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Dengue: Essence of its Causes, Symptoms and Preventive Measures

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ABSTRACT

One of the most prevalent viral diseases spread by mosquitoes in the world, dengue fever has significant fatality and morbidity rates, particularly in tropical and subtropical areas. *Aedes* is the species of mosquito responsible for transmitting dengue. Numerous variables, including geography, rainfall, temperature, and rapid urbanisation or globalisation, have an impact on the spread of the dengue virus. Clinical signs might range from subtle to severe and even lethal. Over the past few decades, the dengue virus (DENV), which causes dengue fever, has been a serious public health concern. This review highlights convenient way of brief representation to understand the transmission and risk factors associated with the transmission, methods for treatment and preventive measures.

Keywords: Dengue, Transmission, DENV, Treatment

1. Introduction

Over the past few decades, the dengue virus (DENV), which causes dengue fever, has been a serious public health concern. Human dengue infection is frequently unnoticeable, and both endemic and epidemic dengue transmission cycles are well-established worldwide[1]. Dengue is a flavivirus illness spread by mosquitoes that has four related but antigenically distinct dengue viruses (DENVs, serotypes 1-4). Dengue is a disease of public health significance. Since it is most frequently found among underprivileged communities in tropical and subtropical areas, dengue is characterised as a "disease of poverty."[2]. The World Health Organization classifies dengue fever as one of the world's 17 neglected tropical diseases (NTDs). The four DENV serotypes (DENV-1 to DENV-4) can infect people and cause dengue, the most common viral disease spread by mosquitoes[3]. A wide range of clinical symptoms caused by DENV infection are possible, from the relatively mild flu-like condition known as dengue fever (DF) to the potentially fatal dengue shock syndrome (DSS). Fever, nausea, vomiting, rash, aches, and pains are among the symptoms of DF, whereas serious haemorrhage and shock can occur in DSS and, if left untreated, fatality rates as high as 20%[4]. More than 100 nations (mainly in Southeast Asia and South America) have dengue as an endemic disease, and it is quickly spreading to new areas with outbreaks that are becoming more and more severe[5].

Over the past 50 years, dengue fever (DF) and dengue hemorrhagic fever (DHF) have been reemerging and spreading at alarming rates around the world[6]. A small percentage of infections progress to severe illness, with rapid onset of capillary leakage accompanied by bleeding, thrombocytopenia, and liver injury; the majority of dengue infected individuals either have no symptoms or have mild self-limited disease (including fever, headache, retroocular pain, muscle and joint pain, nausea, vomiting, and rash)[2]. There is currently no therapeutic option, thus treatment is only supportive. Fluid replacement is the most common illness management strategy. Early indicators of illness progression to severe disease are desperately needed, in addition to early and correct diagnosis[7]. This review highlights convenient way of representation to understand the transmission and risk factors associated with the transmission, methods for treatment and prevention and control measures.

2. Structure of dengue virus

Dengue virions were discovered to be spherical, with a diameter of around 50 nm, a reasonably smooth surface, a well-organized exterior protein layer on the surface of a lipid bilayer, and an inner nucleocapsid core[8]. Figure 1, Three structural proteins—the capsid (C), membrane (M), and envelope (E)—as well as seven nonstructural proteins—NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5—are present in DENV. The spherical immature and mature particles have an ER-derived outer membrane and E and M proteins, which together form an icosahedral-shaped outer glycoprotein surface. Within the lipid bilayer is an RNA-protein core made up of a positive-sense ssRNA genome and capsid proteins (C). It depends on the conformational variations of M and E proteins at various ambient pH levels for DENV mature and immature states to be infectious or non infectious[9]. When moving through the trans-Golgi network (TGN), the morphological structural shift from immature (spiky) to mature (smooth) takes place, mostly caused by structural alterations in the E molecule[10]. E proteins that are linked to membrane proteins alter their shape in the TGN (low pH) prior to DENV maturation. After maturation, the Pr peptide, which has infectious capabilities, is released from the E protein in the extracellular environment (pH 7.0)[11]. The molecular structures of the non-structural proteins NS1, NS2A, NS4A, and NS44B are comparatively little understood. Through the suppression of complement activation, NS1 aids in viral defence as well as RNA replication[12]. The 50 UTR part (untranslated region), the ORF (open reading frame),

and the 30 UTR region make up the RNA genome. The genome lacks a poly (A) tail at the 30 end and has a type I cap (m7GpppAmp) at the 50 end with a single ORF that encodes a polyprotein.

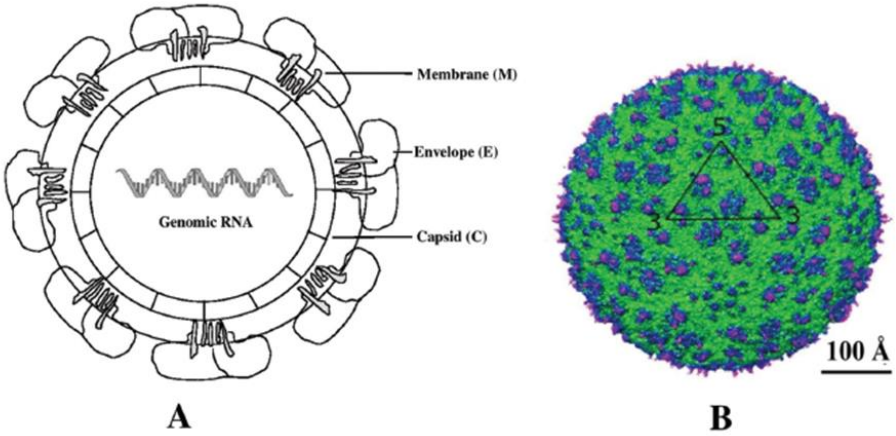

Figure 1 (A) Enveloped and spherical dengue virion with different structural proteins and (B) Cryo-electron Microscopic of the dengue virus DENV-4[13]

3. Causes of dengue fever

The dengue virus can enter our blood and multiply when a mosquito biting someone transmits the disease. The virus can damage blood components that help to create clots and give our blood vessels shape. Internal bleeding may result from this, combined with specific immune system-produced substances, causing blood to flow out of our vessels. This results in the severe dengue symptoms, which can be fatal. Unlike the flu, dengue fever cannot be transmitted from one person to another. Only if a pregnant woman have the disease can contaminate other. If pregnant women get dengue while pregnant or giving delivery, then she could infect her unborn child.

3.1 Transmission

The primary vector of the dengue virus (DENV), which is present in urban centres throughout many tropical and semitropical regions of the world, is the cosmotropical mosquito Aedes aegypti. It is very anthropophilic, feeds on blood, and primarily breeds in stagnant water that may be found in used auto tyres and containers. Importantly, female mosquitoes contribute to the spread of viruses to people[14]. DENV is transmitted in both urban (human transmission cycle) and forested areas (sylvatic transmission cycle). DENV is transmitted between people in urban settings, whereas in forested environments, transmission happens between non-human primates with infrequent spillover into human populations[15]. Due to the complexity of DENV's transmission, eradication is difficult. There have also been reports of non-vector transmission methods such intrapartum and perinatal transmission, bone marrow transplant, and blood transfusion. There is no proof that DENV might be spread by semen like the Zika virus[16-17]. Enhanced globalisation, particularly faster trade and travel, has aided in DENV's quick spread[18]. There is evidence that several DENV genomes have been introduced to the country throughout the years, making Indonesia a continual hub for DENV transmission and mixing. Indonesia has been repeatedly recognised as a source of DENV infection in travellers[19-20]. Aedes albopictus, a mosquito vector that was once only found in Asia, has since taken over the entire world, aiding in the spread of the dengue virus[21-22].

3.2 Risk factor relevent to dengue

The risk factors for dengue transmission include host immunity, vector capacity, circulating DENV, weather or climate, dengue control capability, and population migration. Because of their indirect effects on mosquito life cycles and DENV incubation times within mosquitoes, climatic conditions have an impact on the dengue epidemiology[23]. Both viral and host variables that are still not completely known affect dengue development. Both people with secondary heterotypic DENV infections and newborns born to mothers who have developed primary anti-DENV antibody responses can get severe dengue[24-27]. Open, standing water can serve as a haven for mosquitoes that transmit the dengue virus[28]. The temperature and rainfall affect the spread of mosquito vectors and virus transmission[29]. Studies predict that, in contrast to urban DENV transmission, the sylvatic dengue virus may infect wild animals and have an effect on human health due to cross-species transmission[30].

4. Clinical symptoms of dengue

The clinical spectrum of dengue, a systemic and dynamic disease with mild to severe clinical symptoms, is broad. Following an incubation period, the sickness can typically be divided into three phases: febrile, critical and recovering. During febrile phase patients go through a sudden, high-grade fever that lasts for two to seven days during this phase. Other symptoms include anorexia, nausea, vomiting, sore throat, injected pharynx, conjunctivitis, facial

flushing, skin erythema, body aches, myalgia, arthralgia, headaches, and severe retro-orbital pain[31]. The second crucial stage starts roughly three to seven days after defervescence, or when the fever starts to subside. Defervescence is a brief condition that lasts for about 48 hours and is linked to a higher risk of capillary leakage and haemorrhage[32]. In the subsequent 48–72 hours, extravascular compartment fluid gradually reabsorbs during the last, healing phase[31] The general state of health has improved, the appetite has returned, and the hemodynamic status has stabilised. Chronic symptoms such headaches, pain behind the eyes, sleeplessness, alopecia, myalgia, arthralgia, asthenia, anorexia, dizziness, nausea, and itching are widespread and are linked to changes in certain immunological markers[33]. Typically, younger children and those experiencing their first dengue infection will have a milder illness than older children and adults.

Dengue Shock Syndrome (DSS): DHF with an unstable pulse, a narrow pulse pressure (20 mmHg), restlessness, cold, clammy skin, and circumoral cyanosis is referred to as DSS. Due to disseminated intravascular coagulation and multiple organ dysfunction, patients with DSS have a high death rate. With attentive care, the shock lasts just a short while, and the patients quickly recover from the illness[34].

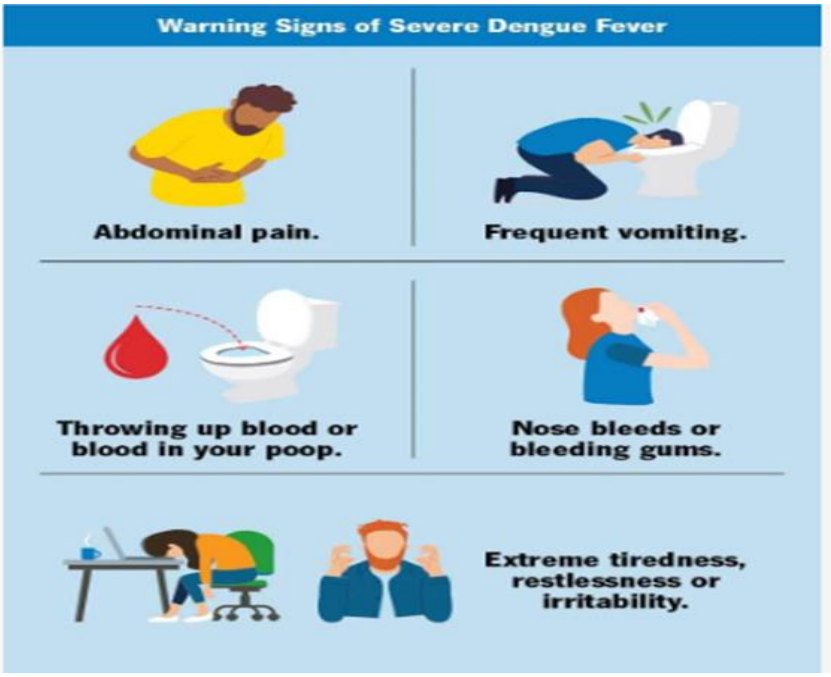

Figure 2: severe signs of dengue (source: google)

5. Treatment & Prevention

In order to save lives through properly executed and timely structured interventions, therapeutic care for dengue illness should be straightforward and inexpensive[35]. There is no specific treatment for dengue fever because it is a virus that must run its course. Treatment for this illness with antibiotics is ineffective. Its symptoms are treated once a person reduces the infection. Painkillers, rest, aspirin-free fever reducers (such acetaminophen), and fluid for rehydration are frequently suggested[36]. The goals of current therapy options are to reduce complication rates and symptom severity. One such essential therapy in the treatment of dengue is fluid therapy. Oral fluid replacement is sufficient for DF (Dengue Fever); however, intravenous fluid replacement for shock avoidance is necessary in cases of severe dengue[37]. Oral prednisolone as an anti-inflammatory drug, carbazochrome sodium sulfonate to stop capillary leakage, lovastatin (statin) as an anti-DENV and anti-inflammatory at the endothelium[38-40].

In small-scale trials, therapies such as single platelet donations or recombinant human (rh) IL-11 have been tested to lessen severe bleeding or speed up the time it takes for bleeding to stop[41-42].

Numerous sulfated polysaccharides derived from seaweeds have been explored in phytomedicine and have demonstrated potent antiviral activity against the dengue virus[43]. Clinical research is currently being conducted to identify the precise antidengue medications[44].

There is no vaccine currently available to prevent dengue fever. Preventing mosquito bites is the primary way to avoid the infection. We can prevent these bites by doing the following is. Spraying mosquito repellant on skin and clothes, wearing long sleeves, long pants, and socks sprayed with mosquito repellant, avoiding being outdoors at dawn and dusk when mosquitoes are most active. Use of pesticides to kill the mosquitoes or the use of repellents to stop them from biting are examples of direct vector control strategies. It is possible to apply indirect vector control techniques by changing the environment, improving cleanliness to eliminate potential larval development sites, or making home renovations to keep mosquitoes out.

6. Conclusion

The most common virus spread by mosquitoes to people is dengue. It is a significant issue for public health in developing nations in Asia and Latin America. Since there is now no very effective vaccine to control the severity of dengue by all serotypes, dengue has evolved into a significant life-threatening burden for humans, and its prevalence has been rising day by day. The best way to protect someone from the dengue virus is unknown. The economic and social repercussions of dengue virus spread by mosquitoes are quite concerning. By performing early diagnosis of high-risk patients and providing appropriate care for severe cases, the morbidity and mortality of dengue and other viral infections spread by mosquitoes can be decreased. An innovative strategy is required for early dengue infection and risk assessment of disease severity.

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