

## Original Article

## MUCOCUTANEOUS MANIFESTATIONS OF DENGUE VIRAL INFECTION DURING 2011 EPIDEMIC IN LAHORE, PAKISTAN

Muhammad Azam Bokhari, Muhammad Ashfaq and Shama Ahmed

**Objective:** To investigate the type and correlate the appearance of mucocutaneous signs and symptoms with different stages and clinical types of Dengue viral infection.

**Material & Methods:** Two hundred patients of dengue virus infection admitted in the dedicated Dengue Unit at Services Hospital, Lahore from 1st September to 31st October 2011 were included in the study. Presenting features were noted. The patients were physically examined for the presence of skin and mucosal lesions and findings were recorded. Serologic tests for anti-dengue immunoglobulin M (IgM) antibodies, Total and Differential Leukocyte Count (TLC and DLC), Platelet count and Liver Function Tests (LFTs) were done in all the patients.

**Results:** Of the 200 patients with dengue infection, 83 (41.5%) were classified as dengue fever (DF), 116 (58%) as dengue hemorrhagic fever (DHF) and one (0.5%) as dengue shock syndrome (DSS). Cutaneous involvement was seen in 160 (80%) of patients. Of these 160 patients, 130 (81.25%) had single while 30 (18.75%) had multiple manifestations. The most common cutaneous finding was pruritis (47.50%), followed by erythema (37.50%), flushing (23.35%), ecchymosis (18.13%), petechiae (16.88%), and macular/scarlatiniform eruption (13.7%). Mucosal involvement was seen in 35.63% of patient, with dry tongue/ cracked lips being the most common (39.7%), followed by mucosal bleed (36.6%), and conjunctival involvement (10.2%). The most common initial presentation was flushing (27 patients) within 1-3 days followed by mucosal involvement (47 patients) during 4-6 days and cracked lips (30 patients) in 7-10 days. Cutaneous involvement was more common in DF (41.5%) while mucosal involvement was more remarkable in DHF (58%).

**Conclusion:** This study describes the variety of mucocutaneous features associated with dengue viral infection which may evolve during the course of the disease. There is a clear correlation between various skin manifestations & stages of infection. Cutaneous signs & symptoms are more commonly observed in DF & mucosal involvement in DHF.

**Key Words:** Dengue fever, Skin lesion, erythema, petechiae.

### Introduction

The word 'dengue' is derived from the Swahili phrase "Ka-dinga pepo", meaning "cramp like seizure caused by an evil spirit".<sup>1</sup> The first record of probable dengue fever is in a Chinese medical encyclopedia from the Jin Dynasty (265-420 AD) which referred to a "water poison" associated with flying insects.<sup>2</sup> The first recognized Dengue epidemics occurred almost simultaneously in Asia, Africa, and North America in the 1780s, shortly after the identification and naming of the disease in 1779. The first confirmed case report dates from 1789 and is by Benjamin Rush, who coined the term "breakbone fever" because of the symptoms of myalgia and arthralgia.<sup>3</sup>

The global prevalence of DF has grown dramatically in recent decades; it is now endemic in more than 100 countries. DHF, a potentially lethal complication of dengue virus infection, was first recognized in Asia in the 1950s and is now a leading cause of

hospital-ization and death among children.<sup>4</sup> During the past decade, DHF epidemics have occurred in China, Sri Lanka, India, the Maldives, Bangladesh and Pakistan.<sup>5</sup> Dengue fever has a growing incidence in Pakistan nowadays.<sup>6</sup> Pakistan experienced the first major outbreak of Dengue in 1994 and the serotype identified was DENV-2.<sup>5</sup> In 2006, largest and severe outbreak of DHF occurred due to serotypes DENV-2 and DENV-3.<sup>7</sup>

DF is an acute febrile infectious disease caused by dengue virus.<sup>8</sup> There are four serotypes, referred to as DENV-1, DENV-2, DENV-3 and DENV-4.<sup>9</sup> Infection with any of the four serotypes can lead to a broad clinical spectrum, ranging from classical dengue fever to a severe, sometimes fatal disease, known as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).<sup>8</sup> Infection with one serotype produces lifelong immunity to it but only short-term protection against other serotypes.<sup>2</sup>

Dengue virus is primarily transmitted by female *Aedes* mosquitoes, particularly *A. aegypti*.<sup>8</sup> Other *Aedes* species that transmit the disease include *A. albopictus*, *A. polynesiensis* and *A. Scutellaris*.<sup>9</sup> Humans are the primary host of the virus. An infection can be acquired via a single bite.<sup>8</sup> A female mosquito, that takes a blood meal from a person infected with dengue fever, becomes itself infected with the virus in the cells lining its gut. About 8-10 days later, the virus spreads to other tissues including the mosquito's salivary glands and is subsequently released into its saliva. The virus seems to have no detrimental effect on the mosquito, which remains infected for rest of its life.<sup>9</sup> *Aedes aegypti* prefers to lay its eggs in artificial water containers, to live in close proximity to humans, and feed on them rather than other vertebrates.<sup>10</sup>

There are three main types of dengue infection: Classical dengue fever, Dengue hemorrhagic fever and Dengue Shock syndrome. The characteristic symptoms of dengue are sudden-onset fever, headache (typically located behind the eyes), muscle and joint pains, and a rash.<sup>11</sup> The classic dengue fever lasts about 6-7 days, with a smaller peak of fever at the trailing end of the disease (the so-called "biphasic pattern"). Most people have a complete recovery without any complication.<sup>12</sup>

Dengue haemorrhagic fever (DHF) usually occurs during a second dengue infection in persons with preexisting actively or passively (maternally) acquired immunity to a heterologous dengue virus serotype. Increased vascular permeability, bleeding & possible Disseminated Intravascular Coagulation (DIC) may be mediated by circulating dengue antigen-antibody complexes, activation of complement, and release of vasoactive amines. In the process of immune elimination of infected cells, proteases and lympho-kines may be released and activate complement coagulation cascades and vascular permeability factors. Cases of Dengue haemorrhagic fever (DHF) also show higher fever, haemorrhagic phenomena, thrombocytopenia and haemoconcentration. A small proportion of cases lead to Dengue Shock Syndrome (DSS), which has a high mortality rate.<sup>13</sup>

Skin lesions are common presenting features of dengue fever and can, at times, be diagnostic. The characteristic combination of fever, rash and headache is called the "dengue triad".<sup>14</sup> The characteristic exanthem of dengue fever occurs in 50% to 82% of patients with DF.<sup>15</sup> The initial rash involves a flushing erythema of face, neck and chest that typically occurs within first 24 to 48 hours of the

onset of symptoms.<sup>16</sup> It is thought to be the result of capillary dilatation. The subsequent rash, seen 3 to 5 days later is characterized by a generalized morbilliform eruption with petechiae and islands of sparing "white islands in a sea of red" and is thought to be an immune response to virus.<sup>17</sup> Some petechiae can appear at this point, as may mild bleeding from the mucous membranes of the mouth and nose.<sup>18</sup>

Skin lesions are common presenting features of dengue fever and can, at times, be diagnostic. General practitioners and other non-dermatologists require a clear understanding of the various types of skin lesions seen in cases of dengue fever.<sup>19</sup> The aim of this study was to determine the frequency and types of mucocutaneous lesions in cases of dengue fever and correlate their appearance with different stages and clinical types of Dengue viral infection.

## Material & Methods

Two hundred cases of dengue viral infection admitted in the dedicated Dengue Unit at Services Hospital, Lahore from 1st September to 31st October were included in the study. Presenting features were noted. The patients were physically examined for the presence of skin and mucosal lesions and findings were recorded. Serologic tests for anti-dengue immunoglobulin M (IgM) antibodies, Total and Differential Leukocyte Count (TLC and DLC), Platelet count and Liver Function Tests (LFTs) were done in all the patients. All ages and both genders were included. The patients with negative serology were excluded. The patients who had other acute or chronic concurrent ailments along with dengue fever were also excluded. The data of the patients including age, gender and duration of illness was recorded. Data analysis was performed through SPSS version 12.0. Categorical variables such as skin lesions were presented as percentages. As it was a case series study so no inferential test was applied.

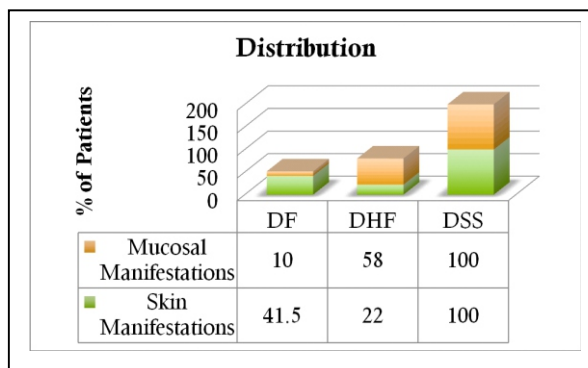
## Results

Two hundred admitted cases of dengue fever with positive IgM serology for dengue virus were seen for the presence of skin and mucosal lesions. 146 (73%) were males and 54 (27%) were females. The youngest patient was 14 years and the oldest was 70 years old. In all those patients, the total leukocyte and platelet counts were found to be lower than the normal range. The Total Leukocyte Counts (TLC) ranged from  $1.2 \times 10^9/L$  to  $3.8 \times 10^9/L$  (normal range  $4-11 \times 10^9/L$ ). The platelet counts ranged from  $16 \times 10^9/L$

Out of 200 patients 83 had Dengue Fever, 116 suffered from DHF and 1 had Dengue Shock Syndrome. 160 (80%) patients had skin lesions, whereas 40 (20%) cases did not have any skin lesions during the course of illness. Of these 160 patients, 130 (81.25%) presented with multiple manifestations while 30 (18.75%) suffered from single manifestation. The most common cutaneous presentation was pruritis seen in 76 (47.50%) patients. Pruritis was generalized in 20.5% and localized in 27% cases. Erythema was seen in 60 (37.50%) patients. Other cutaneous manifestations included flushing (23.35%), ecchymosis (18.13%), petechiae (16.88%), macular/scarlatiniform eruption (13.7%) and urticaria (3.7%). Mucosal involvement was seen in 35.63% of patients, with dry tongue/ cracked lips being the most common (39.7%). Mucosal bleeding was observed in 36.6%. Nose bleed occurred in 19.4% followed by gum involvement in 15% and conjunctival involvement in 10.2%. Herpes simplex virus infection was seen in 18.7% while candidiasis was seen in 12.5% of cases. The frequency of mucocutaneous features in various forms of disease is shown in **Table I**.

With respect to stage of infection, the most common initial presentation was flushing (27 patients) within 1-3 days followed by mucosal involvement (47 patients) during 4-6 days and cracked lips (30 patients) in 7-10 days. The distribution of mucocutaneous manifestations with respect to duration of disease is shown in **figure I & II**.

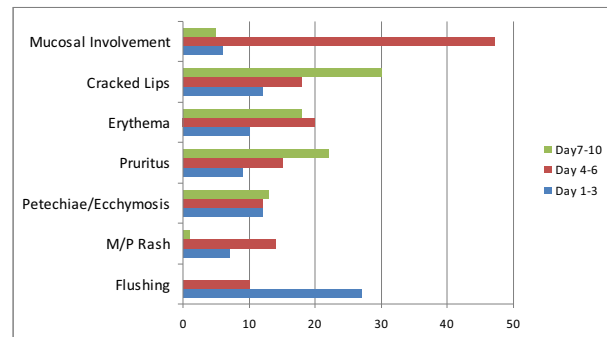
**Table-1:** Mucocutaneous manifestations in various forms of illness.



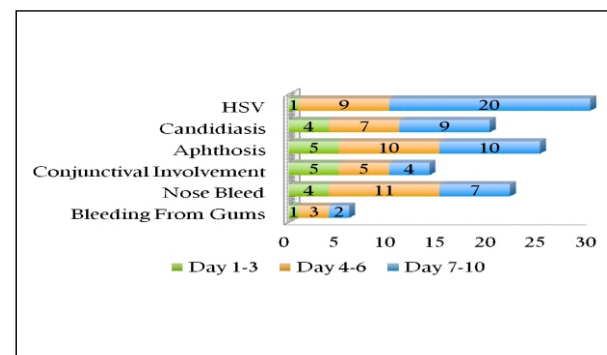
**Discussion**

Dengue fever (DF) is one of the major health hazards, that has erupted in Pakistan within the last few years and has caused loss of lives of many young people.<sup>20</sup> DF usually starts suddenly with a

high fever, malaise, headache, facial flushing, retrobulbar pain,



**Fig-I:** Skin manifestations in relation to stages of infection.



**Fig-II:** Mucosal manifestations in relation to stages of infection.

conjunctival suffusion and severe backache. The illness can last up to 10 days, but complete recovery can take as long as a month. Older children and adults are usually more sick than young children.<sup>21</sup> In some people, the disease proceeds to a critical phase, which follows the resolution of high fever and typically lasts one to two days. During this phase, organ dysfunction and severe bleeding, typically from the gastrointestinal tract, may occur.<sup>4</sup> Shock (dengue shock syndrome) and hemorrhage (dengue hemorrhagic fever) occur in less than 5% of all cases of dengue. However those who have previously been infected with other serotypes of dengue virus (“secondary infection”) are at an increased risk.<sup>22</sup> In this study, majority of cases (80%) had skin lesions as one of the presenting features. This signifies cutaneous manifestations as one of the common presenting features of dengue fever. The most frequent skin presentation seen was pruritis which usually started on 1<sup>st</sup> to 3<sup>rd</sup> day of fever. Pruritis in DF can be either localized to palms and soles or generalized. Blanchable erythema mostly localized to palms was also seen in a considerable number of cases. It was on 5<sup>th</sup> to 7<sup>th</sup> day of illness in majority.

low. The maculopapular/scarlatiniform rash was seen in 13.7% patients. This rash probably occurs when the virus enters the bloodstream. The presence of the virus within the blood vessels, especially in cutaneous blood vessels, causes vasodilatation and increased capillary permeability resulting in generalized blanchable erythema. Mucosal involvement was also observed with most frequent symptom being dryness of lips or tongue. This symptom was observed on 7<sup>th</sup> to 10<sup>th</sup> day of illness in majority of cases. Mucosal bleeding was also seen especially in those who developed DHF. Nose bleeding was more frequent followed by gum bleed and conjunctival hemorrhage. All of these patients had thrombocytopenia. Overall, cutaneous involvement was more in DF while mucosal involvement was predominant in DHF.

## Conclusion

This study describes the variety of cutaneous features associated with dengue viral infection which may evolve during the course of the disease. As a significant proportion of patients showed cutaneous features, these manifestations, together with simple laboratory tests, will be helpful in the early diagnosis of dengue viral infection. There is a clear correlation between various skin manifestations & stages of infection. Cutaneous signs & symptoms are more commonly observed in DF & mucosal involvement in DHF.

*Department of Dermatology  
Services Institute of Medical Sciences, Lahore*  
**theesculapio@hotmail.com**  
**www.sims.edu.pk/esculapio.html**

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