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Research article

CLINICO-PATHOLOGICAL PROFILE IN THE INFANTS AND CHILDREN IN DENGUE 2012 EPIDEMIC, KOLKATA

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ABSTRACT

Background: Dengue fever (DF) is responsible for cyclical and frequent epidemic in different parts of India in its varieties of presentations. In 1992 large number of children died of Dengue hemorrhagic fever (DHF). **Aims and objective:** In this study, we evaluated the demography and clinico-pathological profile in dengue affected infants and children in 2012 Kolkata epidemic**. Materials and methods:** Total 233 patients (between 1-18 years, with either Non structural protein 1 antigen or dengue Immunoglobulin positive) admitted in our hospital. After taking proper history and physical examination, blood were sent for different hematological and biochemical examinations on the day of admission and after 24-48 hours of admission. We differentiated the dengue patients into DF and DHF based on platelet count. **Results:** Male female ratio and DF to DHF ratio were 1: 0.86 and 1: 3.5 respectively. Mean age of DF and DHF were 10.31±5.41 years and 12.6±4.51 years respectively. Mean duration of fever in DF and DHF cases were 5.33±1.13 and 6.08±1.79 days respectively. Headache, backache, nausea/vomiting, rash, anorexia, loose motions were statistically significant in DF. In spite of significant positive tourniquet test in DHF patients (76.92%), only 13 patients showed evidence of bleeding. Hematocrit (Hct) values between 30-40 and below 30 were significant in DHF and DF patients respectively. Leucopenia and increased liver enzymes (SGOT and SGPT) were commonly observed in both DF and DHF patients. Hepatomegaly was observed in 13.72% of DF patients, whereas, isolated hepatomegaly, ascites, combined hepatomegaly with ascites and evidence of pleural effusion were observed in 4.94%, 1.64%, 3.29% and 7.14% of DHF patients respectively. **Conclusion:** In seropositive DHF patients, fever, headache, backache, loose motions were the predominant symptoms associated with hepatomegaly, elevated liver enzymes and evidence of plasma leakage.

Keywords: Clinico-pathology, Dengue epidemic, Infants, Children, Kolkata

INTRODUCTION

Over several decades, Dengue, an Arbo virus infection, is responsible for cyclical and more frequent epidemic in rural as well as urban areas of India, showing a wide variety of presentations from subclinical or mild self limiting disease to severe form of disease, like, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[1] DHF first crept into Kolkata in 1963-65, this was followed by the recurrent occurrence of outbreaks.[2] In the 1992 epidemic, large number of affected children died of DHF/DSS. Dengue may be manifested by its typical clinical features, but its presentation may be variable making the doctor puzzled. Our present study was to evaluate the demography and clinic-pathological profile of

dengue fever in infants and children during the 2012 dengue epidemic in Kolkata.

PATIENTS & METHODOLOGY

Inclusion criteria: In 2012 epidemic, total 233 infants and children between the ages of 1 to 18 years, were admitted in our hospital on and from the month of 1st August to 31st October with either Non structural protein 1 antigen ($NS_{1,}$ antigen) positive or dengue Immunoglobulin M (IgM) positive.

Exclusion criteria: Patient suffering from any infection, viral hepatitis during this period.

Ethical clearance: This study was started after getting approval from Ethical Committee and informed consent form obtained from the patients' parties.

Methodology: Thorough history-taking and physical examination was performed in all these patients. Just after admission, 5 ml. of blood was collected aseptically from each patient. 1 ml of clotted blood was used for non structural protein 1 (NS1) antigen and immunoglobulin M (IgM) antibody by Mac ELISA manufactured by Panibo Diagnostics, remaining 4ml of Blood sample was used for examination of hematological and biochemical profile immediately.

Between the interval of 24 and 48 hours after admission, 4 ml of blood sample was collected. 2 ml of blood was kept in EDTA vial and was sent for platelet count both by manual methods (light microscopy and Neubauer chamber) and Coulter counter method and hematocrit. Rest 2 ml of clotted blood was used for biochemical tests (SGPT, SGOT). Daily platelet count was advised for those patients having platelet count less than 100000/cc.

Imaging studies like, Ultrasonography and chest x-ray were performed to detect Ascites and pleural effusion respectively. We differentiated the dengue patients into Dengue fever (DF) and DHF based on platelet count. (Since there was no DSS detected among in this group). These patients were treated with intravenous fluid, Paracetamol according to WHO protocol.[3] No patient was treated with NSAID. When vital statistics of these patients came to normal; they were discharged from hospital.

Statistics: Then, we compared the demographic data, symptoms, laboratory investigations between DF and DHF by Open stat and Statcalc statistical Calculators. P value of <0.05 was considered as statistical significance.

RESULTS

In our study, all our patients were either NS1 (79%) or IgM (21%) positive. Male female ratio was 1: 0.86, whereas ratio of DF to DHF ratio was 1: 3.5. Male to female ratio in DF was 1: 1 and in DHF, 1:1.16**.** Mean age of DF and DHF were 10.31±5.41 years and 12.6±4.51 years respectively **[table 1]**. All the patients were admitted with fever. Mean duration of fever in DF and DHF cases were 5.33±1.13 and 6.08±1.79 days respectively. Common symptoms were Headache (62.74%, 30.76%), backache (58.82%, 30.76%), nausea/vomiting (62.74%, 47.25%), rash (29.41%, 15.93%), anorexia (60.78%, 13.73%), loose motion (35.29%, 18.68%) in both DF and DHF respectively. In spite of significant positive tourniquet test in DHF patients (76.92%), severe bleeding was seen in only 13 patients. **[Table 2]**. Most of the patients were anemic. Hematocrit (Hct) between 30-40 was significant in DHF patients, whereas, Hct was observed below 30 in significant number of DF patients. Leucopenia and raised liver enzymes (SGOT and SGPT) were commonly observed in both DF and DHF patients without any statistical difference. But, the International normalized ratio (INR) was only elevated more than 1.5 in DHF patients **[Table 3]**. Sonographically, Isolated hepatomagaly observed in 13.72% and 4.94% DF and DHF patients respectively, whereas, ascites and ascites associated with hepatomagaly were observed in 1.64% and 3.29% of DHF patients respectively. Again, chest x-ray showed evidence of pleural effusion in DHF patients only **[Table 4]**.

Table 1: Demographic distribution

Features	DF (51)	DHF (182)	P value
Mean age yrs	10.31 ±5.41	12.6 ±4.51	0.04*
Male sex	26	98	0.35
Female sex	25	84	0.35

*significant

Table 2: Common symptoms

Symptoms	DF (51)	DHF (182)	% Amongst total (233)	P value
Fever (days)	5.33±1.13	6.08±1.79	-	0.0001**
Headache	32 (62.74 %)	56(30.76%)	88 (37.76%)	0.00001***
Backache	30 (58.82%)	56 (30.76%)	86(36.90%)	0.0001**
Nausea/vomiting	32 (62.74%)	86 (47.25%)	136(58.36%)	0.02*
Rash	15 (29.41%)	29 (15.93%)	44 (18.88%)	0.01*
Anorexia	31 (60.78%)	52 (13.73%)	83(35.62%)	0.00001***
Loose motion	18 (35.29%)	34 (18.68%)	52 (22.31%)	0.005**
Retro orbital pain	4 (7.8%)	6 (3.29%)	10 (4.29%)	0.07
Types of bleeding				
Positive tourniquet test	0	140 (76.92%)	140 (60.08%)	
Epistaxis	0	3 (1.64%)	3(1.28%)	
Skin	0	4 (2.19%)	4(1.71%)	
Gum	0	3 (1.64%)	3(1.28%)	
Hematemesis/melena	0	3 (1.64%)	3 (1.28%)	

*-- Significant, **-- Very significant, *** -- Extremely significant

Table 3: Hematological, biochemical distribution:

Parameter	DF (51)	DHF (182)	% amongst total (233)	P value
Hematocrit (L/L)				
≥40 (37)	2 (3.92%)	4 (2.19%)	6 (2.57%)	2.46
(30-40)	20 (39.21%)	120 (65.93%)	140 (60.08%)	0.0003**
(<30)	29 (56.86%)	58 (31.86%)	37.33	0.0006**
Hemoglobin (gm/dl)	10.5±1.4	10.3±1.1	-	
Total leukocyte count				
<1000-3000/cc	20 (39.21%)	60 (32.96%)	80 (34.33%)	0.20
>3000-4000/cc	19 (37.25%)	80 (43.95%)	99(42.48%)	0.19
>4000/cc	12 (23.52%)	42 (23.07 %)	54(23.17%)	0.47
Platelet count				
≤20000/cc (8)	0	8 (4.39%)	8(3.43%)	-
>20000 – 40000/cc	0	28 (15.38%)	28(12.01%)	-
SGOT >3 times normal	15 (29.41%)	66 (36.26%)	81(34.76%)	0.18
SGPT >100 – 200 IU/L	10 (19.60%)	31 (17.03%)	41(17.59%)	0.33
SGPT >200 – 350 IU/L	5 (9.80%)	18 (9.89%)	23 (9.87%)	0.49
SGPT >350 IU/L	2 (3.92%)	14 (7.69%)	16 (6.86%)	0.17
INR >1.5 (21)	0	21 (11.53%)	21 (9.01%)	-

** Very significant, SGOT: Serum aspartate aminotransferase, SGPT: Serum alanine aminotransferase; INR: International normalized ratio

Table 4: Radiological distribution:

Items		DF (51)	DHF (182)	% Amongst total patients (233)
USG	Ascites	0	3 (1.64%)	1.28
	Hepatomegaly	7 (13.72%)	9 (4.94%)	6.86
	Ascites & Hepatomegaly	0	6 (3.29%)	2.57
	Hepatosplenomegaly	0	0	0
Chest x-ray		0	13 (7.14%)	5.57

DISCUSSION

Age group affected by dengue fever as shown by Narayanan et al[4] was 7 to 8 years of age, which was similar to the study done by Kabra SK et al[5] and Banik GB et al.[6] Though dengue fever is a well-known disease of child-age group, but since 1980's there is slight inclination towards higher age group in case of DHF, as shown in various studies in Latin America and South-East Asia. Similarly, in our study, the mean age was 10.31 and 12.6 years in DF and DHF respectively. Though according to previous belief, DHF/DSS is due to either previous infection or passive transfer of antibody from the mother[7], but in our study, DHF occurred at higher age group – so it may be due to antibodies, acquired by the patients at earlier ages. According to some author, it may be due to virulent virus rather than pre-infection antibody status.[8]

Few available hospital studies demoed male-female distribution in dengue fever. Kabra SK et al[5] showed girl preponderance as also seen in the study done by Mittal H et al.[9] Three independent studies in India and Singapore showed that males were twice more common than females.[10, 11] Hospital based study in Delhi showed male to female ratio 2.5:1.[12] Similarly, in our study, there was slight edging of boys over girls. In study done by Mittal et al showed that fever (100%), headache (63%), abdominal pain (71%) and petechiae (35.5%) were more common.[9] Fever, vomiting were most frequent symptoms as shown by Narayanan M et al.[4] Similar pictures were observed in our study, but in addition, headache, anorexia was also frequently found.

In our study, 76.92% DHF patients showed positive tourniquet test, which was much higher than that was observed in the study of Kabra et al.[5] It may be due to thrombocytopenia and capillary fragility, either or both. Low proportion of positivity in tourniquet test in Indian population may be due to darker skin color or dengue strain difference in Indian subcontinent.[13, 14]. The tourniquet test will never correlate with overt bleeding manifestation as shown by Wali et al.[15] It may be due to difference in pathogenesis, like, vascular permeability and/or capillary fragility.

Since in our study, only 13 patients showed evidence of bleeding, amongst them, evidence of epistaxis, gum bleeding and hematemesis were observed in 1.64% of DHF patients, which was very low as compared to other studies [5]. According to WHO's protocol for management of DHF, 1-2 hourly documentation of Hematocrit (Hct) value is very essential for monitoring intravenous fluid therapy. But, if pretreatment Hct value is not known, it is very difficult to demonstrate the percentage of hemoconcentration in DHF. Hemoconcentration is very important factor that correlates platelet count with bleeding manifestations. This was shown in different studies.[16, 17]. In our study, Hct >40 was observed in 3.92% of DF and 2.19% of DHF patients, whereas, Hct >30-40 was observed in 65.93% of DHF patients. So according to our study, it may not be a good indicator of monitoring fluid therapy in infants and children in presence of moderate anemia which was near 10 gm% in our study population.

In our study, leucopenia (<5000/cc) was observed in 76.81% of patients, whereas, Ratageri et al[18] showed 21% of patients suffered from leucopenia and Benerjee[19] et al demonstrated no evidence of leucopenia in their studies. So, leucopenia may be an indicator of virulent dengue strain in our epidemic. Our study showed 182 (78.11%) children suffered from thrombocytopenia, amongst them, 36 (19.77%) had platelet count <40000/cc. Similarly, 82% and 96%rombocytopenic patients were described in the studies of Ratageri et al[18] and Banerjee et al[19] respectively. This thrombocytopenia may be due to decreased production in bone marrow, temporary bone marrow suppression[20], virus-antibody complex mediated immune destruction[21] of platelet or increased consumption of platelet induced by secondary infection associated with release of high level of platelet activating factors or increased adhesiveness of platelet to the vascular endothelial cells.[22]

In DHF, there may be evidence of plasma leakage as evidenced by ascites and pleural effusion. In our study, 13 (7.14%) patients showed evidence of pleural effusion in the chest x-ray, 3 (1.64%) patients suffered from isolated ascites and 6 patients (3.29%) suffered from ascites associated with hepatomegaly. On the contrary, 70% and 54% of children demonstrated pleural effusion and ascites respectively in the study of Ratageri et al.[18] According to some observations, massive T-cell activation producing cytokines (interferon γ, interleukin 2 and TNF α) and infected cell lysis by CD 4+ and CD8+ dengue specific lymphocytes are mainly responsible for plasma

leakage. Interaction between infected cells and immune cells induces release of cytokines directly by macrophages and monocytes.

One important laboratory finding is elevation of liver enzymes, which was reported in various studies.[23-.25]. Similarly, in our study, the rise in SGPT >100 U/L was observed in 34.32% of patients.

Evidence of vomiting, hepatomegaly and elevated liver enzymes may be a clue to the diagnosis of dengue in the background of the epidemic.

CONCLUSION

Dengue fever is more prevalent in Kolkata. Mean age of DF and DHF patients were 10.31 and 12.6 years respectively. Male to female ratio was 1.13:1. In seropositive DHF patients, fever, headache, backache, loose motions were the predominant symptoms associated with hepatomegaly, elevated liver enzymes and evidence of plasma leakage. Leucopenia may be due to a virulent strain of dengue virus.

Key-massage: Evidence of fever, vomiting, backache with or without bleeding associated with hepatomegaly, elevated liver enzymes and thrombocytopenia may be a clue to the diagnosis of dengue hemorrhagic fever. Due to the high prevalence of anemia, rise in Hematocrit is not at all helpful to the diagnosis of DHF.

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Competing interests: Nil.

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