Original Article

A clinico - pathological correlation of patients with dengue hemorrhagic fever at tertiary health care center

Bhavesh B Shah[1*], Sara Dhanawade[2]

[1]Assistant Professor, Department of Paediatrics, Government Medical College, Miraj, Maharashtra, INDIA.
[2]Professor and Head Dept of Paediatrics, Bharati Vidyapeeth Deemed University Medical College, Sangli, Maharashtra, INDIA.
Email: shahbhavesh1010@rediffmail.com, sarasubodh@yahoo.com

Abstract

Background: Dengue fever is an infectious disease which is difficult to distinguish from other viruses as there are no specific markers that can diagnose the disease early. **Aims and Objectives:** To Study Clinico- Pathological correlation of patients with Dengue Hemorrhagic fever at tertiary health care center. **Methodology:** It was a hospital based prospective study done over a period of one year from 1st July 2002 to 30th June 2003 in the Department of pediatrics, wanless hospital and Government medical college, Miraj. Fifty children admitted to pediatric intensive care unit during the above period with clinical diagnosis of DHF/DSS were included in the present study. Children of 1 month to 16 years of age, fulfilling WHO criteria for the diagnosis of DHF/DSS were included. **Result:** In our study, we have found that Out of 50 patients, 35 (70%) aged 6 to 12 years, 9 (18%) patients aged 13 to 16 years while 6 (12%) aged less than 5 years, youngest being 7 month old infant. Of total 50 patients, 15 (30%) patients had grade I and 17 (34%) had grade II severity. While 12 (24%) patients had grade III and 6 (12%) had grade IV severity. Tourniquet test was positive in 15 (100%) patients with Grade-I, and 9 (52.9%) patients with Grade II severity. Only 4 (33.3%) patients with grade III and I (16.7%) patients with Grade IV severity had positive tourniquet test. In 7 (14%) patients it was less than 4,000 (leucopenia) while 12 (24%) patients had count more than 11,000. (Leukocytosis). All fifty patients had thrombocytopenia (<1,00,000/mm3) of which 26 (52%) had moderate thrombocytopenia while 16 (32%) patients had severe and 8 (16%) had mild thrombocytopenia. Rise in Hct. Concentration by >20% was observed in 31 (73.8%) of the 42 patients in whom it could be computed. Elevated liver enzymes were found in a total of 34 (68%) patients of which 24 (70.6%) had predominantly SGOT rise while 10 (29.4%) had predominantly SGPT rise. Thirty-one (62%) of the 50 patients were found to have hypoproteinemia. **Conclusion:** It can be concluded from our study that the most common, age group in our study found to be 6 to 12 years; WHO grade I and Tourniquet test was most common in Grade I , Most of the patients showed Thrombocytopenia, Raised Hematocrit seen in 20 % persons also some patients showed Elevated liver enzymes.

Key Words: Dengue Hemorrhagic, DHF/DSS, WHO Grades of DHF.

[*]**Address for Correspondence:**
Dr. Bhavesh B. Shah, Assistant Professor, Department of Paediatrics, Government Medical College, Miraj, Maharashtra, INDIA.
Email: shahbhavesh1010@rediffmail.com
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INTRODUCTION

Dengue fever is an infectious disease which is difficult to distinguish from other viruses as there are no specific markers that can diagnose the disease early. Because it is a disease that can evolve with serious consequences and even be fatal, this study aimed at analyzing clinical and epidemiological data and laboratory dynamics in order to try to identify biomarkers that are predictive of severity. Dengue is caused by a virus belonging to the flaviviridae family (single stranded, positive, non-segmented RNA virus). It has four distinct serotypes DEN 1, DEN 2, DEN 3 and DEN 4[1,2,4]. Infection with one serotype confers

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immunity to only that serotype and hence a person may be infected up to four times[1,2,4]. Humans are the main reservoir of dengue virus[1,2 ,3]. Dengue presents as dengue fever, dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS).[1,2,34,5]. It has been suggested that baseline microvascular permeability in children is greater than that of adults and this could partly explain, why DHF is more frequent in children[3,5,6,7,8].

MATERIAL AND METHODS

It was a hospital prospective study done over a period of years from 1st July 2002 to 30th June 2003 in the department of pediatrics, wanless hospital, Government medical college, Miraj. Fifty children admitted to pediatric intensive care unit during the above period with clinical diagnosis of DHF/DSS were included in the present study. Children of 1 month to 16 years of age fulfilling WHO criteria for the diagnosis of DHF/DSS were included. The case definition criteria follows the procedures outlined in the "technical guide for diagnosis, treatment, surveillance, prevention and control of dengue hemorrhagic fever", prepared by technical advisory committee on dengue hemorrhagic fever for the south-east Asia and western pacific regions, world health organization.(W.H.O). Accordingly the case definition of DHF consisted of the presence of Fever, Hemorrhagic manifestations-including at least a positive tourniquet test and/or minor or major bleeding phenomenon like, petechiae, purpura, ecchymosis (skin bleeds), epistaxis, gum bleeding, hematemesis and/or melena etc., Thrombocytopenia i.e. platelet count ≤ than 1,00,000/mm3, Hemoconcentration I.e. rise in the hematocrit (Hct.) by 20% or more or objective evidence of increased capillary permeability (ascites and/or pleural effusion). The case definitions of DSS consisted of the presence of the criteria listed for DHF with presence of narrow pulse pressure i.e. less than 20 mm of Hg or hypotension for respective age and sex. Once included according to above criteria and enrolled in the study, patients are roofed under a common title "dengue like disease" until a specific serological diagnosis was established. Patients fulfilling case definition criteria of dengue fever syndrome (DF) without evidence of thrombocytopenia and objective evidence of plasma loss i.e. hemoconcentration, ascites and/or pleural effusion, were excluded from the study. The ratio was computed to evaluate the degree of hemoconcentration in our patients, as follows: Highest (pack) Hct.-Recovery hct.×100 Recovery Hct. A value of 20% or more was considered as evidence of significant hemoconcentration.

RESULT

Table 1: Distribution of cases according to Age:

Age	Number of cases (%) N=50
1 month to 1 years	01(2%)
2 to 5 years	05(10%)
6 to 8 years	20(40%
9 to 12 years	15(30%)
13 to 16 years	09(18%)
Total	**50(100%)**

Out of 50 patients, 35 (70%) aged 6 to 12 years, 9 (18%) patients aged 13 to 16 years while 6 (12%) aged less than 5 years, youngest being 7 month old infant.

Table 2: Distribution of cases according to W.H.O. Grades of severity

W.H.O. Grades	Number of cases (%) N=50
DHF-I	15(30%)
DHF-II	17(34%)
DHF-III	12(24%)
DHF-IV	06(12%)
Total	**50(100%)**

Of total 50 patients, 15 (30%) patients had grade I and 17 (34%) had grade II severity. While 12 (24%) patients had grade III and 6 (12%) had grade IV severity, together called DSS (shock) group.

Table 3: Distribution of cases according to sites of hemorrhagic manifestations

Sr. No	Hemorrhagic manifestations	Number of cases (%)
1	Petechia/Ecchymoses(skin bleeds)	21(65.6%)
2	Hematemesis and/or melena	15(46.9%)
3	Epistaxis	09(28.1%)
4	Gum bleed	04(12.5%)
5	Hematuria	01(03.1%)
6	Intracranial hemorrhage	00(0%)

Of the total 32 patients with bleeding 21 (65.6%) patients had skin bleeds, 15 (46.9%) had hematemesis and/or melena while epistaxis was seen in 9 (28.1%) patients. Gum bleeds and hematuria were seen in 4 (12.5%) and 1 (3.1%) patients respectively. Intracranial hemorrhage was not seen in any patients.

Table 4: Distribution of positive tourniquet test according to the grades of severity of DHF/DSS

Grades	Number of case N=50	Positive tourniquet test number of cases (%) (N=29)
I	15	15(100%)
II	17	09(52.9%)
III	12	04(33.3%)
IV	06	01(16.7%)
Total	**50**	**29(58.0%)**

Tourniquet test was positive in 15 (100%) patients with Grade-I, and 9 (52.9%) patients with Grade II severity. Only 4(33.3%) patients with grade III and I (16.7%) patients with Grade IV severity had positive tourniquet test.

Table 5: Distribution of cases according to hematological laboratory findings

Sr. No	Investigations	Cases (%)
1	**Total leukocyte count/mm^3**	**(N=50)**
	Leucopenia:<4,000	07(14%)
	Normal :4,000 to 11,000	31(62%)
	Leukocytosis:>11,000	12(24%)
2	**Platelet count/mm^3(thrombocytopenia)**	**(N=50)**
	Mild:50,000-1,00,000	08(16%)
	Moderate: 20,000-50,000	26(52%)
	Severe:<20,000	16(32%)
3	**Hemoconcentration**	**(N=42)***
	Rise in Hct. Concentration by>20%	31(73.8%)

*(computation of rise in Hct. Concentration could be possible in 42 of the total 50 patients)

Total leukocyte count in 31 (62%) patients was normal. In 7(14%) patients it was less than 4,000 (leucopenia) while 12(24%) patients had count more than 11,000. (Leukocytosis). All fifty patients had thrombocytopenia (<1,00,000/mm^3) of which 26(52%) had moderate thrombocytopenia while 16(32%) patients had severe and 8(16%) had mild thrombocytopenia. Rise in Hct. Concentration by >20% was observed in 31(73.8%) of the 42 patients in whom it could be computed.

Table 6: Distribution of cases according to other laboratory findings

Sr No.	Investigation	Number of Cases (%)
1	Liver enzymes	N=50)
	SGOT(>40u/l), SGPT(<40u/l)	34(68%)
2	Serum total protein	(N=50)
	(<5.5 gm/dl)	31(62%)
3	Coagulation profile	(N=42)*
	Pt(<control) and APTT(>control)	22(52.4%)
4	Mac ELISA	(N=42)*
	IgM antibodies to dengue 2 virus	34(80.9%)

*(coagulation profile tests and mac ELISA test were done in 42 of the total 50 patients)

Elevated liver enzymes were found in a total of 34 (68%) patients of which 24 (70.6%) had predominantly SGOT rise while 10 (29.4%) had predominantly SGPT rise. Thirty-one (62%) of the 50 patients were found to have hypoproteinemia. Overall, coagulation profile (PT and APTT) was deranged in 22 (52.4%) patients. Of the 42 samples collected at admission 34(80.9%) were positive for IgM antibodies to dengue 2 virus by Mac ELISA test.

DISCUSSION

In our study, we have found that Out of 50 patients, 35 (70%) aged 6 to 12 years, 9 (18%) patients aged 13 to 16 years while 6 (12%) aged less than 5 years, youngest being 7 month old infant. Of total 50 patients, 15 (30%) patients had grade I and 17 (34%) had grade II severity. While 12 (24%) patients had grade III and 6 (12%) had grade IV severity, together called DSS (shock) group. Of the total 32 patients with bleeding 21 (65.6%) patients had skin bleeds, 15 (46.9%) had hematemesis and/or melena while epistaxis was seen in 9 (28.1%) patients. Gum bleeds and hematuria were seen in 4 (12.5%) and 1 (3.1%) patients respectively. Intracranial hemorrhage was not seen in any patients. Tourniquet test was positive in 15(100%) patients with Grade-I, and 9(52.9%) patients with Grade II severity. Only 4 (33.3%) patients with grade III and I (16.7%) patients with Grade IV severity had positive tourniquet test. Total leukocyte count in 31 (62%) patients was normal. In 7 (14%) patients it was less than 4,000 (leucopenia) while 12 (24%) patients had count more than 11,000. (Leukocytosis). All fifty patients had thrombocytopenia (<1,00,000/mm^3) of which 26 (52%) had moderate thrombocytopenia while 16 (32%) patients had severe and 8 (16%) had mild thrombocytopenia. Rise in Hct. Concentration by >20% was observed in 31(73.8%) of the 42 patients in whom it could be computed. Elevated liver enzymes were found in a total of 34 (68%) patients of which 24 (70.6%) had predominantly SGOT rise while 10 (29.4%) had predominantly SGPT rise. Thirty-one (62%) of the 50 patients were found to have hypoproteinemia. Overall, coagulation profile (PT and APTT) was deranged in 22 (52.4%) patients. Of the 42 samples collected at admission 34 (80.9%) were positive for IgM antibodies to dengue 2 virus by Mac ELISA test. This was similar to Mane V *et al* 13The most common clinical feature of dengue in their study was high fever. The fever rash was typically macular or maculopapular, often becoming confluent and sparing small islands of normal skin. The rash was not associated with scaling or pruritus[1,2,10,11,12]. Pervin *et al*[12], reported occurrence of rash in 33% of patients. Hepatomegaly was observed in more than 30% of our patients. Hepatomegaly is more common in patients with secondary infection and some of these may be associated with a increase in liver transaminases. Myalgia was observed in 72% of patients. Pervin *et al*, reported myalgia in 84.5% of patients. Hemoconcentration was seen in more than 50% of patients[12]. Mane V13 *et al* they found Thrombocytopenia (platelets < 1,00,000/cmm) was seen in 80% of patients. The platelet count in these patients ranged between 4,000-1,00,000/cmm. None had any bleeding manifestations. Platelet count was evaluated by Nihon Kohden 5 part diferential cell counter as well as on peripheral blood smear. The counter gives a false low reading when large platelets are present. Such cases were obviated by assessment of platelets on smear. Ratagiri *et al*[12], reported thrombocytopenia in 82%, DHF in 60%, DSS in 22% and DF in 18% of patients. Our study on the other hand reflected DF in 96%. Leucopenia was observed in 26% of patients by Ratagiri *et at*[12]. Leucopenia was observed in

more than 60% of patients in the study of Mane V *et al*[13]. Development of antibodies potentially cross-reactive to plasminogen (due to a similarity in 20 amino acid sequence of dengue E glycoprotein and a family of clotting factors) could have a role in causing haemorrhage in DHF[9,10,12]. The increased destruction or decreased production of platelets could result in thrombocytopenia. Virus-antibody complexes have been detected on the platelet surface of DHF patients suggesting a role for immune-mediated destruction of platelets13. The release of high levels of platelet-activating factor by monocytes with heterologous secondary infection may explain the haemorrhage, given that platelet-activating factor may induce platelet consumption and augment adhesiveness of vascular endothelial cells resulting in thrombocytopenia11. The presence of IgM antibodies in the sera DHF cases that cross-reacted with platelets has been demonstrated[1,3,6,9]. These autoantibodies could be involved in the pathogenesis of the disease. IgM and IgM antibodies assay by ELISA is the commonest diagnostic test. The test based on an increase in the IgG titre by a factor of four is difficult in routine clinical care because a second blood sample is required at the convalescent stage. Cross reactions with other flaviviruses interfere with serologic testing, particularly the ELISA for IgG and this affects the interpretation of test results in travellers exposed to other flavivirus infections, including those previously vaccinated against flavivirus infections, such as yellow fever and Japanese encephalitis[7,12,13]. Rheumatoid factor may lead to an IgM capture assay that is false positive for dengue and like many other flavivirus infections (albeit lesser than with dengue IgG assays)[8].

CONCLUSION

It can be concluded from our study that the most common, age group in our study found to be 6 to 12 years; WHO grade I and Tourniquet test was most common in Grade I, Most of the patients showed Thrombocytopenia, Raised Hematocrit was seen in 20 % patients also more than 50 % patients showed Elevated liver enzymes.

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