez JG, Clark GG, Gubler DJ, Reiter P, Sanders EJ, Vorndam AV. Dengue and dengue haemorrhagic fever. The Lancet. 1998; 352: 971-977.
13. Simmons CP, Farrar JJ, van Vinh Chau N, Wills B. Dengue. New England Journal of Medicine. 2012; 366: 1423-1432.
14. Ralapanawa DMPU, Kularatne SAM, Jayalath WATA. Guillain-Barre syndrome following dengue fever and literature review. BMC Research Notes. 2015; 8: 729.
15. Singhi S, Kissoon N, Bansal A. Dengue and dengue hemorrhagic fever: management issues in an intensive care unit. Jornal de Pediatria. 2007; 83: S22-S35.
16. Gupta N, Srivastava S , Jain A, Chaturvedi UC. Dengue in India. Indian J Med Res. 2012; 136: 373-390.

17. World Health Organization. Dengue Guidelines For Diagnosis, Treatment, Prevention And Control. New edition. 2009.

18. Ministry of Health - Sri Lanka. National Guidelines on Management of Dengue Fever & Dengue Haemorrhagic Fever in Adults. 2012.

19. Kalayanarooj S. Clinical manifestations and management of dengue/DHF/DSS. Tropical Medicine and Health. 2011; 39: S83-S87.

20. Heilman JM, de Wolff JF, Beards GM, Basden BJ. Dengue fever: a Wikipedia clinical review. Open Medicine. 2014; 8: 105-115.

21. WHO. Dengue vaccine research. 2017.

22. Staples JE, Breiman RF, Powers AM. Chikungunya fever: an epidemiological review of a re-emerging infectious disease. Clinical Infectious Diseases. 2009; 49: 942-948.

23. Centers for Disease Control and Prevention. Clinical Evaluation & Disease. 2018.

24. Kularatne SAM, Weerasinghe S, Gihan C, Wickramasinghe S, Dharmarathne S, Abeyrathna A, et al. Epidemiology, Clinical Manifestation, and Long-Term Outcomes of a Major Outbreak of Chicungunya in a Hamlet in Sri Lanka, in 2007: A Longitudinal Cohort Study. Journal of Tropical Medicine. 2012.

25. Kularatne SAM, Gihan MC, Weerasinghe SC, Gunasena S. Concurrent outbreaks of Chikungunya and Dengue fever in Kandy, Sri Lanka, 2006-2007: a comparative analysis of clinical and laboratory features. Post Grad Med J. 2009; 85: 342-346.

26. Panning M, Wichmann D, Grywna K, Annan A, Wijesinghe S, Kularatne SAM, et al. No evidence of chikungunya virus and antibodies shortly before the outbreak on Sri Lanka. Med Microbiol Immunol. 2009.

27. WHO. Chikungunya. 2017.

28. WHO. A Global Brief on Vector-Borne Diseases. 2014.

29. World Health Organization. Guidelines on clinical management of chikungunya fever. 2008.

30. Chikungunya Virus. Transfusion. 2009; 49:59S-61S.

31. Swaroop A, Jain A, Kumhar M, Parihar N, Jain S. Chikungunya fever. JIACM. 2007; 8: 164-168.

32. Weaver SC, Osorio JE, Livengood JA, Chen R, Stinchcomb DT. Chikungunya virus and prospects for a vaccine. Expert Review of Vaccines. 2012; 11: 1087-1101.

33. Petersen LR, Jamieson DJ, Powers AM, Honein MA. Zika virus. New England Journal of Medicine. 2016; 374: 1552-1563.

34. Basarab M, Bowman C, Aarons EJ, Cropley I. Zika virus. BMJ. 2016; 352: i1049.

35. Paixão ES, Barreto F, da Glória Teixeira M, da Conceição N, Costa M, Rodrigues LC. History, epidemiology, and clinical manifestations of Zika: a systematic review. American Journal of Public Health. 2016; 106: 606-612.

36. Ralapanawa U. Zika: Next big treat. The KSM Newsletter. 2016.

37. Plourde AR, Bloch EM. A Literature Review of Zika Virus. Emerging Infectious Diseases. 2016.

38. Chibueze EC, Tirado V, da Silva Lopes K, Balogun OO, Takemoto Y, Swa T, et al. Zika virus infection in pregnancy: a systematic review of disease course and complications. Reprod Health. 2017; 14: 28.

39. Atif M, Azeem M, Sarwar MR, Bashir A. Zika virus disease: a current review of the literature. Infection. 2016.

40. Musso D, Gubler DJ. Zika virus. Clin Microbiol Rev. 2016; 29: 487-524.

41. Malone RW, Homan J, Callahan MV, Glasspool-Malone J, Damodaran L, Schneider AD, et al. Zika virus: medical countermeasure development challenges. PLoS Negl Trop Dis. 2016; 10: e0004530.

42. Sampathkumar P, Sanchez JL. Zika Virus in the Americas: A Review for Clinicians. Elsevier. 2016; 91: 514-521.

43. De Carvalho NS, De Carvalho BF, Fugaça CA, Dóris B, Biscaia ES. Zika virus infection during pregnancy and microcephaly occurrence: a review of literature and Brazilian data. The Brazilian Journal of Infectious Diseases. 2016; 20: 282-289.

44. WHO. Laboratory testing for Zika virus infection Interim guidance. 2016.

45. Garske T, Van Kerkhove MD, Yactayo S, Ronveaux O, Lewis RF, Staples JE, et al. Yellow Fever in Africa: estimating the burden of disease and impact of mass vaccination from outbreak and serological data. PLoS Med. 2014; 11: e1001638.

46. WHO. Yellow Fever, Fact sheet. 2016.

47. Tomori O. Yellow fever in Africa: public health impact and prospects for control in the 21st century. Biomedica. 2002; 22: 178-210.

48. Cutts F, Vainio J, World Health Organization. Yellow fever.

49. Wasserman S, Tambyah PA, Lim PL. Yellow fever cases in Asia: primed for an epidemic. International Journal of Infectious Diseases. 2016; 48: 98-103.

50. WHO. Technical Guidelines On Detection And Control Of Epidemic Yellow Fever. 1998.

51. WHO, Yellow fever in Angola. 2016.

52. Karunamoorthi K. Yellow Fever Encephalitis: An Emerging and Resurging Global Public Health Threat in a Changing Environment. INTECH Open Access Publisher. 2013.

53. Reiter P. Yellow fever and dengue: a threat to Europe. Euro Surveill. 2010; 15: 19509.

54. Yellow fever Epidemiology in New Zealand. 2012.

55. Barnett ED. Yellow fever: epidemiology and prevention. Clinical Infectious Diseases. 2007; 44: 850-856.

56. Guidance. Yellow fever. Green Book Chapter. 2014.

57. Barrett AD. Yellow Fever in Angola and Beyond-The Problem of Vaccine Supply and Demand. New England Journal of Medicine. 2016; 375: 301-303.

58. Cetron MS, Marfin AA, Julian KG, Gubler DJ, Sharp DJ, Barwick RS, Weld LH, Chen R, Clover RD, Deseda-Tous J, Marchessault V. Yellow fever vaccine recommendations of the Advisory Committee on Immunization Practices (ACIP), 2002. MMWR Recomm Rep. 2002; 51: 1-11.

59. Lee HL, Rohani A, Khadri MS, Nazni WA, Rozilawati H, Nurulhusna AH, et al. Dengue vector control in Malaysia-challenges and recent advances. Intern Med J Malaysia. 2015; 14: 11-16.

60. WHO. Chapter 5 Vector Surveillance and Control.

61. Baly A, Toledo ME, Vanlerberghe V, Ceballos E, Reyes A, Sanchez I, et al. Cost-effectiveness of a community-based approach intertwined with a vertical Aedes control program. Am J Trop Med Hyg. 2009; 81: 88-93.

62. Guidelines For Integrated Vector Management For Control Of Aedes Mosquito. Directorate General of Health Services, Ministry of Health & Family Welfare, India.

63. Kunst RL. Vector control for Dengue and other mosquito-borne diseases. 2008.

64. Aedes aegypti vector control and prevention measures in the context of Zika, Yellow Fever, Dengue or Chikungunya. WASH Regional Group. 2016.

65. Benelli G. Spread of Zika virus: The key role of mosquito vector control. Asian Pacific Journal of Tropical Biomedicine. 2016; 6: 468-471.