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**Abstract:**

Dengue hemorrhagic fever is the second most common mosquito-borne diseases after Malaria. Dengue is one of the leading cause of death and morbidity in children dwelling in Southeast part of Asia, Africa and parts of South America. It is a viral infection caused by the vector mosquito *Aedes aegypti* commonly found breeding in contaminated waters thus seen surfacing during the rainy season. It is a debilitating form of disease if not diagnosed earlier may increase the chance of fatality. Dengue features the

classical triad consisting of fever, muscle/joint pain and skin rash, oral findings are fairly less common and include mucosal bleeding and other minor manifestations. Although oral findings are secondary to general finding, they may serve as an early indicator for dengue fever. A detailed description of oral features seen in dengue is lacking in the literature. Thus this review attempts to find the significance of oral manifestation presented with dengue fever by analyzing various clinical scenarios found

in literature and bring about a cohesive review article on this matter thereby providing information for the dental practitioner to aid in the early detection of this insidious condition.

**Keywords:** Dengue fever, oral manifestation, mucosal bleeding, candidiasis.

## INTRODUCTION

Dengue fever (DF) or Dengue hemorrhagic fever (DHF) is viral infection transmitted by the mosquito *Aedes aegypti* characterized mainly by high fever and severe thrombocytopenia. Dengue fever has emerged as a serious global threat with almost half of the world's population at risk for infection.<sup>[1]</sup> It does not show much age variation or gender predilection. Some evidence suggests that risk for disease, with different serotypes, varies by age; however, the relationships have never been strongly quantified.<sup>[2]</sup> Although adults are more likely

than young children to have clinical dengue and some studies show a male predominance.<sup>[3]</sup> Most people infected with dengue viruses commonly develop dengue fever (DF), the signs and symptoms of which include high fever, myalgia, arthralgia, severe headache, retro-orbital pain and maculopapular rash. Some patients sometimes develop non-specific symptoms, such as nausea, vomiting, cough, dizziness, and diarrhea.<sup>[4]</sup>

Oral manifestations of dengue infection have commonly been described by most clinical guidelines as gingival bleeding and included by the WHO as an unspecific finding of the disease.<sup>[5]</sup>

## ETIOPATHOGENESIS:

The dengue virus belongs to the genus Flavivirus of the Flaviviridae family with 4 serotypes of the dengue virus (DENV1-4).<sup>[6]</sup> Various theories have been formulated for the cause of dengue infection such as

replication of the virus occurring primarily in the macrophages<sup>[7]</sup> and skin infection directly by the virus during blood meal.<sup>[8]</sup> Infection by any of viruses is thought to confer lifelong immunity against variants of the same serotype, but only partial and transient cross-protection against infections caused by other serotypes.<sup>[9, 10]</sup>

Flow chart 1 depicts etiopathogenesis of dengue fever.<sup>[7,8,9]</sup> The immune pathogenic events of dengue infection are usually related to disruptions in endothelium leading to micro vascular permeability and coagulatory mechanisms, leading to an increased rate of vascular leakage and edema. It has been postulated that endothelial cell activation caused by monocytes, T-cells, the complement system, and various inflammatory molecules mediate plasma leakage, which is linked with useful rather than damaging effects on endothelial cells. Thrombocytopenia may be associated with alterations in megakaryocytopoiesis,

elicited by the infection of human hematopoietic cells and impaired progenitor cell growth, which result in platelet dysfunction, destruction, or consumption, leading to significant hemorrhages.<sup>[11, 12]</sup>

### CLINICAL FEATURES

According to World Health Organization, the dengue virus (DENV) causes three clinical syndromes:

- Dengue fever
- Dengue hemorrhagic fever
- Dengue shock syndrome<sup>[13]</sup>

The disease is characterized by:

- Sudden onset of fever
- Frontal headache
- Muscle and joint pain and
- Skin rashes<sup>[14]</sup>

Mild phase: Includes fever, generalized pain, nausea, vomiting and occasionally petechiae  
<sup>[15, 16]</sup>

Severe phase: After the resolution of fever, there is fluid accumulation in the chest, abdominal cavity as well as decreased blood supply to vital organs <sup>[16]</sup>

Dengue viral infection may result in illness varying from a mild undifferentiated fever to severe life-threatening forms. There are four classifications of dengue:

- Undifferentiated febrile illness or viral syndrome
- Classic dengue fever(DF)
- Dengue hemorrhagic fever (DHF)
- Dengue shock syndrome (DSS)

**Undifferentiated Fever:**

This frequently follows a primary infection but can also occur during the initial phase of a secondary infection.

**Classic Dengue Fever:**

The symptoms usually start with a sudden onset of high fever lasting for 4-8 days.

- Intense headache
- Retro-orbital pain

- Fatigue
- Muscle and joint pain,
- Loss of appetite unpleasant metallic taste in mouth,
- Vomiting, diarrhea, and abdominal pain.

Manifestations of the skin commonly occur as rashes on the face, extremities and spread to the trunk.

In few patients, a severe erythematous prototype with islands of normal skin is seen as macular, papular rash.

The other features, which could be present, are minor epistaxis or bleeding gums, heavy menstrual periods, petechiae, and gastrointestinal bleeding.

Several individuals with DF have been reported with a positive tourniquet test.

**Dengue Hemorrhagic Fever:**

Generally follows a secondary infection. It is characterized by:

- Pyrexia
- Hemorrhagic phenomena

- Hepatomegaly and features of circulatory failure.

The clinical progression of DHF is alienated into three stages:

- Febrile stage
- Leakage stage
- Convalescent stages.

Bleeding manifestations and rashes appear in the initial febrile stage. The fever persists for 2-7 days and then falls to usual or subnormal levels when the patient recuperates or progresses to plasma leakage stage. Patients remain ill, despite normalization of temperature. In severe cases with high plasma leakage, frank shock is apparent with low pulse pressure cyanosis, hepatomegaly, pleural effusions, pericardial effusion and ascites and in some cases a severe ecchymosis and gastrointestinal bleeding followed by epistaxis. During convalescence period, decreased heart rate and confluent petechial rashes, erythema and pallor are seen. The threatening stage in DHF is signs

of circulatory failure and hemorrhagic tendencies. Hematological investigations usually show platelet count,  $\leq 100,000/\text{mm}^3$  as an evidence of a vascular leak syndrome.

#### **Dengue shock syndrome:**

Is defined as DHF associated with:

- weak rapid pulse
- narrow pulse pressure ( $< 20 \text{ mmHg}$ )
- cold, clammy skin
- restlessness
- circumoral cyanosis
- high mortality

Patients with DSS die due to progressively worsening shock and multi-organ failure and disseminated intravascular coagulation. The phase of shock is transient, and the patient promptly recuperates with right supportive therapy<sup>[17, 18]</sup>.

#### **ORAL MANIFESTATIONS**

Oral lesions are seen to involve in approximately 15-30%<sup>[19]</sup> and seen more in patients with the DHF variety.

Oral mucosal manifestations that are considered to be prominent in dengue includes:

- Spontaneous gingival hemorrhage
- Petechiae, purpura, ecchymosis
- Vesicles involving the soft palate
- Erythema and crusting of lips
- Brown color plaques with a rough surface on the buccal mucosa<sup>[20]</sup>
- Xerostomia<sup>[21]</sup>
- Oral candidiasis(pseudomembranous type)
- Hemorrhage can also occur in the Sub-lingual, tongue and tonsillar area
- Hematomas in lips, palate tongue.

#### **Some of the reported clinical scenarios of oral manifestations in dengue:**

An 18-year-old male complaining of an asymptomatic, reddish lesion on the anterior portion of the maxilla that had been present for 1 week. Intraoral examination revealed the existence of a

huge, painless, soft, reddish swelling in the anterior upper gingival and lip resembling a hematoma, as well as small maculopapular lesions in the lower lip and left cheek mucosa that impaired adequate oral functions and hygiene<sup>[21]</sup>.

A 29-year-old woman was diagnosed with dengue. Intraoral examination revealed several white plaques located on the soft palate. The clinical diagnosis was pseudo-membranous candidiasis<sup>[22]</sup>.

A middle-aged female patient had sought our consultation for blisters in her mouth, bleeding gums, and difficulty in swallowing for the past 1 week. Intraoral examination revealed the presence of raised hemorrhagic plaques both on the right and left buccal mucosa as well as on the dorsum of the tongue near the tip<sup>[23]</sup>.

A study from South Asia investigated 104 children diagnosed with Dengue infection, who were admitted during period of three

months and the clinical findings showed that oral/or pharyngeal candidiasis was reported in 19 patients<sup>[24]</sup>.

## INVESTIGATIONS

Laboratory diagnosis:

Confirmation of dengue infection is by serology or detection by virus isolation and by reverse transcriptase polymerase chain reaction. The timing of clinical course plays a major role in the Laboratory diagnosis of dengue

Serological diagnosis:

Basic serologic tests such as:

- Hemagglutination-inhibition
- Complement fixation test
- Neutralization test
- Immunoglobulin M capture enzyme-linked immunosorbent assay
- ELISA.

Serologic diagnosis depends upon the increase in the titer of specific antibodies

between acute- and convalescent-phase serum samples.

Viral serotypes:

Reverse transcriptase-polymerase chain reaction (RT-PCR) provides a rapid serotype-specific diagnosis.

This method:

- Rapid
- Sensitive
- Simple
- Reproducible [<sup>18, 25</sup>].

## MANAGEMENT

- Fever is usually treated with paracetamol
- Sponging is helpful in the early phase of infection
- Oral fluids given to the patients are increased, and in the presence of dehydration, intravenous fluids should be administered with follow-up hematocrit and platelet counts
- Patients with signs of circulatory compromise should immediately receive rapid volume replacement with

10-20 ml/kg/hour of crystalloid solution. If no improvements noted, oxygen should be administered, and the crystalloid solution should be replaced with colloid (if hematocrit rising) or blood (if hematocrit falls).

- In the management of severe case blood transfusion may be necessary. <sup>[18]</sup>

## CONCLUSION

Literature has viewed Dengue to be a serious health condition which had resulted in countless epidemics. This progressively emerging disease has taken over the globe causing morbidity and mortality worldwide. In India Dengue becomes a primary concern especially after the monsoon. Oral health is the index of general health implying the need for both Dentist and General physician to know their significance. Oral manifestation may be rare in Dengue but seem to play a significant role in early diagnosis. Improper knowledge of oral

presentation of dengue can lead to misdiagnosis or delayed diagnosis of this condition. Thus to accentuate accurate diagnosis of such diseases the gravity of oral manifestation needs to be remembered.

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