Clinical Profile of Muco-Cutaneous Lesions in Dengue Fever in Children at a Tertiary Care Hospital

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Abstract

Background: Dengue is arthropod borne viruses, they use mosquitoes as vector. Aedes Albopictus although could be a suitable vector, the Aedes aegypti work as the most efficient carrier, vectors also serve to amplify viral replication. The frequency of Dengue and its complications has increased over the past few years, especially in rural area. Dengue has a wide spectrum of clinical presentation, unpredictable clinical evolution and outcome, especially in children. Subjects and Methods: The study was conducted over a period of two years on Dengue cases in Paediatrics department of Medical College and Research Hospital. Children with fever of acute onset, with clinical features suggestive of Dengue fever as described in WHO 2012 Guidelines. Children with age less than 18 years, admitted as Dengue fever based on clinical features as described in WHO 2012 Guidelines and positive Ns1Ag and/or Dengue IgM. Results: Dengue fever had fewer mucosal manifestations compared to cutaneous manifestations. 144 cases had mucosal manifestations. Scleral Congestion/Conjunctival Haemorrhage was the most common manifestation seen in 69 cases (47.92%), followed by Erythema and Crusting of Lips and Tongue (31.94%), vesicles on soft palate or throat congestion (29.86%) and Palatal Haemorrhage and Gingival bleeding (11.80%). Conclusion: Flushing is the most common cutaneous manifestation in our study followed by macular rash, petechiae and pruritus. Flushing is an early feature occurring around day 2 of illness, whereas, pruritus is a late manifestation, occurring around day 5 of illness. Thus, Dengue should be strongly considered in any child presenting with fever and flushing.

Keywords: Muco-cutaneous lesions, Dengue fever, Children.

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Introduction

Dengue disease is an acute infectious disease caused by four serotypes of dengue virus, and is the most prevalent mosquito-borne viral disease in humans, occurring in tropical and subtropical countries of the world where over 2.5 billion people are at risk of infection. The World Health Organization has estimated 50 million cases of dengue fever and several hundred thousand cases of dengue haemorrhagic fever occur each year, depending on the epidemic activity. Some 1.8 billion of the population at risk for dengue worldwide live in member states of the WHO South-East Asia Region and Western Pacific Region, which bear nearly 75% of the current global disease burden due to dengue. Four related yet antigenically distinct viruses belonging to Flaviviridae family cause dengue illnesses. Infection with one dengue serotype provides lifelong immunity to that particular virus, but other serotypes have no cross protective immunity. Humans and mosquitoes are the principal hosts of dengue virus. Dengue is arthropod borne viruses, they use mosquitoes as vector. Aedes Albopictus although could be a suitable vector, the Aedes aegypti work as the most efficient carrier, vectors also serve to amplify viral replication. The frequency of Dengue and its complications has increased over the past few years, especially in rural area. Dengue has a wide spectrum of clinical presentation, unpredictable clinical evolution and outcome, especially in children. Early prediction of Dengue infection during any febrile illness, using clinical and laboratory markers, is essential for initiating early appropriate management. Muco-cutaneous manifestations may be the presenting feature of dengue fever. It needs to be differentiated from other infectious and non-infectious causes of fever with rash. Hence, a clear understanding of muco-cutaneous manifestations may help in the clinical diagnosis of dengue fever and institution of early appropriate management. Until now only a very few studies are available regarding the spectrum of muco-cutaneous features of dengue fever in children.

Subjects and Methods

Study Design
Hospital based Prospective Observational study.

Source of Data
The study was conducted over a period of two years on Dengue cases in Paediatrics department of Medical College and Research Hospital.

**Study Population**
Children with fever of acute onset, with clinical features suggestive of Dengue fever as described in WHO 2012 Guidelines.

**Inclusion Criteria**
Children with age less than 18 years, admitted as Dengue fever based on clinical features as described in WHO 2012 Guidelines and positive Ns1Ag and/or Dengue IgM.

**Exclusion Criteria**
A. Children who cannot be followed up till 7 days.
B. Muco-cutaneous changes due to drugs or blood transfusion.
C. Children with pre-existing diseases on Chronic medications.
D. Children with pre-existing skin diseases.
E. Children with Dengue fever associated with other illnesses. example: chikungunya, malaria, typhoid, etc.

**Results**
Out of 372 clinically suspected dengue patients, 296 cases were confirmed as dengue fever by Dengue antigen and serology test. Those 296 patients were included in the study.

**Table 1:** Categorization According To Serology (N=372)

| Serology Group | No of Cases | Percentage |
|----------------|-------------|------------|
| Dengue (+)     | 296         | 79.57      |
| Dengue (-)     | 76          | 20.43      |
| Total          | 372         | 100        |

Out of 296 dengue cases, 211 cases had obvious mucocutaneous manifestations, (i.e. 71.28%).

**Table 2:** Dengue Fever With and Without Mucocutaneous Manifestations (N=296)

| Mucocutaneous Manifestations | No of cases | Percentage |
|------------------------------|-------------|------------|
| Dengue fever with mucocutaneous manifestations | 211 | 71.28 |
| Dengue fever without mucocutaneous manifestations | 85 | 28.72 |
| Total                         | 296         | 100        |

Out of 296 dengue cases, 211 cases had obvious mucocutaneous manifestations, (i.e.71.28%).

**Table 3:** Different Cutaneous Manifestations of Dengue

| Cutaneous Manifestations | No of Cases | Percentage |
|--------------------------|-------------|------------|
| Macular Rash             | 96          | 45.50      |
| Papular Rash             | 32          | 15.17      |
| Pruritus                 | 90          | 42.65      |
| Morbilliform Rash        | 30          | 14.22      |
| Erythema                 | 12          | 5.69       |
| Desquamation             | 15          | 7.11       |
| Petechia                 | 87          | 41.23      |
| Flushing                 | 198         | 93.84      |

560 cutaneous manifestations were seen in 203 cases. Many patients had more than one cutaneous manifestations. Predominant Cutaneous manifestations of dengue fever were flushing, macular rash and petechie. Flushing was the most common manifestation seen in 198 cases (93.84%), followed by Macular rash seen in 96 cases (45.50%), Pruritus in 90 cases (42.65%), and Petechia in 87 cases (41.23%).

**Table 4:** Different Types of Mucosal Manifestations

| Mucosal Manifestations                                  | No of Cases | Percentage |
|--------------------------------------------------------|-------------|------------|
| Oral (Vesicles on Soft Palate) Throat Congestion       | 43          | 29.86      |
| Erythema and Crusting of Lips and Tongue               | 46          | 31.94      |
| Scleral Congestions/ Conjunctival Haemorrhage          | 69          | 47.92      |
| Nasal/Palatal Haemorrhage/gingival bleeding            | 17          | 11.80      |

**Dengue fever had fewer mucosal manifestations compared to cutaneous manifestations. 144 cases had mucosal manifestations.**

**Table 5:** Cutaneous Manifestation with Day of Occurrence

| Cutaneous Manifestations | Occurrence in Days | Mode in Days | Average No of Days (Mean ± SD) |
|--------------------------|--------------------|--------------|-------------------------------|
| Macular rash             | 2-4                | 3            | 2.98±0.57                     |
| Papular rash             | 2-4                | 3            | 3.16±0.51                     |
| Morbilliform rash        | 3-5                | 4            | 4.44±0.64                     |
| Pruritus                 | 5-7                | 5            | 5.54±0.57                     |
| Erythema                 | 4-6                | 4            | 4.33±0.65                     |
| Desquamation             | 4-6                | 5            | 5.14±0.64                     |
| Petechia                 | 3-6                | 4            | 3.87±1.17                     |
| Flushing                 | 2-4                | 2            | 2.45±0.50                     |

**Table 6:** Mucosal Manifestations with Day of Occurrence

| Mucosal Manifestation                                  | Occurrence in Days | Mode in Days | Average No of Days (Mean ± SD) |
|--------------------------------------------------------|--------------------|--------------|-------------------------------|
| Vesicles on Soft Palate/Throat congestion              | 3-4                | 3            | 3.48±0.50                     |
| Erythema and Crusting of Lips and Tongue               | 3-4                | 4            | 3.66±0.48                     |
| Scleral Congestion/ Conjunctival Haemorrhage           | 2-5                | 3            | 3.42±0.60                     |
| Nasal or Palatal Haemorrhage / Gingival Bleeding       | 4-5                | 4            | 4.28±0.49                     |

All the Cutaneous Manifestations of Dengue Fever were further analysed statistically for the day of occurrence -range, mode in days and average no of days of occurrence with mean and standard deviation. Flushing was early
manifestations commonly occurring on day 2 of illness, whereas pruritus and desquamation were late manifestations occurring commonly on or after day 5 of illness.

Discussion

In the present study, various cutaneous manifestations were observed in children with Dengue Fever. Those were compared with various other studies as follows. All variables expressed in percentage.

In the present study, the most common cutaneous manifestation in dengue patients is flushing, seen in 198 cases (93.84%) followed by macular rash in 96 cases (45.50%), pruritus in 90 cases (42.65%), petechia in 87 cases (41.23%), papular rash in 32 cases (15.17%), morbilliform rash in 30 cases (14.22%), desquamation in 15 cases (7.11), last was ecchymosis in 12 cases (5.69%).

Flushing is the most common manifestation seen in 93.84% of the dengue cases similar to study done by Mahboob A et al.\(^5\) where he found it in 77.08% of dengue cases. Nadiya A et al.\(^6\) found flushing in 28.7% of dengue patients. Flushing was early feature, transient in nature which usually started between day 2 to day 4, commonly occurring on day 2 of illness, and mostly involving face.

Study done by Nadia A et al from Lahore, stated that dengue rash was a generalized, macular eruption in 31.7% while a papular rash was seen in 11.2%.\(^7\) In a study by Saleem K et al done in Karachi, a macular rash was reported in 65% of cases.\(^8\) In the present study, macular rash is seen in 45.50% of cases and Papular rash is seen in 15.17% of cases. This variation of incidence maybe due to different strains of the virus.\(^9\) In present study, Macular and Papular rash both commonly occurred around day 3 of onset of illness, with a range between 2-4 days.

In present study, generalized morbilli form rash was present in 14.22%. In studies from Pakistan and India generalized morbilli form rash was observed in 65%, 81.73%, and 48.3% respectively, whereas in a study from France\(^10\) morbilliform rash was observed in 33% cases. Morbilliform rash occurred between day 3 to day 5 from the onset of fever with most common day being day 4 of illness.

Haemorrhagic manifestations are considered to be a hallmark of Dengue Fever, especially of Severe Dengue. In present study, petechiae were present in 41.23% of the cases other study from Lahore by Nadia Ali et al. reported that petechia in 20% cases and Saleem and Shaikh\(^8\) from Karachi in 35% cases in their study. In studies from Pakistan and India ecchymotic spots were observed in 4%, 13.8% and in 35% of dengue patients respectively. In the present study, ecchymosis was seen in 5.69% of the cases. These haemorrhagic cutaneous manifestations including petechiae, purpura and ecchymosis occur mainly on day 3 or day 4 of illness.

Desquamation was observed as a late feature in patients of dengue fever. In present study, it was found in 7.11% patients. Another study by Nadia et al.\(^6\) found desquamation in 12.3% of dengue patients. Desquamation was mostly seen in late stages of dengue fever. It appeared commonly on day 5 with range being day 4 to day 6.

Pruritus is also quite common in dengue cases. We found Pruritus in 42.65% of patients and is generally observed as late feature, occurring commonly around day 5 of illness. Pruritus is reported in different studies, ranging from 16% to 27.6%. This observation was consistent with reports from Karachi by Saleem K et al. Who found Pruritus in 43.0%\(^8\) and in Brazil by Noqueiro et al. who found Pruritus in 50.5% patients\(^11\)

Mucosal involvement is estimated to occur in 15% to 30% of patients with dengue viral infections which is less compared to cutaneous manifestations. In the present study mucosal manifestation were noted in 48% of the cases. In another study from Lahore by Mahboob A et al., mucous membrane involvement was quite common and was seen in 85.38%.\(^5\) Another study from France stated the mucosal involvement of 46.15% in their study.\(^10\) The mucosal manifestations noted in Dengue viral infections in present study, are conjunctival and sceleral injection, small vesicles on the soft palate/throat congestion, erythema and crusting of lips and tongue and palatal haemorrhage and gingival bleeding. According to study by Nadiya A, the most frequent mucosal involvement was oral mucosal involvement i.e. 43.58%.\(^6\) In this present study, oral mucosal involvement in the form of Vesicles on soft palate, erythema of buccal mucosal and throat congestion was found to be 30.06%. Study from Lahore by Mahboob A et al.\(^5\) found oral mucosal involvement to be 66.67%. Oral mucosal involvement usually appears between day 3 to day 4 from the onset of illness. The most common finding of oral mucosa was erythema of buccal mucosa. In present study, erythema and crusting of lips and involvement of tongue was found to be 32.02%. Mahboob A from Lahore in his study, found involvement of lips to be 4.8%, palate to be 2.4% and tongue to be 1.6% cumulative to be 10.41%.\(^8\) Saleem K et al in his study found 30.0% involvement of the lips and tongue.\(^8\) These manifestations usually start by day 3 and day 4 from the onset of illness.

Gingivae were hyperaemic and bleeding from gums was seen in11.80% patients from the study by MahboobA\(^9\), while in other study from Pakistan, 7% of patients had bleeding from gums. In one study from Pakistan, haemorrhagic manifestations of Dengue fever in gums were seen in 40% of patients, while in a study from Japan gum bleeding was more common in adults. In the present study, Nasal bleeding, palatal haemorrhage and gingival bleeding was seen in 3.32%. Nasal bleeding, Gingival bleeding and palatal haemorrhage are seen in cases with Severe Dengue. They usually occur during critical phase. They usually appear on day 4 to day 5 from the onset of illness.
Other mucosal manifestations included nasal membrane congestion and epistaxis, which was seen in 23.5%. Similarly, 26% of patients from Liaquat National Hospital had nasal bleeding. In another study from Japan\textsuperscript{[71]} nasal bleeding was most common in children with Dengue.

**Conclusion**

Mucosal manifestations are seen in 48% of children with Dengue fever with scleral congestion and conjunctival haemorrhage being the most common mucosal manifestation.

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