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A Prospective and Observational Immunological Correlation Analysis of Non Classical with Classical Clinical Spectrum of Dengue Disease at Tertiary Health Centre

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Introduction

Dengue is a mosquito borne viral disease caused by Dengue virus (DEN-1, 2, 3&4). Dengue is endemic in more than 100 countries[1]. Dengue constitutes a major cause of pediatric morbidity and mortality in South East Asian countries[2]. Dengue fever (DF) has been reported from India over a longtime, but dengue hemorrhagic fever (DHF) was first reported in 1963 from Calcutta city[3]. Since then several outbreaks of dengue fever have been reported from India with a major epidemic of dengue hemorrhagic fever that occurred in Delhi in 1996 when 10,252cases and 423 deaths were reported[3]. Manifestation in children and adults differ in many ways. In a study, children had higher proportion of DHF I (42.9%) cases, whereas 51% adults were of DHF II. Some clinical manifestations, such as petechiae, melena, headache, retro-orbital pain, joint pain, myalgia, nausea and vomiting were more common in adult patients[8]. This study was undertaken to evaluate clinical profile and outcome of adult admitted with DHF/Dengue Shock Syndrome (DSS), dengue like illnesses amongst the adult admitted ii ABG Hospital Delhi from 2017.

Subjects & Method

This was a hospital based retrospective study. During from the year 2017 dengue positive, 100 cases suspicion of dengue fever were hospitalized in the Department of Medicine ABG Hospital, Delhi, India during the period of from 2017. An approval from the head of the department was taken. Medical records of these 100 Adult were analyzed. Criteria used for clinical diagnosis were.

Probable Dengue Fever (DF)

Acute febrile illness with 2 or more of the following manifestations:

1. Headache 2. Retro-orbital pain
3. Myalgia 4. Arthralgia
5. Rash 6. Haemorrhagic manifestations
7. Leucopenia;

Confirmed DF

Cases having positive ELISA test for Anti dengue IgM antibody

Dengue Hemorrhagic Shock (DHF)

All of following must be present

1. Confirmed dengue fever through laboratory
2. Fever for 2-7 days
3. Bleeding evidenced by at least one of the following:
   a. Positive tourniquet test (TT),
   b. Petechiae, ecchymosis, or purpura,
   c. Bleeding from the mucosa, GI tract, inj.site
   d. Haematemesis or malaena
   e. Thrombocytopenia (100,000 /mm3 or less),
4. Evidence of plasma leakage due to increased vascular

Permeability, manifested by at least one of the following:

   a. Rise in the haematocrit > 20% above average for age, sex & population.
   b. Drop in the haematocrit following volume replacement treatment > 20%
   c. Signs of plasma leakage e.g., pleural effusion, ascites, hypoproteinaemia

Dengue Shock Syndrome (DSS)

1. Four criteria of DHF
2. Plus signs of circulatory failure manifested as

a. Rapid and weak pulse

b. Narrow pulse pressure (<20mmHg)

c. Hypotension for age (Sys Press<80mmHg for <5yrs,

<90mmHg for>5yrs)

d. Cold, clammy skin

e. Restlessness

Thrombocytopenia was further categorized, depending on severity as those with platelet count less than 50,000/cumm and with platelet countless than 20,000/ cumm. Disease severity was assessed according to the WHO grading system:

- Grade I: Positive tourniquet test
- Grade II: Spontaneous bleeding
- Grade III: Circulatory failure
- Grade IV: Undetectable blood pressure and pulse

Grades III and IV DHF also referred to as DSS.

Hemoglobin, hematocrit, platelet count and total leukocyte count was done in all cases. Platelet count was monitored as and when required in certain cases. Liver function test, renal function test were done in all those cases where it was possible. Chest X-ray and ultrasound abdomen was done in some patients. Serological diagnosis was carried out with IgM ELISA. Patients in whom the serological tests were negative but presented with characteristic features of DHF or DSS, were classified under Viral Hemorrhagic Fever and those with features of dengue fever were classified as Dengue like illness.

Observations

Total 100 cases of suspected dengue were admitted in the hospital during the study period, of these total 57 (57%) cases came out positive out . In 7 of the cases IgM was positive by Card method but Negative with ELISA so these cases were not included amongst positive. The findings observed are as follows: Amongst the cases admitted adult was of 18 year of age and maximum were in the age group & near 90 yrs.

Table 1: Agewise distribution of IgM+ve and Suspected Dengue cases

Age group	IgM+ve cases	Suspected Dengue
1. <20 yr	10	14
2. 20-40 yr	23	25
3. 40-60 yr	19	20
4. 60 -80 above	05	07

Table 2: Clinical manifestations among IgM+ve and Suspected Dengue cases

Clinical Feature	*IgM +ve Cases*
1. *Fever+C/R*	*23*
2. *Fever-C/R*	*09*
3. *Rashes*	*10*
4. *Anorexia*	*01*
5. *Nausea & vomiting*	*01*
6. *Headache*	*05*
7. *Body ache*	*01*
8. *Abdo. pain*	*02*
9. *Cough & coryza*	*02*
10. CNS	*03*

Table 3: Bleeding manifestations among IgM+ve and Suspected Dengue cases

Bleeding manifestations	IgM +ve Cases	Suspected Dengue
1. Hess's Test		
Positive	05	21
Negative	20	20
Not applicable	11	42
2. Petechiae	29	47
3. Epistaxis	5	20
4. Gum Bleed	1	3
5. Hematemesis	3	15
6. Malena	4	16
7. Hematochezia	3	5
8. Bruise @ inj site	2	2

Table 4: Evidence of fluid leakage

Condition	IgM +ve Cases	Suspected Dengue
1. Edema	11	19
2. Ascitis	06	14
3. Effusion	01	06
Bilateral	0	1

Table 5: Incidence of organomegaly

Organomegaly	IgM +ve Cases	Suspected Dengue
1. Hepatomegaly	21	36
Tender	7	30
Nontender	11	34
2. Splenomegaly	3	36
Diagnosis	**Number**	
1. Dengue F	27	
2. DHF I	7	
3. DHF II	23	
4. DHF III	2	
5. DHF IV	2	

Discussion

In this study most of the cases were between 18-90 yrs of age. In a study by Faridi et al, 76 % of all cases of DHF /DSS[10]. In a study by Anju et al, 45% cases presented with DHF/DSS[11].

In our study, Dengue fever was present in 27 cases of IgM Positive out of 57 final diagnosed cases. DHF II was present in 23 of cases o IgM positive out of 57 final diagnosis while DHF I, III & IV each were present in near 5% of cases. In a study by Dhooria et al 92% of cases presented in Grade II and 7.4% cases presented in Grade III of WHO classification. No patient presented in Grade IV severity. Patients with Grade I disease did not require admission[4]. In a study by Ratageri et al, dengue fever was present in 18%, DHF in 60% and DSS in 22% of cases[9]. In a study of 134 cases by Anju et al 67% of cases were of DHF whereas remaining 33% were of DSS[11].

In this study, common symptoms seen were fever with chills n rigors(57.5%),fever without chills n rigors in 42.5% cases, vomiting (23%), bodyache (37.5%), abdominal pain (37.5%), headache (27.5%), anorexia (2.5%), Cough n coryza (7.5%), and CNS symptoms (15%). Hepatomegaly was seen in 20 cases (50%), splenomegaly was found in 3 cases (7.5%) while pleural effusion was noted in 15% cases and all were on right side. In a study by Dhooria et al common symptoms seen were fever (91%), vomiting (41%), poor intake (21%), abdominal pain(16%) and significant bleeding (15%). Hepatomegaly was seen in 60% of cases[4]. Ratageri et al reported fever (100%), vomiting (82%), abdominal pain (61%), restlessness (65%), headache (22%), and hepatomegaly (87%)[9]. The mean duration of fever prior to admission was 5.47 days (2-12 days)[9] which was 6 days(2-15 days) in our study. In a study by Kabra et al pleural effusion occurred in 19 patients (90%/o), and 18 (86%) exhibited each of the following: vomiting, thrombocytopenia. Hepatomegaly was observed in 15 patients (71%) and splenomegaly in three (14%).

In our study the most common bleeding manifestation was petechiae in 35% .Significant bleeding in form of melena (10%), hematemesis (7.5%), heamtochezia (7.5%), epistaxis (12.5%), gum bleed (2.5%) and bruises at injection site (5%) was seen. In a study by Dhooria et al petechiae was seen in 85% of cases, melena (6%), ecchymosis (2.5%) and epistaxis (2.5%)[4]. In a study by Ratageri et al, common bleeding manifestations were GI bleeding (22%) and petechiae (18%)[9]. Gastrointestinal tract was reported as the commonest site of bleeding (61%) in a study by Ahmed et al[13] as well as Rachel et al[12]. In our study, gastrointestinal bleeding in the form of melena, hematochezia and hematemesis

was seen in 25% of cases. Gastrointestinal bleeding is secondary to microvascular damage leading to increased permeability (particularly when platelet function is decreased) or actual disruption and local hemorrhage[14]

The main pathogenic feature of dengue is an increase in vascular permeability leading to loss of plasma from blood vessels, which causes hemoconcentration, low blood pressure and shock. This may also be accompanied by hemostatic abnormalities such as thrombocytopenia, vascular changes and coagulopathy[15]. A drop in platelet count to below 100,000/cumm and an increase of 20% or more in the hematocrit, both resulting from increased vascular permeability, are consistent findings. Other signs of plasma leakage include pleural effusion, ascites and hypoproteinemia. In the study the mean hematocrit at presentation was 28.3 gm% and since pre illness hematocrit was not known it was difficult to document hemoconcentration. These observations suggest that hemoconcentration may not be a good indicator for diagnosis and monitoring of fluid if pre-illness hematocrit is not known, particularly because there is a high prevalence of anemia in the population[13].

In the current study, out of 40 cases only 6 patients (15.5%) had platelet count over 1,00,000/cumm and 50% cases had platelet count less than 50,000/cumm and 10.5% cases had platelets less than 20,000/cumm. In the study by Dhooria et al on DHF cases all patients had platelet counts less than 100,000/cumm (part of case definition of DHF), while 59% of cases had platelet count less than 50,000/cumm. There was poor correlation between thrombocytopenia and bleeding diathesis indicating thereby that the abnormal platelet aggregation rather than reduction in absolute numbers was the cause of bleeding diathesis. In the study by Kamath et al, platelet counts less than 50,000/cumm were noted in 62.3%[16]. Dengue infection can cause neurological manifestation ranging from non-specific symptoms to encephalitis and rarely Guillain- Barre Syndrome[17]. Apart from abnormal neurology secondary to cerebral hypoperfusion

on account of shock other significant reasons for neurological presentations include cerebral edema, direct neurotropic effect of dengue virus resulting in encephalitis/ encephalopathy, or secondary to hepatic dysfunction and metabolic derangements such as hypoglycemia and hyponatremia [18-21]. Encephalopathy is known to occur in 0.5% of patients with DHF[22]. Malavige et al reported acute liver failure (73%), electrolyte imbalances (80%) and shock (40%) as factors contributing to encephalopathy[23]. In study by Dhooria et al, of the 3 patients (3.7%) which presented with altered sensorium, 1 patient had persistent low GSC and seizures in spite of correction of shock[4]. Soloman et al found that altered consciousness and convulsions are the major manifestations of dengue infection in CNS[24]. In our study 6 out of 40 had some CNS complaints, 3 of which had seizures and unconsciousness & drowsiness was complained by 1 patient each while the other had irritability none of these patient had shock or dyselectrolytemia.

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