

Dengue and its serotypes: A comprehensive review of epidemiology, clinical features and prevention strategies.

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ABSTRACT:- Dengue fever is a viral disease transmitted by Aedes mosquitoes, Aedes aegypti being the most common. This disease is enzootic in tropical and subtropical areas and is a major global public health problem. This review offers an all-encompassing view of the dengue virus, covering transmission, clinical manifestations, diagnosis, therapy, prevention, and epidemiology of the disease. Furthermore, we have discussed the pathophysiology, possible complications of the disease and the latest developments in the field. Vaccine development.

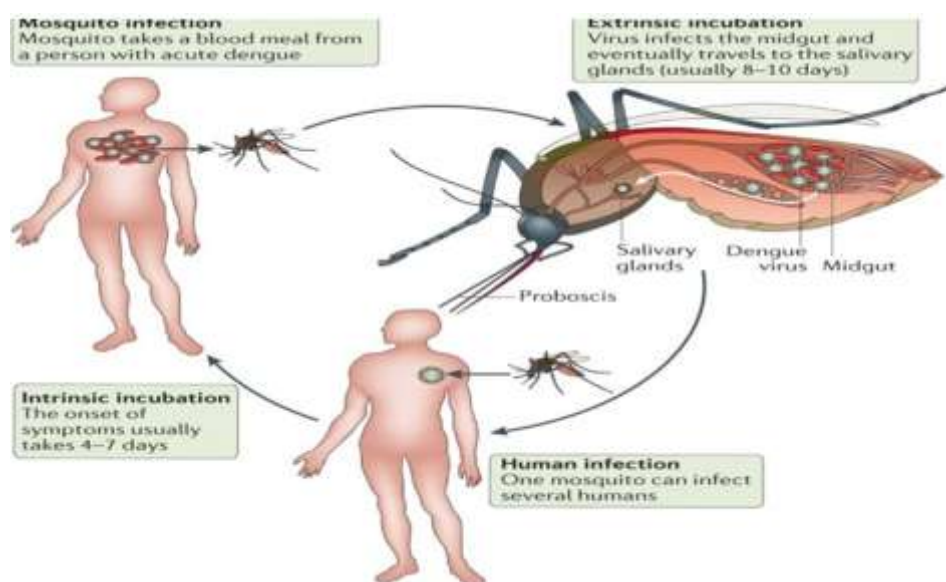
Keywords: Dengue virus, dengv-1, dengv-2, dengv-3, dengv-4, dengue hemorrhagic fever (dhf), dengue shock syndrome (dss), antibody-dependent enhancement (ade), Aedes Aegyptus, Aedes albopictus, ns1 antigen, Dengvaxia vaccine, flavivirus, epidemiology, prevention strategies.

I. INTRODUCTION:-

Dengue fever, transmitted by the dengue virus (denv), is one of the most widespread mosquito-borne viral diseases worldwide. The virus comes in four different forms of serotypes: dengv-1, dengv-2, dengv-3, and dengv-4. This virus is spread by Aedes aegypti mosquitoes, the main vectors of this virus, in tropical and subtropical areas, resulting in numerous outbreaks in many countries. This illness has its symptoms; they include high fever, severe pain, and rash; and in the worst cases, it can lead to fatal diseases, including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS.).

• Clinical Features:-

The incubation period for dengue typically spans 4 to 10 days following exposure to an infected mosquito.



• **Pathophysiology :-**

The dengue virus, for instance, has a preference for immune cells such as monocytes, In macrophages the and severe dendritic forms increased of cells, vascular the which permeability disease, enables and the the resulting immune virus in response to bleeding may travel and lead in plasma to the leakage. A bloodstream. This cytokine plasma storm leakage that is the causes a

evolution crucial of factor dengue in hemorrhagic fever (DHF) and dengue shock syndrome (DSS).

Type of dengue virus:-

- **Denv-1**
- **Denv-2**
- **Denv-3**
- **Denv-4**

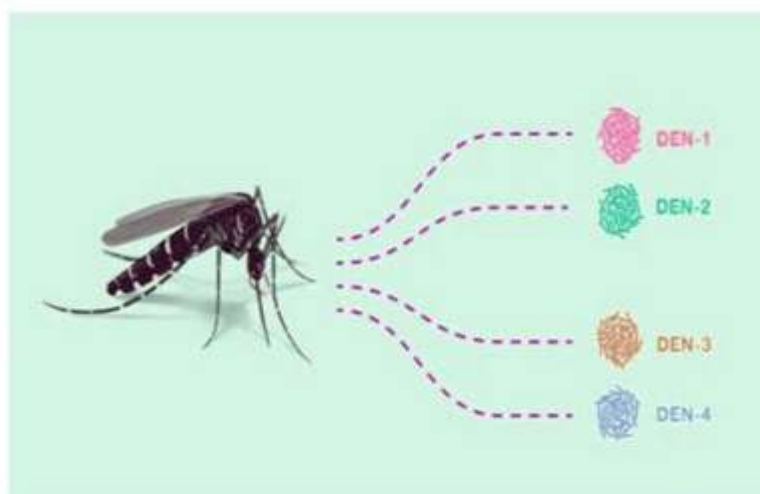


Figure 2 : Serotypes of Dengue Virus

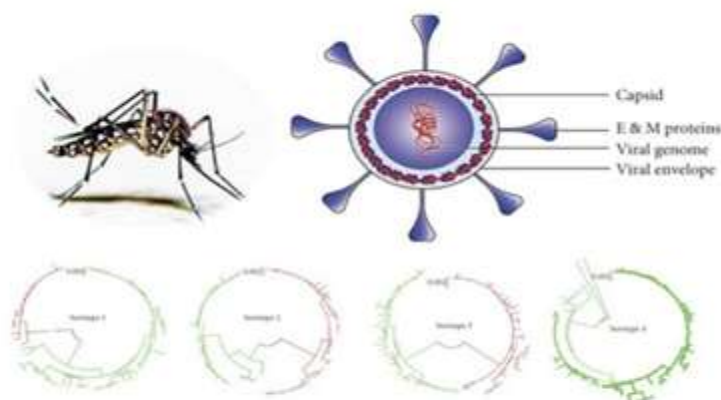


Diagram with dengue virus and its four serotypes.

1)DENV -1(dengue virus serotype-1):-

Denv-1 refers to dengue virus serotype 1, one of the four serotypes of the dengue virus. The dengue virus unequivocally consists of four distinct serotypes: denv-1, denv-2, denv-3, and denv-4. This mosquito-borne flavivirus is primarily

transmitted through Aedes aegypti and Aedes albopictus mosquitoes.

Key points about DENV-1:

1. **Genome:** It is a single-stranded positive-sense RNA virus that belongs to the Flaviviridae family.
2. **Symptoms:** The symptoms of Dengue infection are clearly defined and include fever, headache, retro-orbital pain, muscle and joint pain—commonly known as “break bone fever”—rash, and mild bleeding tendencies. In severe instances, it can lead to dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS).
3. **Immunity:** An infection with DENV-1 provides lifelong immunity solely to this serotype. However, it is critical to understand that it does not provide immunity against the other serotypes (denv-2, denv-3, denv-4). This lack of cross-protection can lead to severe dengue during secondary infections due to antibody-dependent enhancement (ADE).

4. Epidemiology:

DENV-1 is widespread and holds a significant presence globally, especially in tropical and subtropical regions. The prevalence of specific serotypes distinctly varies across different geographic areas and over time, with the majority of cases occurring in Southeast Asia, the western Pacific, the Americas, and Africa. Dengue is firmly endemic in these regions, underscoring its substantial impact on global health. Especially in tropical and subtropical regions. The prevalence of specific serotypes distinctly varies across different geographic areas and over time, with the majority of cases occurring in Southeast Asia, the western Pacific, the Americas, and Africa. Dengue is firmly endemic in these regions, underscoring its substantial impact on global health. Especially in tropical and subtropical regions. The prevalence of specific serotypes distinctly varies across different geographic areas and over time, with the majority of cases occurring in Southeast Asia, the western Pacific, the Americas, and Africa. Dengue is firmly endemic in these regions, underscoring its substantial impact on global health. Over 100 countries report endemic dengue, with around dengue fever poses significant public health challenges worldwide, with approximately 390 million infections reported annually, of which around 96 million manifest as symptomatic cases. To effectively combat this issue, targeted interventions are especially important in high-risk areas, such as urban and semi-urban regions that are characterized by dense populations and limited

vector control measures. The dengue virus (denv) comprises four distinct serotypes: denv-1, denv-2, denv-3, and denv-4. The primary vectors for its transmission are the *Aedes aegypti* and *Aedes albopictus* mosquitoes.

5. Climatic and Seasonal considerations:

Understanding the relationship between environmental conditions and dengue outbreaks is vital for prevention efforts. The virus tends to thrive in climates with high humidity and elevated temperatures, leading to a noticeable increase in cases during and after the rainy season when mosquito breeding conditions are optimal.

6. Understanding Stereotypes:

The geographical distribution of the different DENV serotypes changes over time, presenting both challenges and opportunities for public health strategies. Notably, DENV-2 has been associated with more severe disease manifestations, while DENV-4 is less frequently linked to severe outcomes. By monitoring these variations, public health officials can better tailor their response efforts and resources to effectively manage and mitigate the impact of dengue fever. Dengue fever, especially related to DENV-1, highlights the importance of understanding its prevalence and patterns to inform effective public health strategies. By focusing on these aspects, we can enhance our interventions and better manage the impact of dengue on communities. Ineffective strategies for prevention and management.

7. Affected Age Groups:

While children have historically faced the highest rates of dengue infection, recent trends reveal a growing incidence among adolescents and adults. This shift underscores the need for targeted awareness campaigns and educational efforts to address immunity changes across age groups.

8. Urbanization and Globalization:

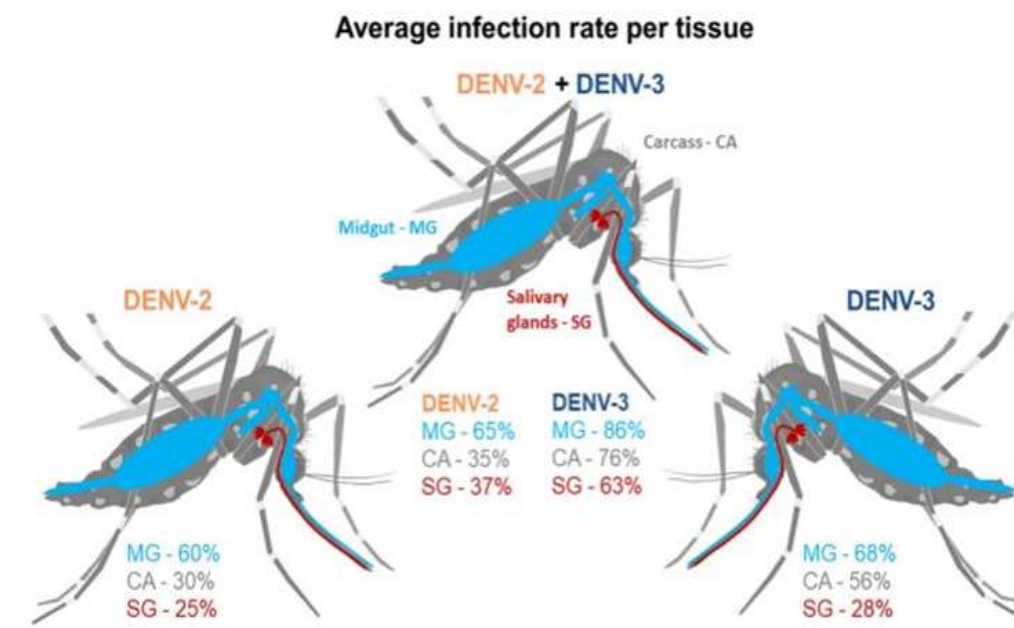
The rapid pace of urbanization creates conditions that support mosquito breeding, facilitating the spread of dengue. Additionally, the increase in global travel introduces the virus to new regions, including parts of Europe and the USA. By implementing effective public health measures and community engagement, we can mitigate these risks and enhance resilience against outbreaks.

9. Outbreak patterns:

Dengue outbreaks typically follow a cyclic pattern, marked by severe epidemics that

occur periodically. Proactively raising awareness and improving preparedness within communities

are essential steps to effectively manage these outbreaks and reduce their impact.



2) DENV-2 (dengue virus serotype2):-

Key points about DENV-2:

- 1. Genome:** DENV-2 is a single-stranded positive-sense RNA virus that belongs to the flaviviridae family.
- 2. Symptoms:** The symptoms of DENV-2 infection include fever, headache, retro-orbital pain, and muscle and joint pain, often referred to as "break bone fever." Other manifestations can include rash and mild bleeding tendencies.
- 3. Immunity:** Infection with DENV-2 provides lifelong immunity to this serotype. However, it's essential to note that this immunity does not extend to DENV-1, DENV-3, or DENV-4. This lack of cross-protection significantly elevates the risk of severe dengue during subsequent infections due to the phenomenon known as antibody-dependent enhancement (ADE).
- 4. Epidemiology:** DENV-2 is prevalent and makes a notable impact globally, especially in tropidengue, which is a significant viral infection frequently found in tropical and subtropical regions. The prevalence of specific serotypes varies across different geographic areas and evolves over time. Most cases arise in Southeast Asia, the Western Pacific, the Americas, and Africa, where dengue has become endemic. This situation presents an important opportunity for enhanced global

health initiatives aimed at effectively addressing and mitigating the impacts of dengue.

- 5. Diagnosis And Management:** To improve diagnosis and management, the NS1 antigen test serves as a valuable tool by detecting viral proteins during early infections. Additionally, RT-PCR is crucial for confirming both the presence of the virus and its serotype. Serological testing also plays a critical role: igm indicates early infections, while igg helps identify secondary infections.

When it comes to clinical indicators, patients typically present with fever accompanied by warning signs such as abdominal pain and persistent vomiting.

In terms of epidemiological impact, dengue is widespread, especially in Asia, South America, and Africa. This highlights the need for collaborative public health efforts. By working together on strategies to combat dengue, we can make significant progress in protecting communities around the world. Major outbreaks in countries like India, Thailand, Brazil, and Sri Lanka suggest opportunities for enhanced surveillance and intervention strategies.

- 6. Severe outbreaks:** The Asian genotype of DENV-2 has been a key factor in notable

outbreaks, especially in Cuba (1981) and India (1996). Understanding the cyclical nature of DENV-2 outbreaks, which tend to recur every 3–5 years, can help in planning proactive measures and resource allocation.

7. Management strategies: Treatment: The management of dengue largely depends on supportive care, which includes fluid replacement, effective fever control, and careful monitoring for complications. Although there is no specific antiviral therapy available, these supportive measures are crucial for patient recovery.

8. Prevention: Addressing vector control is vital in strengthening prevention initiatives against the dengue virus. The Dengvaxia vaccine has shown effectiveness for seropositive individuals; therefore, adhering to specific eligibility criteria will enhance its safe and successful implementation in at-risk populations.

3) Denv-3 (dengue virus serotype 3):

DENV-3 is one of the four identified dengue virus serotypes and presents unique health challenges. Acknowledging its potential impact opens pathways for targeted research and community education, which are essential for managing dengue outbreaks effectively. Its high mutation rate allows it to adapt effectively, making it an important focus for public health initiatives.

Key characteristics:

- 1) Genetics:** DENV-3 is an RNA virus within the flaviviridae family. It shows considerable genetic variability, resulting in multiple genotypes (i–v).
- 2) Transmission:** The virus is primarily spread through *Aedes aegypti* and *Aedes albopictus* mosquitoes, highlighting the importance of vector control strategies.
- 3) Epidemiology:** DENV-3 often contributes to large-scale outbreaks, leading to serious health outcomes. Its re-emergence in regions where it was previously less dominant calls for renewed vigilance and strategy adjustments.
- 4) Virulence:** The virus can lead to secondary infections, some of which may result in severe manifestations like dengue hemorrhagic fever (DHF) and dengue shock syndrome. This underscores the need for effective monitoring and response systems to mitigate its impact on health. By focusing on these aspects, we can

develop more effective interventions and strategies to combat the challenges posed by DENV-3 (DSS). Its high mutation rate significantly enhances its adaptability and pathogenicity.

5) Clinical features:

- 1). Primary infection:** symptoms include high fever, retro-orbital pain, rash, joint and muscle pain, and mild bleeding.
- 2). Secondary infection:** There is an increased risk of DHF/DSS due to antibody-dependent enhancement (ADE). Severe symptoms may involve plasma leakage, thrombocytopenia, hypotension, and organ dysfunction.

6) Diagnosis:

Laboratory tests:

1) NS1 antigen test: This test is crucial for the early detection of infection.

2) RT-PCR: This method confirms the serotype and verifies the presence of the virus, providing vital diagnostic clarity.

7) Serology: The detection of IgM and IgG antibodies confirms the stage of the infection, allowing for informed clinical decisions.

8) Clinical indicators: Warning signs: Persistent vomiting, abdominal pain, and mucosal bleeding are critical indicators that guide the suspicion of severe dengue.

9) Epidemiological impact:

1) Global distribution: Dengue is prevalent in tropical and subtropical regions, with significant outbreaks reported in India, Brazil, Sri Lanka, and the Philippines.

2) Severe outbreaks: The DENV-3 serotype has played a substantial role in severe dengue cases, particularly noted in Sri Lanka (1989) and South America (2002).

3) Re-emergence: This virus often resurfaces after long absences, resulting in serotype shifts and more severe epidemics, which require vigilant public health strategies.

10) Management:

- **Treatment:** Supportive care is paramount, emphasizing hydration, fever control, and careful monitoring for shock. Currently, there is no specific antiviral therapy available.

- **Prevention:** Effective vector control is crucial; this includes eliminating mosquito breeding sites, utilizing repellents, and enhancing public awareness. Additionally, the Dengvaxia

vaccine may provide protection for individuals previously exposed, though it is not universally applicable across all serotypes.

4) DENV-4 (dengue virus serotype ;

1) Characteristics:

DENV-4 is an RNA virus that belongs to the flaviviridae family. It is transmitted by the *Aedes aegypti* and *Aedes albopictus* mosquitoes. Though it is the least prevalent among the four dengue serotypes, it has the potential to cause significant outbreaks.

2) Epidemiology:

DENV-4 is primarily found in tropical and subtropical regions. While it is less frequently implicated in outbreaks compared to DENV-1, DENV-2, and DENV-3, notable outbreaks have occurred in Brazil, India, and Southeast Asia. Re-emergence in areas with low immunity can lead to severe epidemics, underscoring the importance of monitoring.

3) Clinical features:

The symptoms of DENV-4 include fever, headache, retro-orbital pain, myalgia, rash, and mild bleeding. Primary infections are usually mild; however, secondary infections pose a higher risk of developing dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS) due to antibody-dependent enhancement (ADE). Severe symptoms

may include plasma leakage, thrombocytopenia, hypotension, and organ dysfunction.

4) Diagnosis:

Early detection of DENV-4 is achieved via the NS1 antigen test. Confirmation of the serotype is done through RT-PCR, while serology tests for IgM and IgG antibodies help in staging the infection.

5) Warning signs to monitor:

Be vigilant for warning signs such as persistent vomiting, severe abdominal pain, and mucosal bleeding, as these may indicate a severe progression of the disease.

6) Prognosis:

The majority of dengue cases are mild and respond well to supportive care. However, severe dengue, including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), can be life-threatening without prompt treatment. Early detection and appropriate medical management are essential for enhancing patient outcomes.

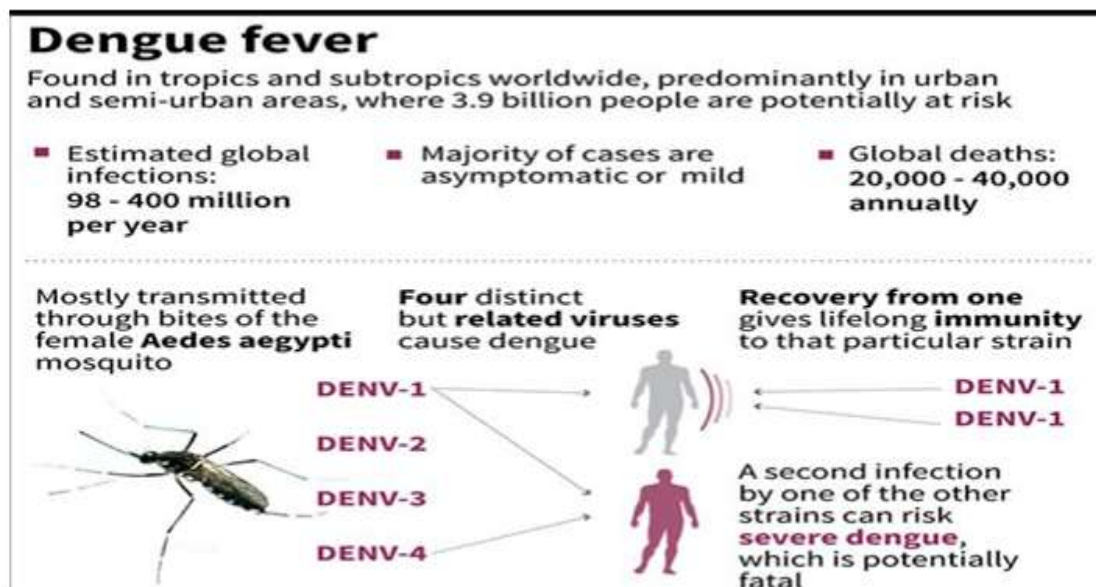
Treatment for Dengue Fever and Its Serotypes

1. General Supportive Care:

Hydration:

Oral rehydration for mild cases.

Intravenous fluids for severe cases with plasma leakage or hypotension.



2. Fever and Pain Management: Use (Acetaminophen) for fever and pain.

Avoid NSAIDs and Aspirin due to increased bleeding risk.

3. Monitoring:

Regularly monitor vital signs, hematocrit, and platelet counts.

Look for warning signs such as severe abdominal pain, persistent vomiting, mucosal bleeding, or rapid breathing.

4. Severe Dengue Management:

Administer intravenous fluids for plasma leakage and hemodynamic stability.

Provide blood transfusions for severe bleeding or thrombocytopenia.

Use oxygen therapy in cases of respiratory distress.

5. Prevention of Complications:

Hospitalize patients with severe symptoms for close monitoring.

Promptly manage symptoms to prevent progression to DHF or DSS.

Preventive Strategies

Eliminate mosquito breeding grounds and stagnant water.

Use insect repellents, mosquito nets, and protective clothing.

6. Vaccination:

Dengue vaccines are designed to target the four serotypes of the dengue virus (DEN-1, DEN-2, DEN-3, and DEN-4). The most widely used vaccine is Dengvaxia, developed by Sanofi Pasteur.

- **Dengvaxia:**

It is a live-attenuated vaccine, meaning it contains weakened versions of all four dengue serotypes.

It is administered in three doses, spaced 6 months apart.

Recommended for individuals aged 9–45 years who have had a prior dengue infection, as it has shown increased risk of severe dengue in those who have never been infected before.

It provides better protection against DEN-2, DEN-3, and DEN-4 but less effectiveness against DEN-1.

- **Other vaccines:** There are several vaccines under research or in limited use, such as the TAK-003 vaccine by Takeda, which also targets all four serotypes and has shown promising results in clinical trials.

7. Community Awareness:

Educate on symptom recognition, early treatment, and personal protection.

- **Community Engagement and Education:**

Local Health Campaigns: Organize community meetings, street plays, and health talks in neighborhoods to inform people about dengue prevention.

School Programs: Educate children in schools about dengue and involve them in spreading the message at home. Schools can distribute educational materials like posters, leaflets, and pamphlets.

Health Workers and Volunteers: Train local health workers and volunteers to engage with community members, explain preventive measures, and distribute awareness materials.

Social Media Campaigns: Leverage social media platforms to spread awareness, share prevention tips, and remind people to take preventive actions. Use local influencers and community groups for wider reach.

II. RESULTS:

The review underscores the complexity of dengue as a significant global health challenge, driven by four distinct serotypes: dengv-1, dengv-2, dengv-3, and dengv-4. Each serotype plays a critical role in the overall disease burden, with DENV-2 and DENV-3 often linked to severe outbreaks, while DENV-4, though less prevalent, has the potential to trigger significant epidemics. The interaction among these serotypes heightens the risk of severe disease, making awareness and preventive measures paramount, antibody-dependent enhancement (ADE), particularly during secondary infections.

The study emphasizes the need for early diagnosis using tools like NS1 antigen tests and RT-PCR, as well as the importance of recognizing warning signs to prevent complications. Supportive care remains the cornerstone of management, as no specific antiviral treatment is available. Preventive strategies, including vector control and vaccination with Dengvaxia, are crucial, though limitations in vaccine applicability highlight the need for continued research.

Globally, urbanization, climate change, and increased travel contribute to the rising incidence of dengue, requiring integrated and sustainable public health strategies. Enhanced surveillance, education, and advancements in diagnostic and therapeutic options are essential to

reduce the disease burden and control its spread effectively.

III. CONCLUSION:-

Dengue fever remains a significant health concern in many tropical and subtropical countries. While there is no specific antiviral treatment, early diagnosis and supportive care significantly improve patient outcomes. Vector control and preventive measures, such as vaccination and personal protection, are key to reducing the incidence and spread of the disease. In conclusion, dengue remains a significant global health concern, driven by the complex interplay of its four serotypes (denv-1 to denv-4), increasing urbanization, climate change, and global travel. Each serotype poses unique challenges, with denv-2 and denv-3 often linked to severe cases, while denv-1 and denv-4 also contribute to outbreaks and disease burden. The risk of severe dengue during secondary infections underscores the need for robust surveillance and early diagnosis. Utilizing tools such as NS1 antigen tests and RT-PCR is vital for managing dengue. While supportive care remains the foundation of treatment, proactive measures like vector control and targeted vaccination—specifically Dengvaxia for seropositive individuals—are essential. The absence of a universal vaccine and specific antiviral therapies underscores the critical need for continued research in this area. Comprehensive efforts that integrate public health strategies, community involvement, and scientific advancements are imperative to reduce disease burden and prevent future outbreaks.

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