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Dengue Disease Treatment And Prevention

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Dengue infection ranks highly among new and newly emerging arthropod borne viral diseases affecting humans. It affects a large proportion of the population mainly in tropical and subtropical countries causing high morbidity and mortality due to rising incidence of DHF. The rapidly expanding global footprint of dengue is a public health challenge with a high economic burden. Appropriate management of the burden of dengue is hindered by several issues including lack of understanding of the exact pathophysiology of the disease failure to control the vector population effectively lack of specific treatment for the disease and technical obstacles in developing a vaccine. This review provide an overview on the epidemiology natural history and management strategies of adult dengue patients.

Keywords : types of dengue ,epidemiology,structure , transmission,diagnosis treatment

INTRODUCTION

Dengue (break-bone fever) is a viral infection that spreads from mosquitoes to people. It is more common in tropical and subtropical climates. Most people who get dengue won't have symptoms. But for those that do, the most common symptoms are high fever, headache, body aches, nausea and rash. Dengue is one of the most common mosquito borne disease in India.

It causes a high fever and a rash. Unlike most mosquitoes, dengue causing mosquitoesbites during the day. These mosquitoes breed in warm, humid weather and in stagnantwater. This is why the number of cases of dengue go up high during monsoon season.

Dengue virus are arboviruses capable of infecting human and causing diseases. A Prevalence of Aede. aegypti and Aede. albopictus together with the circulation of dengue virus of more than one type in a particular area tends to be associated with outbreak of dengye hemorrhagic fever and dengue shock syndrome.

The earliest known documentation of dengue fever like illness was in the Chinese Encyclopedia of symptoms in Chin Dynasty The illness was called Water poison and was associated with flying insects near water. Outbreak of febrile illnesses compatible with dengue fever have been recorded throughout history, with first epidemic described in 1635 in West Indies. In 1779-1780 the first confirmed, outbreak reported, almost simultaneously in Asia, North America and Africa. Benjamin Rush coined the term break bone fever to describe the intense symptoms reported by one of his patients. A dengue like epidemic in East Africa in the early 1820 s was called, in Swahili,ki denga pepo(it is a sudden taking over by the spirit). The English version of this term Dandy Fever was applied to an 1827-28 Caribbean outbreak, and in the Spanish Caribbean colonies, the term was altered to dengue

Dengue is an acute fever caused by a virus. It occurs in two form; Dengue fever and Dengue Hemorrhagic Fever. Dengue fever is marked by the onset of sudden high fever, severe headache and pain behind the eyes, muscles and joints.

Dengue Hemorrhagic fever (DHF) is more severe form, in which bleeding and sometimes shock occurs leading to death. It is most serious in children. Symptoms of bleeding usually occur after 3-5 days of fever. The high fever continues for five to six days. It comes down by the third or the fourth day but rises again. The patient feels much discomfort and is very weak after the illness.

Recognition of Dengue Fever includes sudden onset of high fever, pain behind the eyes, nausea or vomiting, sudden headache (mostly in the forehead), body ache and joint pains.

Recognition of Dengue Hemorrhagic fever and Shock includes symptoms similar to Dengue fever,any one of the following: severe and continuous pain in abdomen, frequent vomiting with or without blood, excessive thirst(dry mouth),restlessness or sleepiness, bleeding from the nose, mouth and gums or skinbruising,black stools like coal tar, pale, cold skin.

Dengue mosquitoes bite during the daytime. Protect yourself from the bite by wearing full sleeve clothes, use of repellent, mosquito coils, nets, protection of people sick with dengue.

Prevention of Dengue involves all efforts of control is directed against mosquitoes. It is important to take control measures to eliminate the mosquitoes and their breeding place. Howerver, the efforts should be intensified before the transmission season (during and after the rainy season) and at the time of the epidemic.

Dengue is caused by one of four serotype of this flavivirus (DEN-1, DEN-2, DEN-3 and DEN-4). Dengue virus **603** | 6 0 3 infection tends to be seasonal and can be expected to be highest during a recognized outbreak of dengue infection. Dengue virus affects both the sexes and all age groups. In South East Asia, where dengue is hyper endemic, dengue

hemorrhagic fever usually affects children below 15years of age.

Dengue viruses are transmitted to humans through the bites of infective female Aedes aegypti mosquitoes. In children the most common symptoms are fever, cough and mild gastrointestinal symptoms and a mild running nose. The only method of controlling and preventing dengue and dengue hemorrhagic fever is to combat the vector mosquitoes.

TYPES OF DENGUE

There are three types of Dengue fever-

1. Classical (simple) Dengue Fever

2. Dengue Hemorrhagic Fever (DHF)

3. Dengue Shock Syndrome (DSS)

1. Classical (simple) Dengue Fever

Sudden onset of high fever with feeling of chills.

Severe Headache, Pains in muscles and joints.

Pain behind the eyeball especially on pressing the eyes or on moving the eyeballs. Extreme weakness, Loss of appetite, felling of nausea.

Change in taste sensation in mouth.

Pain in abdomen by itself or on touching.

Mild pain in throat.

Patient feels generally depressed and very sick.

Rash on skin pinkish red appears on the skin in the form of diffuse flushing, mottling or pinhead eruptions on the face, neck and chest. later on, rash become more prominent. The entire duration of classical dengue fever lasts for about 5-7 days and the patient recovers.

2. Dengue Hemorrhagic Fever (DHF)

Dengue hemorrhagic fever is also called as severe dengue. The mosquito borne viral infection dengue ocassionally develops into potential lethal complication called dengue hemorrhagic fever. Dengue Haemorrhagic Fever was first recognized in the 1950s during dengue epidemics in the Philippines and Thailand. Today, severe dengue affects most Asian and Latin American countries and has become a leading cause of hospitalization and death among children and adults in these regions. It has similar features to dengue fever but it may be severe as compared to the former. It usually occurs if a person has had dengue more than once but most of the patients recover quickly if they follow appropriate medical treatment.

3. Dengue Shock Syndrome (DSS)

Shock syndrome is a dangerous complication of dengue infection and is associated with high mortality. he onset of shock in dengue can be dramatic, and its progression relentless. If you are aware of the signs and symptoms of dengue shock syndrome which sets in after dengue hemorrhagic fever, the patient can survive by undergoing proper medical treatment.

EPIDEMIOLOGY

Dengue is one of the most important emerging viral disease of humans in the world afflicting humanity in terms of morbidity and mortality. Currently the diseaseis endemic in all continents except Europe. The Epidemiology of dengue is acomplex phenomenon that mainly depends upon an intricate relationship betweenthe 3 epidemiological factors: the host (man and mosquito), the agent (virus) and the environment (abiotic and biotic factors). The complexity of relationship amongthese factors eventually determines the level of endemicity in an area.

STRUCTURE OF DENGUE

The dengue viruses are the members of the genus flavivirus. These small (50nm) viruses contain single RNA. There are four virus serotypes, which aredesignated as DEN-1, DEN-2, DEN-3 and DEN-4.Although all four serotypes are antigenicaly similar, they are different enough to elicit cross-protection only for a few months after infection by any one of them. Infection with any one serotype confers lifelong immunity to the virus serotype. Man and mosquito are reservoirs of infection. Transovarian transmission (infection carried over to next progeny of mosquitoes through eggs) has made the control more complicated. At present DENI and DEN2 serotypes are widespread in India.

STRUCTURE

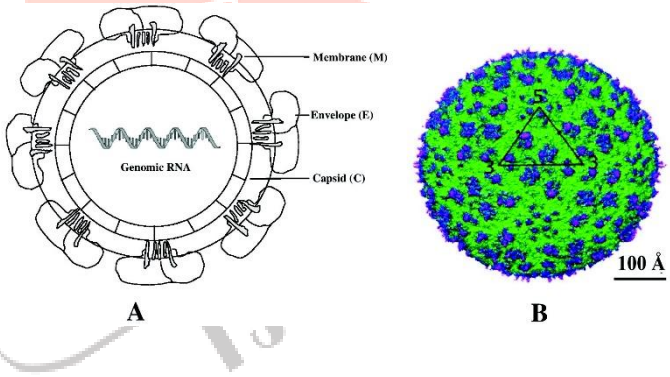

fig. 1. (A) Enveloped and spherical dengue virion with different structural proteins and (B) Cryo-electron Microscopic structure of the dengue virus (DENV-4)

Electron micrographs revealed that dengue virions are spherical and characterized by a relatively smooth surface, with a diameter of approximately 50 nm, a well-organized outer protein layer on the surface of a lipid bilayer, and an inner nucleocapsid core (Kuhn et al. 2002) (Fig. 2A). DENV contains three structural proteins, namely, the capsid (C), membrane (M) (having a membrane precursor or PrM), envelope (E), and seven non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5) (Perera and Kuhn 2008). Table 1 lists the structural and non-structural proteins of DENV and their descriptions.

TRANSMISSION OF DENGUE

Transmission of dengue viruses occur in three cycles:

(1) Enzootic cycle:

A primitive sylvatic cycle maintained by monkey-Aedes-monkey cycle as reported from South Asia and Africa. Viruses are not pathogenic to monkeys and viraemia lasts 2 3 days. 19 All the four dengue serotypes (DENV-1 to -4) have been isolated from monkeys.

(2) Epizootic cycle:

The dengue virus crosses over to non-human primates from adjoining human epidemic cycles by bridge vectors. In Sri Lanka, the epizootic cycle was observed among touqe macaques (Macaca sinica) during 1986 1987 in a study area on a serological basis. Within the study area (three kilometres), 94% macaques were found affected.

(3) Epidemic cycle:

The epidemic cycle is maintained by human-Aedes aegypti-human cycle with periodic/cyclical epidemics. Generally, all serotypes circulate and give rise to hyperendemicity. Ae. aegypti has generally low susceptibility to oral infection but its strong anthrophily with multiple feeding behaviour and highly domesticated habitats makes it an efficient vector. The persistence of dengue virus, therefore, depends on the development of high viral titres in the human host to ensure transmission in mosquitoes.

Transmission of DF/DHF

For transmission to occur the female Ae. aegypti must bite an infected human during the viraemic phase of the illness that manifests two days before the onset of fever and lasts 4 5 days after onset of fever. After ingestion of the infected blood meal the virus replicates in the epithelial cell lining of the midgut and escape.

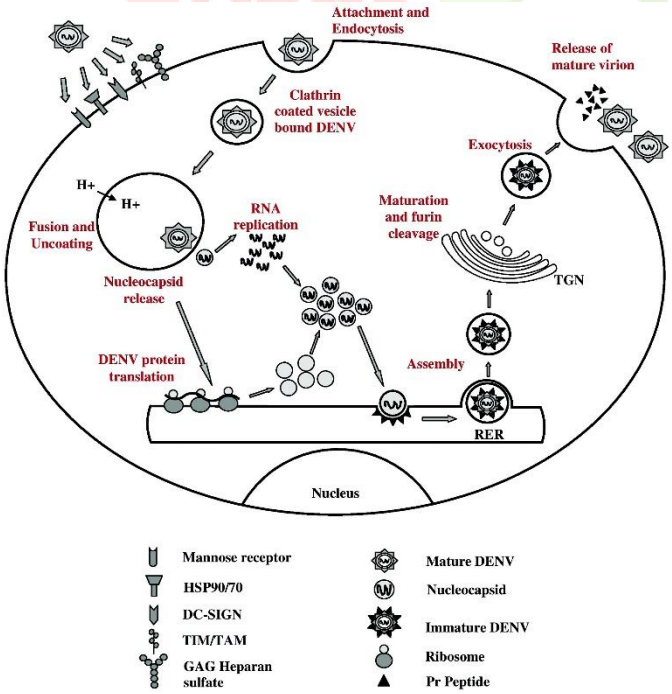

Fig. 2. Step-by-step processes of dengue virus entry in the host cell and its life cycle (adapted from Urcuqui-Inchima et al. 2010; Rodenhuis-Zybert et al. 2010).

Symptoms

- Mild symptoms of dengue can be confused with other illnesses that cause fever, aches and pains, or a rash.

The most common symptom of dengue is **fever** with any of the following:

- Nausea, vomiting
- Rash
- Aches and pains (eye pain, typically behind the eyes, muscle, joint, or bone pain)

Symptoms of dengue typically last 2–7 days. Most people will recover after about a week.

FIG -3

CLINICAL PRESENTATION

The severe forms of disease are defined as a patient that has dengue with one of the following: severe plasma leakage that leads to shock and/or fluid accumulation with respiratory distress; severe bleeding, and severe organ impairment (1) [16]. As noted above, dengue-induced shock occurs at defervescence and at a time when viral levels are falling (), indicating(FIG 4) likely immune-mediated pathology [27]. The hypovolemic shock that occurs is a result of prolonged increased vascular permeability causing plasma leakage [28]. Patients with DSS initially suffer from asymptomatic capillary leakage progressing to compensated shock to hypotensive shock, eventually leading to cardiac arrest [29, 30]. Dengue shock patients need to be closely monitored, as the time between warning signs and the development of compensated shock and hypotensive shock may only be a matter of hours [28]. Only minutes may separate hypotensive shock and cardiorespiratory collapse and cardiac arrest [28]. For a more in-depth review of the clinical presentation of severe dengue and patient management, consult the WHO Handbook for clinical management of dengue [16].

Dengue virus infection can result in either asymptomatic or symptomatic infection [18]. Roughly 20% of all infections are

symptomatic, with individuals experiencing disease symptoms that cover a broad clinical spectrum of nonsevere to severe

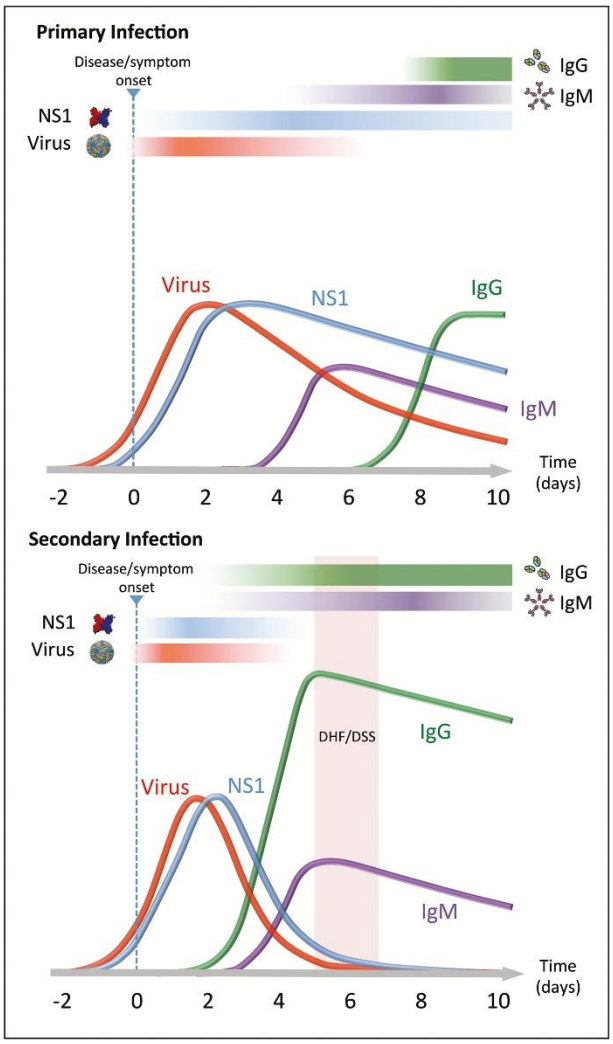

FIG -4

clinical manifestations [19]. Illness caused by dengue has an abrupt onset with 3 broadly identifiable phases: febrile, critical, and recovery [16]. Appropriate viral diagnosis and evaluation of warning signs of progression to severe disease are critical for effective patient management.

The initial febrile phase is characterized by rapid onset, initially with sudden high-grade fever [18]. This phase lasts between 2 and 7 days, with the febrile phase of the disease being characterized by a facial flushing skin erythema, generalized body ache, myalgia, arthralgia, retro-orbital eye pain, photophobia, rubeliform exanthema, and headache [20]. Sore throat, anorexia, nausea, and vomiting are also common [20]. During this phase, a positive tourniquet test is able to differentiate dengue from other diseases presenting with similar symptoms [21]. The acute febrile phase may also be accompanied by hemorrhagic symptoms ranging from a positive tourniquet test and petechiae to spontaneous bleeding from the gastrointestinal tract, nose, gums, and other mucosal sites [16]. The severity of symptoms during this phase is not a predictor of progression to severe dengue; therefore, monitoring of early warning signs needs to be undertaken during the critical phase of disease [16].

Laboratory Diagnosis

Rapid and accurate dengue diagnosis is of paramount importance for: (i) epidemiological surveillance; (ii) clinical management; (iii) research; and (iv) vaccine trials. Epidemiological surveillance requires early determination of dengue virus infection during the outbreak for urgent public health action towards control as well as at sentinel sites for detection of circulating serotypes/genotypes during the inter-epidemic periods for use in forecasting possible outbreaks. Clinical managementrequires early diagnosis of cases, confimation of clinical diagnosis and for

differential diagnosis from other flaviviruses infection agents The following laboratory tests are available to diagnose dengue fever and DHE

-Virus isolation serotypic/genotypic characterization

- Viral nucleic acid detection

- Viral antigen detection

-Immunological response based tests IgM and IgG antibody assays -Analysis for haematological parameters

Diagnostic tests and phases of disease

Dengue viraemia in a patient is short, typically occurs 2 3 days prior to the onset of fever and lasts for four to seven days of illness. During this period the dengue virus, its nucleic acid and circulating viral antigen can be detected. Antibody response to infection comprises the appearance of different types of immunoglobulins; and IgM and IgG immunoglobulin isotypes are of diagnostic value in dengue. IgM antibodies are detectable by days 3 5 after the onset of illness, rise quickly by about two weeks and decline to undetectable levels after 2 3 months. IgG antibodies are detectable at low level by the end of the first week, increase subsequently and remain for a longer period (for

many years). Because of the Inte appearance of IgM antibody, i.e. after five days of onset of fever, serological tests based on this antibody done during the first five days of clinical illness are usually negative. During the secondary dengue infection (when the host has previously been infected by dengue virus), antibody titres rise rapidly. IgG antibodies are detectable at high levels, even in the initial phase, and persist from several months to a lifelong period. IgM antibody levels are significantly lower in secondary infection cases. Hence, a ratio of IgM/IgG is commonly used to differentiate between primary and secondary dengue infections. Thrombocytopenia is usually observed between the third and eighth day of illness followed by other haematocrit changes.

Isolation virus

Isolation of dengue virus from clinical specimens is possible provided the sample is taken during the first six days of illness and processed without delay Specimens that are suitable for virus isolation minclude: acute phase serum, plasma or washed buffy coat from the patient, autopsy tissues from fatal cases (especially liver. spleen, lymph nodes and thymus), and mosquitoes collected from the affected areas. For short periods of storage (up to 48 hours), specimens to be used for virus isolation can be kept at +4 °C to +8 "C. For longer storage the serum should be separated and frozen at 70 °C and maintained at such a temperature that thawing does not occur. If isolation from leucocytes is to be attempted, heparinized blood samples should be delivered to the laboratory within a few hours. Whenever possible, original material (viraemic serum or infected mosquito pools) as well as laboratory-passaged materials should be preserved for future study Tissues and pooled mosquitoes are triturated or sonicated prior to inoculation. Different methods of inoculation and methods of confirming the presence of dengue virus.The choice of methods for isolation and identification of dengue virus will depend on local availability of mosquitoes, cell culture and laboratory capability. Inoculation of serum or plasma into mosquitoes is the most sensitive method of virus isolation, but mosquito cell culture is the most cost-effective method for routine virological surveillance. It is essential for health workers interested in making a diagnosis by means of virus isolation to contact the appropriate virology laboratory prior to the collection of specimens. The acquisition, storage and shipment of the samples can then be organized to have the best chances of successful isolation.

Reverse transcriptase-polymerase chain reaction (RT-PCR)

In recent years, a number of RT-PCR assays have been reported for detecting dengue virus. They offer better specificity and sensitivity compared with virus isolation with a much more rapid turnaround time. A BSL2 laboratory with equipment for molecular biology and skilled professionals are needed to carry out this test. All nucleic acid detection assays involve three basic steps: (1) nucleic acid extraction and purification; (ii) amplification of the nucleic acid, and (ii) detection of the amplified product. False positive results can occur, and this can be prevented by proper isolation.

Viral antigen detection

The NS1 gene product is a glycoprotein produced by all flaviviruses and is essential for replication and viability of the virus. The protein is secreted by mammalian cells but not by insect cells. NS1 antigen appears as early as Day 1 after the onset of the fever and declines to undetectable levels by 5 6 days. Hence, tests based on this antigen can be used for early diagnosis.ELISA and dot blot assays directed against the envelop/membrane (EM) antigens and nonstructural protein 1 (NS1) demonstrated that this antigen is present in high concentrations in the sera of the dengue virus- infected patients during the early clinical phase of the disease and can be detected in both patients with primary and secondary dengue infections.

IgM-capture enzyme-linked immunosorbent assay (MAC-ELISA)

MAC-ELISA has become widely used in the past few years. It is a simple and rapid test that requires very little sophisticated equipment. MAC-ELISA is based on detecting the dengue-specific IgM antibodies in the test serum by capturing them out of solution using anti-human IgM that was previously bound to the solid phase. If the patient s serum has antidengue IgM antibody, it will bind the dengue antigen that is added in the next step and can be detected by subsequent addition of an enzyme- labelled anti-dengue antibody, which may be human or monoclonal antibody. An enzyme-substrate is added to produce a colour reaction.

IgG-ELISA

An indirect IgG-ELISA has been developed and compares well with the HI test. This test can also be used to differentiate primary and secondary dengue infections. The test is simple and easy to perform, and is thus useful for high-volume testing. The IgG-ELISA is very non-specific and exhibits the same broad cross-reactivity among flaviviruses as the HI test; it cannot be used to identify the infecting dengue serotype. These tests can be used independently or in combination, depending upon the type of the sample and test available in order to confirm the diagnosis

Treatment

No specific treatment for dengue fever exists

While recovering from dengue fever, drink plenty of fluids. Call your doctor right away if you have any of the following signs and symptoms of dehydration:

Decreased urination

Few or no tears

Dry mouth or lips

Lethargy or confusion

Cold or clammy extremities

The over-the-counter (OTC) drug acetaminophen (Tylenol, others) can help reduce muscle pain and fever. But if you have dengue fever, you should avoid other OTC pain relievers, including aspirin, ibuprofen (Advil, Motrin IB, others) and naproxen sodium (Aleve). These pain relievers can increase the risk of dengue fever bleeding complications.

If you have severe dengue fever, you may need:

Supportive care in a hospital

Intravenous (IV) fluid and electrolyte replacement

Blood pressure monitoring

Transfusion to replace blood loss

Carica papaya leaf extract used in treatment of dengue

Carica papaya leaves have been used in folk medicine for centuries. In addition to the nutritional value of its fruit, the leaves of C. papaya possess medicinal properties and are widely used in traditional medicines. This study was conducted to determine the effect of C. papaya leaves extract capsules (CPC) in acute febrile illness with thrombocytopenia. An observational. prospective, uncontrolled, open label. single centre study in Indian patients. Total 80 patients were enrolled in the study. These subjects were randomized into two groups of 40, including the control and intervention groups (received two CPC three times daily). The result showed that CPC had significant increased the platelet count ($p<0.05$) and maintained stability of hematocrit in the normal level. Carica papaya leaf extract could be used as an additional or as a complementary drug in acute febrile illness patients with thrombocytopenia; it accelerates the increase in the platelet count and shorten the hospitalization thereby reducing the cost of hospitalization significantly

Prevention

In May 2019Trusted Source, the FDA approved the first dengue vaccine. It can prevent dengue caused by all four viruses.

It is for people who:are ages 9–16 years

have had dengue in the past

live in areas where dengue is common, including Puerto Rico, American Samoa, Guam, and the U.S. Virgin Islands

People who are not eligible for the vaccine can lower their risk by taking steps to avoid mosquito bites.

Tips include

wearing clothes that cover the body

using mosquito repellents on the body

using mosquito nets

using window and door screens

treating camping gear or clothes with insect repellent before Alvarez D.E., De Lella Ezcurra A.L., Fucito S., Gamarnik A.V. Role of RNA structures present at the 3′ UTR of dengue virus on translation, RNA synthesis, and viral replication. Virology. 2005;339(2):200–212. doi: 10.1016/j.virol.2005.06.009. [PubMed] [CrossRef] [Google Scholar]use

if possible, avoiding being outside at dawn, dusk, and early evening

remove any stagnant water around the home and avoid camping near still water

check that drains, plant pots, and other features are not collecting water

CONCLUSION

There is no specific treatment for the dengue diseases in medical field but carica papaya leaf e .xtract used in treatment of dengue. Dengue disease continues to involve newer areas, newer populations and is increasing in magnitude.epidemic after epidemic. Every aspect of dengue viral infection continues to be a challenge; the pathogenesis of severe dengue disease is not known, no vaccine is yet available for protection and the vector control measures are inadequate. Dengue virus was isolated in India in 1944, but the scientific studies addressing various problems of dengue disease have been carried out at limited number of centres. Though clinical studies have reported on dengue disease in India, but these are largely based on diagnosis made by kits ofdoubtful specificity and sensitivity. A lot more remains to be achieved for creating an impact.

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