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Review Article

Prevalence, Clinical Manifestation and Mode of Transmission of Dengue Fever

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Abstract

Background: Dengue fever (DF) is a serious flu-like illness affecting individuals (infants, teenagers, adolescents, and adults) of all ages. In humans, it is the most severe acute systemic arthropod-borne viral infection [1,2]. Human transmission occurs via the Aedes aegypti mosquito and occurs primarily during the rainy season.

Aim: In this review, we will look into the prevalence, clinical manifestation, mode of transmission and management of dengue fever.

Conclusion: Educating travelers on mosquito bite prevention by covering exposed skin and using bed nets, mosquito repellents and indoor insecticides is necessary. Mosquito breeding areas should be eradicated, such as standing water. And public consciousness must be raised about the manner in which dengue fever is transmitted by health awareness campaigns.

Keywords: *Dengue Fever; Management of Dengue Fever; Manifestations of Dengue Fever; Mode of Transmission of Dengue Fever*

Introduction

Dengue fever (DF) is a serious flu-like illness affecting individuals (infants, teenagers, adolescents, and adults) of all ages. In humans, it is the most severe acute systemic arthropod-borne viral infection [1,2]. Human transmission occurs via the Aedes aegypti mosquito and occurs primarily during the rainy season [3].

The disease has been known as water poison and has been linked to flying insects. It was reported as global public health issue, spreading to most subtropical parts of the world from tropical regions, leading to human misery and significant socio-economic losses [1,4,5]. Also, it was known as break bone fever owing to the difficulty of muscle twinges and joint pain, dandy fever, or known as seven-day fever due to the usual duration of symptoms [6].

Over 50% of the world's population live in areas where they are at risk of the disease, and nearly 50% live in dengue endemic countries, so it is formerly considered the most sever arboviral disease globally [7,8].

The escalation of dengue as a hazard to health, finance and health services has risen dramatically in the past decade [9]. Bhatt., *et al.* in his research reported that cases of dengue infection increased more than three times per year, with 67 to 136 million cases clinically manifested at any degree of severity annually [10].

Dengue is also believed to be responsible for 20,000 deaths each year [11,12]. In numerous regions, particularly in Asian and Latin American countries, severe dengue has become a leading cause of hospitalization and death among children and adults [13].

The dengue virus, a member of the Flavivirus genus of the Flaviviridae family, comprises four separate serotypes of the dengue virus [14]. Serotypes are mentioned to as DENV-1, DENV-2, DENV-3, and DENV-4, and infection with each of the four viruses is associated with lifelong immunity to that particular serotype [15]. Individually, each of the four serotypes was found to be responsible for dengue epidemics and to be associated with more extreme dengue [16]. Any of the four dengue serotypes, DENV-1 to 4, may cause the disease and its clinical range varies from asymptomatic form to undifferentiated fever to acute fever; hemorrhage, plasma leakage, and organ failure can occur in the most extreme form [17].

DENV is an enclosed virus with a single-stranded, positive-sense 10.7 kilobase RNA genome [18]. The virus reaches target cells after the E protein stick to cell surface receptors in primary DENV infection, such as dendritic cell-specific intercellular adhesion molecule-3-grabbing non-integrin (DC-SIGN) on dendritic cells [19]. Virus genome duplication occurs within the endoplasmic reticulum (ER) in discrete domains. The virus assembly occurs in the ER, and through Golgi-derived secretory vesicles, virions are exocytotic [20].

The Dengue virus achieves entrance through the skin into the host organism after an infected bite of the mosquito. The development of the disease includes humoral, cellular, and innate host immune responses, and the more serious clinical signs arise after the rapid clearance of the virus from the host organism [21].

There is currently no approved antiviral therapy or vaccine in use and the treatment is supportive in nature, patients can rest and use acetaminophen, and it is very necessary to balance fluids and electrolytes [22]. Mosquito control is the primary means of dengue prevention and concerted inter-organizational efforts are needed to control the epidemic [23].

In this review, we will look into the prevalence, clinical manifestation, mode of transmission and management of dengue fever.

Epidemiology

A small number of countries reported extreme dengue epidemics prior to 1970 [24]. However, the disease is now widespread in more than 100 countries in the most severely affected regions of Africa, the Americas, the Eastern Mediterranean, South East Asia and the Western Pacific [25]. The number of cases of dengue infection reported mainly in urban and semi-urban areas has risen in recent years and has thus become a significant universal community health alarm.

With growing regional expansion into new countries and, in the current decade, from urban to rural settings, the incidence has risen 30-fold over the last 50 years. Global figures differ, but about 50 million to 200 million dengue infections, 500,000 extreme dengue (DHF/DSS) episodes, and over 20,000 dengue-associated deaths occur every year [26,27]. It led to approximately 60 million symptomatic infections in 2013 globally, with 18% admitted to hospital and approximately 13,600 deaths [28].

It is clear that dengue is now a global problem, but nearly 75% of the global population exposed to dengue lives in the Asia-Pacific region [29,30]. Twelve countries in Southeast Asia is reported to have about 3 million infections and 6,000 deaths annually for the decade of the 2000s [31]. The Philippines have announced a national dengue epidemic in 2019 because of the deaths that year, reaching 622 people [32].

Almost all countries in the Americas now have hyper-endemicity of indigenous dengue transmission, considering the absence of dengue transmission in the middle of the 20th century [33]. More than 1.6 million dengue cases were registered in the Americas alone in 2010, of which 49,000 were extreme dengue [34].

While dengue is not officially reported by African countries to the WHO and dengue is likely to be under-recognized, evidence indicates that outbreaks in the region are growing in size and frequency [33]. It is recorded in at least 22 African countries, but is likely to be pres-

ent in all countries, with 20% of the population at risk [35]. Four serotypes of the dengue virus have been observed in Africa, but most epidemics tend to have been caused by DENV-2 [35].

In Europe, the last recorded dengue outbreak was in Greece between 1926 and 1928 [33]. In Europe today, there is a very significant and obvious danger of outbreaks of dengue. Imported cases are regularly seen in passengers and local transmission of dengue was recorded in both Croatia and France in 2010 [33,34].

Dengue is known as an emerging disease in the Eastern Mediterranean region; cases have only been officially reported to the WHO for the last 2 decades, during which time there have been several outbreaks in three countries, Saudi Arabia, Pakistan and Yemen [33]. In Pakistan, the main dengue outbreak associated with 21,685 confirmed cases and 350 deaths was recorded in the city of Lahore, mainly due to DENV-2 [36,37].

Clinical manifestation

Infection with the Dengue virus in humans causes a range of diseases from inapparent to moderate febrile disease to serious and lethal hemorrhagic disease. People infected with dengue virus are typically asymptomatic (80%) or have only mild symptoms such as uncomplicated fever, some have more serious disease (5%) and they are life-threatening to a limited degree [38,39]. Incubation cycles range from 3 to 14 days (4 to 7 days on average) [40].

Beginning of symptoms is characterized by a biphasic, high-grade fever lasting for 3 days to 1week, severe headache (mainly retrobulbar), lassitude, myalgia and painful joint, metallic taste, appetite loss, diarrhea, vomiting, and stomachache are the other reported manifestations [41,42].

Dengue is associated with myalgia and pain in joints so, it was referred as break bone fever [43]. Specific cutaneous rash has also been recorded in 50 - 82% of patients which arising from capillary dilatation and presenting as a transient erythema of facial flushing, usually occurring before or within the first 1 - 2 days of fever [44]. Bleeding episodes are rarely seen in DF, while epistaxis and gingival bleeding, substantial menstruation, petechiae/purpura, and gastrointestinal tract (GIT) hemorrhage can occur [41].

Children also have symptoms similar to common cold and gastroenteritis (vomiting and diarrhea) and are at higher risk of serious complications, while initial symptoms are usually mild but include elevated fever [45,46].

Mode of transmission

The numerous serotypes of the dengue virus are spread to humans through the bites of infected *Aedes* mosquitoes, principally *Ae. aegypti*. It is a tropical and subtropical species widely distributed around the world, mostly between latitudes 35°N and 35°S [47]. While another less effective vector Aedes albopictus is also unexpectedly responsible for the spread of this disease in recent years [46].

During daylight hours, the adult mosquitoes feed on humans. There are two peaks of biting activity, 2 to 3 hours after daybreak in the early morning and several hours before dark in the afternoon. During a single blood meal, *Aegyptii* females sometimes feed on multiple individuals, thus increasing the rate of transmission [48]. In order to prevent DENV transmission, protective clothing and mosquito repellent sprays are therefore necessary, as Aedes mosquitoes are active during the day, thus reducing the use of bed nets.

Additionally, Dengue can a be spread by blood products that are contaminated and by organ donation [49]. However, there is evidence that maternal transmission is possible (from a pregnant mother to her baby) [50]. There have also been records of other person-to - person modes of transmission, including sexual transmission, but they are quite unusual [51].

Diagnosis

A conclusive diagnosis of dengue infection can only be made in the laboratory and relies on the isolation of the virus, the detection of serum or tissue viral antigen or RNA, or the detection of particular antibodies in the serum of the patient [52]. As soon as possible after the onset of suspected dengue fever, an acute-phase blood sample should always be taken, and a convalescent-phase sample should preferably be taken 2 to 3 weeks later. Also, on the day of discharge from hospital, a second blood sample should always be obtained from hospitalized patients [53].

Dengue fever-related clinical laboratory findings include neutropenia accompanied by lymphocytosis, frequently characterized by atypical lymphocytes. Thrombocytopenia is also normal in dengue fever; 34% of patients with reported dengue fever who were tested had platelet counts lower than 100,000/mm in the above epidemic [54]. In addition, serum liver enzyme levels may be elevated; the elevation is normally mild, but alanine aminotransferase and aspartate aminotransferase levels exceed 500 to 1,000 U/liter in some patients. In one DEN-4 outbreak, elevated levels were observed in 54% of confirmed patients with data reported on liver enzymes [54].

By virus culture, polymerase chain reaction (PCR), or serological assays, a confirmed diagnosis for a DENV infection is identified. The cultivation of the virus requires an acute patient serum with adequate virus levels, and the timeline for effective isolation of DENV in the patient serum is limited. Virus cultivation is both time- and labor-intensive; infectious patient material must be kept cold, and a level 3 bio-safety laboratory is required, requiring professional staff training. The use of this diagnostic tool, especially in rural areas is restricted by these requirements [55].

Serological diagnosis is accessible more readily. The presence of cross-reactive antigenic determinants shared by all four serotypes of the dengue virus and members of the flavivirus family complicates this [56]. For the diagnosis of dengue infection, five specific serologic tests have been routinely used: hemagglutination-inhibition (HI), complementary fixation (CF), neutralization (NT), immunoglobulin M (IgM) capture enzyme-linked immunosorbent assay (MAC-ELISA) and indirect immunoglobulin G ELISA [52].

HI is the most widely used; it is sensitive, simple to perform, needs only minimal equipment, and, if properly performed, is very reliable [52]. A significant test for the routine diagnosis of dengue is the enzyme-linked immunosorbent assay (ELISA) with a sensitivity and specificity of approximately 90% and 98%, respectively [46]. The first immunoglobulin to manifest is the IgM antibody. Then, at the end of the first week of the disease, IgG antibodies may be measurable and then slowly increase. But, often, even in the acute process, high IgG levels are present [57]. Additionally, the nonstructural protein 1 (NS1) of the dengue viral genome has been shown to be a useful test for the diagnosis of acute dengue infections [46].

RT-PCR is a valued diagnostic tool with high sensitivity and specificity even before dengue-specific antibodies are produced. Generally, molecular methods (nucleic acid detection assays) can usually identify viruses within 24 - 48 hours, but these techniques are costly and require skilled staff [46].

Management

Dengue infection is a disease with complex clinical manifestations; therefore, therapeutic management should be simple, low cost yet effective in saving lives through correctly performed and timely institutionalized interventions [24]. No specific medication is available for dengue infection and no antiviral therapy has demonstrated benefit to date [58]. The recommended treatment after the febrile phase is fluid substitution and antipyretic treatment with paracetamol. Non-steroidal anti-inflammatory drugs such as aspirin or ibuprofen should be avoided due to the fact that these anti-inflammatory drugs work by thinning the blood, and blood thinners can worsen the prognosis in patients at risk of bleeding [46].

In order to preserve organ perfusion during the critical process, sensible and optimal fluid resuscitation is necessary, which simultaneously promotes favorable results [59]. The aim of fluid resuscitation is to stop vein leakage and hypovolemic shock complications [60]. Transfusion of blood products, such as packaged red cells, platelets, or fresh-frozen plasma, can be life-saving in patients with serious bleeding. However, evidence does not justify the use of prophylactic platelet transfusion in patients with serious thrombocytopenic dengue without any sign of a bleeding manifestation [60].

Due to a lack of available care, dengue management currently relies on successful methods of vector control, which are minimal.

Conclusion

Educating travelers on mosquito bite prevention by covering exposed skin and using bed nets, mosquito repellents and indoor insecticides is necessary. Mosquito breeding areas should be eradicated, such as standing water. And public consciousness must be raised about the manner in which dengue fever is transmitted by health awareness campaigns.

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