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Original article:

Clinico-epidemiological study of dengue illness: A paediatrics study in North Western India

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ABSTRACT

INTRODUCTION: Dengue, an acute febrile illness caused by dengue virus (DENV) is a major cause of symptomatic dengue infection transmitted mainly by the *Aedes aegypti* mosquito and also by the *Aedes albopictus* mosquito. A complete clinico-laboratory profile and clinical outcome with comprehensive understanding of disease severity in dengue fever by analyzing plasma samples from various stages of dengue illness have great clinical relevance in the light of diagnostic and prognostic point of view. Therefore, this study has immense importance in early identification as well as progression of infection in children below 16 year. This longitudinal study is highly suited for studying disease pathogenesis and to monitor dengue fever severity and enhanced our understanding of dengue fever pathogenesis.

MATERIAL AND METHODS: This prospective study was conducted at Department of Paediatrics, Sardar Patel Medical College, Bikaner. Total 80 patients were included in the study with features of dengue illness along with positive dengue serology and 50 healthy controls were included in the study.

RESULTS: In this study Out of total 80 children, 22 (27.5%) children were suffering from DFNWS (dengue fever with non-warning symptoms), 52 (65%) suffering from DFWS dengue fever with warning symptoms) and only 6 (7.5%) suffering from SD (severe dengue). In our study, fever was the most common manifestation of dengue infection and was present in all children (100%) while vomiting, myalgia, headache, pain abdomen, positive tourniquet, rash were also pesent significantly. Thrombocytopenia was present in total 73.7% of cases and overall mean platelet count in DFNWS group was 99.12±37.7, in DFWS group 85.07±33.98 and in SD it was 35.89±13.8 with statistically significant difference ($p<0.01$). Only one child expired and he had severe dengue while 75 patients were discharged and 4 patients were discharged on request.

CONCLUSION: In the present study highest number of case were found in age group 10-15 years with male predominance. These results provide insights into the mechanisms of severe dengue pathogenesis which might serve as therapeutic targets to alleviate severe dengue.

KEYWORDS: Dengue, clinic epidemiological.

INTRODUCTION

Dengue, an acute febrile illness caused by dengue virus (DENV) is a major cause of symptomatic dengue infection with an estimated 390 million infections occurring every year, nearly 100 million of which are clinically apparent. It is the most important arboviral disease globally and a major source of morbidity and

mortality in tropical and subtropical regions of the world[1]. It is a mosquito borne viral infection transmitted mainly by the *Aedesaegypti* mosquito and also by the *Aedesalbopictus* mosquito. The viral infection has four serotypes and each serotype has unique characteristics and exhibit diverse manifestations in a particular population depending upon its interaction with the host response. DENV infection results in a broad spectrum of clinical symptoms, ranging from mild fever to dengue hemorrhagic fever (DHF), the latter can advance to dengue shock syndrome (DSS) and death. The majority of dengue patients recover uneventfully after 5–7 days of acute illness. In a small proportion of patients, however, the initial febrile period is followed by a rapid onset of vascular leakage, thrombocytopenia and hemorrhage indicating DHF. The continual loss of intravascular volume from plasma leakage can very rapidly lead to hypotension and cardiovascular collapse which, if not carefully managed, can result in death. In the absence of an effective antiviral drug, the management of dengue patients is primarily supportive. Early recognition of patients with plasma leakage is thus critical for the initiation of appropriate fluid management to prevent onset of hypovolemic shock. However, because these symptoms become evident only in the critical phase of infection, it is currently not possible to distinguish DF and DHF accurately during the early stages of illness, when the disease is less well differentiated[2]. Therefore, this study has immense importance in early identification as well as progression of infection in children below 16 years.

AIM

To study Clinico-epidemiology of patients suffering from dengue fever.

METHODS

This Prospective observational hospital based study was conducted on total 80 patients with features of dengue illness along with positive dengue serology and 50 healthy controls fulfilling inclusion criteria (<16 years and ruled put malaria infection) and exclusion criteria (Other concomitant illness like malaria, enteric fever, chikungunya etc.) by consecutive sampling during one year (2019) in Department of Paediatrics, Sardar Patel Medical College, Bikaner. After approval of the Institutional Ethics Committee and written informed consent was obtained, detailed history was taken regarding duration and type of fever, abdominal pain, headache, vomiting, myalgia, urine output and bleeding tendencies since day first of admission. Thorough clinical examination was done. Temperature, pulse, respiratory rate, blood pressure, pallor, petechiae/ecchymosis, liver and spleen size and consistency were recorded. Other systemic examination was done in case of relevant history. All the findings were recorded on predesigned proforma. Categorization of dengue illness was made according to WHO Guideline 2009. Further Complete blood cell count, Serum glutamic oxaloacetic transaminase (SGOT), Serum glutamic pyruvic transaminase (SGPT), Serum creatinine blood urea, prothrombin time (PT) with international normalized ratio (INR), blood culture and urine analysis including culture were done in all dengue infected patients. Arterial blood gas analysis, chest radiograph, electrocardiogragh (ECG), ultrasonogram of abdomen, computerized tomography (CT) were done on specific indications. Appropriate blood tests were performed to rule out co-morbid infections like; typhoid fever (widal test and specific blood culture), chikungunya (enzyme immunoassay for the differential detection of IgG and IgM antibodies), peripheral blood film and rapid diagnostic test to rule out malaria parasite. Cases were managed as per standard treatment protocol recommended by WHO (2009). All collected data was entered into excel sheet and analyzed with the help of Epi Info software, from CDC.

RESULTS

In this study Out of total 80 children, 22 (27.5%) children were suffering from DFNWS (dengue fever with non-warning symptoms), 52 (65%) suffering from DFWS dengue fever with warning symptoms) and only 6 (7.5%) suffering from SD (severe dengue). maximum patients 47.5% belonged to age group 10-15 years with mean age 10.02±3.19 years. male predominance over female (although not significant) where total 58.8% were males and 41.2% were females and male to female ratio was 1.42:1, 77.5% were from urban area, majority of patients 48.75% belonged to lower middle socioeconomic status. In our study, fever was the most common manifestation of dengue infection and was present in all children (100%) while vomiting (71.2%), myalgia (60%), headache (55%), pain abdomen (58.7%), positive tourniquet (46.2%), rash (23.7%) were also pesent significantly. Thrombocytopenia was present in total 73.7% of cases and overall mean platelet count in DFNWS group was 99.12±37.7, in DFWS group 85.07±33.98 and in SD it was 35.89±13.8 with statistically significant difference ($p<0.01$). coagulopathy was present in total 6 (7.5%) children, whole blood was required only in 3 patients belonged to SD group, platelet transfusion was required in 9 children DFWS (3) and SD (6) group, while fresh frozen plasma was required in 8 children DFWS (2) and SD (6) groups respectively. When we compared different parameters with dengue severity, the difference between overall Hb, haematocrit, mean TLC and Dengue severity was found statistically insignificant ($p>0.05$), blood urea and serum creatinine had an insignificant difference ($p>0.05$) while SGOT and SGPT had a highly significant difference ($p<0.001$), sodium had insignificant difference ($p>0.05$) and potassium had a significant difference ($p<0.01$). Only one child expired and he had severe dengue while 75 patients were discharged and 4 patients were discharged on request.

Table: 1. Sociodemographic profile

Age Group (years)	No.	(%)
0-<5	6	7.5
5-<10	36	45
10-15	38	47.5
Gender		
Male	47	58.8
Female	33	41.2
Residential Area		
Rural	18	22.5
Urban	62	77.5
Socioeconomic Status		
Upper	1	1.25
Upper Middle	5	6.25
Lower Middle	39	48.75
Upper Lower	23	28.75
Lower	11	13.75

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Table: 2. **Clinico-laboratory profile of dengue in relation to severity of dengue fever**

Presenting Complaints	Severity of Dengue Fever						Total	
	DFNWS		DFWS		SD			
	No.	%	No.	%	No.	%	No.	%
Fever	22	100	52	100	6	100	80	100
Vomiting	13	59.1	40	76.9	4	66.7	57	71.2
Headache	10	45.5	31	59.6	3	50	44	55
Pain Abdomen	3	13.6	41	78.8	4	66.7	47	58.7
Myalgia	13	59.1	32	61.5	3	50	48	60
Retro-Orbital Pain	2	9	7	13.4	2	33.3	11	13.7
Rash	3	13.6	15	28.8	1	16.7	19	23.7
Lethargy	0	-	6	11.5	4	66.7	10	12.5
Shock	0	-	0	-	5	83.3	5	6.25
Hepatomegaly	5	22.7	32	61.5	4	66.7	41	51.2
Positive Torniquet test	7	31.1	26	50	4	66.7	37	46.2
Bleeding Manifestations	0	-	24	46.1	6	100	30	37.5
Ascites	0	-	8	15.3	6	100	14	17.5
Pleural Effusion	0	-	7	13.4	5	83.3	12	15
Edema	1	4.5	14	26.9	3	50	18	22.5
Thrombocytopenia	5	22.7	48	92.3	6	100	59	73.7
Elevated liver Enzymes	3	13.6	21	40.4	4	66.7	28	35

Graph 1. Statistical analysis of Platelet Count at different days

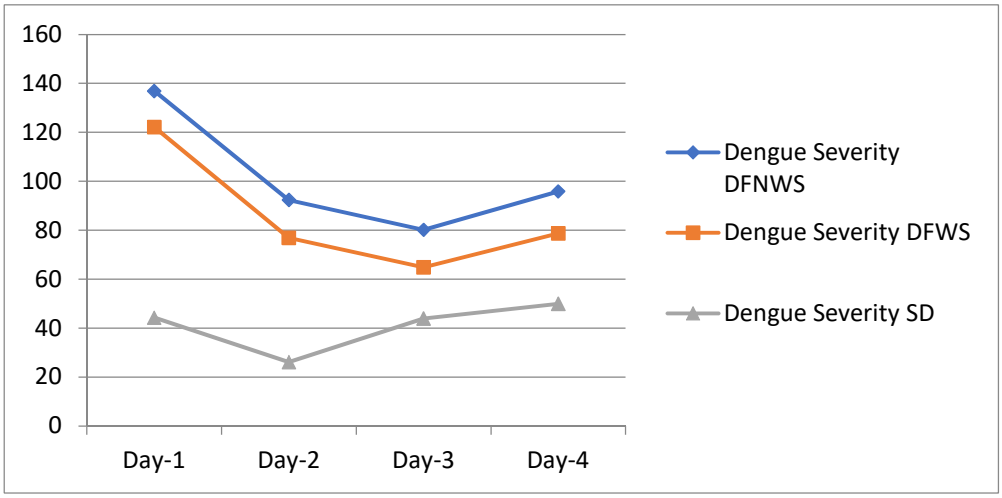

Table 3 **Statistical analysis of different parameters**

Parameters	Dengue Severity						P Value
	DFNWS		DFWS		SD		
	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev	
Haemoglobin (Hb)	10.8	1.84	10.6	1.37	10.5	2.83	0.868
Haematocrit (HCT)	35.5	4.2	35.2	3.7	33.7	8.6	0.664
Platelet count (Thousand)	99.12	37.7	85.07	33.98	35.89	13.8	0.001
Total Leucocyte Count (TLC) (Thousand)	4.9	1.4	4.4	1.3	4.39	2.5	0.383
Blood Urea (mg/dl)	28.59	5.76	28.9	5.9	33.6	15.3	0.262
S. Creatinine (mg/dl)	0.79	0.14	0.91	1.21	0.95	0.63	0.881
SGOT (IU/L)	34.45	9.8	41.5	36.4	206.6	172.3	0.001
SGPT (IU/L)	32.13	10.8	37.5	29.7	157.1	50.3	0.001
Sodium (mEq/L)	136.65	4.05	135.50	4.84	137.8	21.06	0.654
Potassium (mEq/L)	4.1	0.36	4.17	0.37	3.38	0.64	0.001

Table 4. **Distribution of cases according to USG Abdomen**

USG Abdomen	DFNWS n(%)	DFWS n(%)	SD n(%)	Total
Hepatomegaly	6 (27.2)	34 (65.4)	5 (83.3)	45
Splenomegaly	0	2 (3.84)	1 (16.7)	3
Cholecystitis	0	3 (5.7)	3 (50)	6
Ascites	0	9 (17.3)	6 (100)	15
Pleural Effusion	0	8 (15.4)	5 (83.3)	13
Total	22	52	6	

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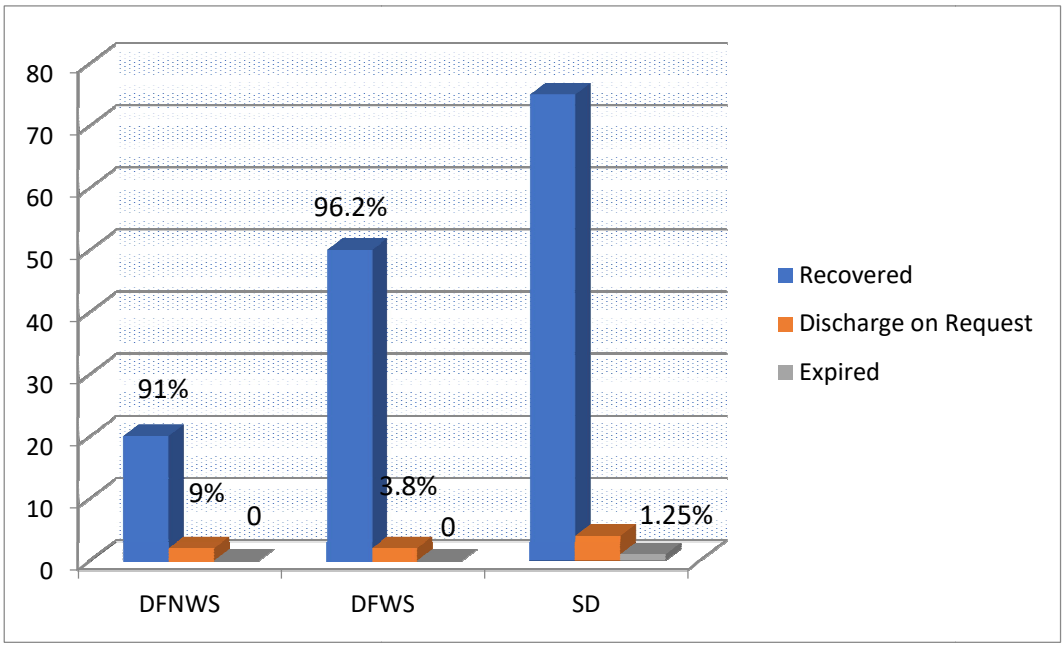
GRAPH: 2. **Distribution of cases according to outcome**



DISCUSSION

This prospective study was conducted in Department of Paediatrics, Sardar Patel Medical College, Bikaner from August 2018 to October 2019 with the objectives to study clinico-laboratory profile with clinical outcome and correlation of identified plasma biomarkers with disease severity in all admitted children suffering from serological diagnosed dengue infection. Total 100 children were admitted with features of dengue illness along with positive dengue serology in this duration. Out of them 18 children had other co-infection; 9 were positive for malaria parasite, 5 had urinary tract infection, 4 had enteric fever and guardian of 2 children refused for written consent, so excluded from current study. Thus, 80 admitted children were enrolled in this study for further analysis.

In our study maximum patients 47.5% belonged to age group 10-15 years followed by those between 5-<10 years 45% and those between 0-5 years were 7.5% with mean age 10.02±3.19 years. A study conducted in Punjab by Dhooria et al[3]observed that children between 10-15 years were most commonly affected (59%) which is quite similar to our study. A study was conducted in a tertiary care hospital in Maharashtra by Nishikant et al[4]on dengue fever which shows that highest number of children were found in age group 6-12 years (61%) followed by 35% in age group of 1-<6 years and 4% children fell in <1 year age group. Oncog et al[5]showed different endemicity pattern with more prevalent age group to be affected as children between 4to7 year old (47.59%) followed by 30% in 8-11 years old and 12.22% in 12-14 years old and least prevalence in 0-3 years old (10.19%). Thus in our study it is observed that the age group between 10-15 years is more susceptible for dengue infection most probably due to more outdoor activities of this age group.

In our study there was increased preponderance of dengue infection in male children (58.8%) as compared to female children (41.2%) with M:F ratio 1.42:1. Mittal et al[6] found M: F ratio 1.32:1 and Chandrakanta et al[7]found M: F ratio 1.6:1 which is quite similar to our study.

In our study, 77.5% children belonged to urban background and remaining 22.5% were from rural background, Oncog et al[5]also found that high population density area had higher incidence of dengue infection as compared to low density. Durani et al[8]found 56.8% children from urban area and 43.2% children from rural area that is similar to present study.

In our study majority of patients 48.75% belonged to lower middle socioeconomic status. Pavanet al[9]observed burden of dengue to be 72% in low socioeconomic group. Soghaier et al[10] showed that increase household density is more likely to get dengue infection compared with those who live in less crowded accommodation and household density itself is always associated with low socioeconomic status and poverty. Both studies stated that low socioeconomic status associate with high incidence of dengue infection, which is in favor of the present study.

In our study 80 children admitted with Dengue infection, 22 (27.5%) were classified as Dengue fever with no warning sign (DFNWS); 52 (65%) were as Dengue fever with warning signs (DFWS); and remaining 6 (7.5%) were labeled severe dengue (SD) as per WHO guidelines 2009. Wanigasuriya et al[11] revealed DFNWS in 17.9%, DFWS in77.4%, SD in 4.7%. Mulay et al[12] distributed patients as dengue without warning sign 15.9%, dengue with warning sign 55.7% and severe dengue 28.4%. Sahana et al[13]found that DFNWS was present in 48.11% children, DFWS was present in 27.2% and severe dengue was present in 24.7% of children. In our study children with severe dengue were less in number than other studies due early detection of severity and proper fluid management.

In present study according to presenting complaints, fever was the most prominent complaint. Vomiting was second most common and present in 71.2% children, myalgia in 60%, headache in 55%, pain abdomen in 58.7%, rash in 23.7%, retro-orbital pain in 13.7%. The features of plasma leakage in present study as ascites, pleural effusion, edema and shock were noticed in 17.5%, 15%, 22.5% and 6.25% respectively. Khan et al[14] found ascites and pleural effusion 14.66% and 11.33% respectively, similar to our study. Rahim et al[15] observed that 14.8% children developed ascites and 27.8% developed pleural effusion.

Based on clinical signs and symptoms; 22 children were classified as dengue fever with no warning sign (DFNWS), 52 children as dengue fever with warning sign (DFWS) and 6 children as severe dengue (SD). Mia MW et al[16] (2010) observed results in similar sequence that were fever in 98%, vomiting in 76%, myalgia in 61%, headache in 34%, abdominal pain in 14% and retro-orbital pain in 13%. Ghalige et al[17] show almost similar results stastically; fever 100%, vomiting 67%, pain abdomen 61%, headache 60%, retro-orbital pain 23%. In current study positive tourniquet was in 46.2% children. Arif et al[18] and Malavige et al[19] observed positive tourniquet test in 43.63% and 47.5% respectively just like current study while Daniel et al[20] observed positive tourniquet in 33.67% children.

Thrombocytopenia was observed in 73.7% children in our study. Mean platelet count at the time of admission in DFNWS group was 136.9±69.75/mm^3, for DFWS was 122.2±102.8/mm^3 for SD was 44.3±32.4/mm^3. Alam et al[21] observed thrombocytopenia in 68.5% children similar to our study. Usman et al[22] found in 50% patients, Mulay et al[12] observed thrombocytopenia in 78.4%. Kumar et al[23] had 61820±7620 for non SD and 30980±2465 for severe dengue. Mittal et al[6]showed that a total of 92.6% of children had thrombocytopenia with mean platelet count 38800mm^3 on day of admission. Kirtilaxmi et al[24] observed mean platelet count 1.39 lakh with minimum of ten thousand and maximum of 6.85 lakh.

In present study on day 1st65% of the children showed platelet count <1.5 lakh/mm.[3] 16.25% between 0-20000, 18.75% between 20000-50000 and 30% between 51000-100000, 15% between 1.01-1.5 lakh and 20% >1.5 lakh. Kiritilaxmi et al[24] found that 79% of patient showed thrombocytopenia, 19% <50000, 20% were between 50000-1lakh, 22% were between 1 lakh to 1.5 lakh, 21% patients had platelet count >1.5 lakh which almost similar to our study.

coagulopathy was present in total 6 (7.5%) children similarly Lokanatha et al[25], Karnataka showed prolonged PT in 23.1% of non-severe dengue and 77.3% of SD. Bashir et al[26]observed that PT was prolonged in 9% patients with or without hemorrhage.

whole blood was required only in 3 patients belonged to SD group, platelet transfusion was required in 9 children DFWS (3) and SD (6) group, while fresh frozen plasma was required in 8 children DFWS (2) and SD (6) groups respectively. Requirement of all 3-blood components was significantly associated with severe dengue. Shah et al[27] reported 29.4% patient required fresh frozen plasma, 26.5% patients required platelet transfusion and 11.8% patients required blood transfusion. The requirement of transfusion of blood products was much more in Shah et al[28] study due to more number of children of DSS (41.2%) in comparison to present study (6%).

SGOT was more than 1000 IU/l in 3 children with severe dengue. Mean SGOT was found 34.45±9.8, 41.5±36.4, 206.6±172.3 in patients with DFNWS, DFWS and SD, respectively whereas mean SGPT was found 32.13±10.8 (DFNWS), 37.5±29.7 (DFWS), 157.16±50.3 (SD). Blood urea was found 28.59±5.76 (DFNWS), 28.9±5.95 (DFWS), 33.6±15.3 (SD). Serum Bilirubin was raised in only 10 (12.5%) patients. According to ultrasonography hepatomegaly was the most common finding in 45 (56.25%) followed by ascites in 15 (18.75%), pleural effusion in 13 (16.25%), cholecystitis in 6 (7.5%) and splenomegaly in 3 (3.75%). Shukla et al[29] found hepatomegaly in 51.4 % patients just similar to our study. Khurram et al[30] observed that mild ascites and pleural effusion were the most common finding. Sravani et al[31] found hepatomegaly in 47.1%, ascites in 35.7%, cholecystitis in 25.7%, splenomegaly in 18.6% as in our study. Most of the studies like Basawaraj et al[32], Santhosh et al[33] observed that cholecystitis was the most common ultrasonographic finding which is different from our study. Ultrasound features like ascites, pleural effusion, cholecystitis, hepatomegaly, splenomegaly strongly favour the diagnosis of dengue fever.

In our study 20 (25%) children out of 80 showed hyponatremia. Lumpaopong et al[34] found hyponatremia in 61% patients which was much higher than our study while Mekmullica et al[35] reported hyponatremia in 18.4% patients which was almost similar to our study.[36]

In our study, 7 (8.75%) children out of 80 have hypokalemia {1 child of DFNWS (mean 4.18±0.36meq/l) and 2 children of DFWS (mean 4.17±0.37meq/l)) and 4 children from SD (mean 3.38±0.64meq/l)}. Lumpaopong et al[34] also showed hypokalemia like our study.

In our study 80 children were admitted for dengue, 75 (93.75%) recovered, 4 (5%) discharged on request and 1 (1.25%) expired. Case fatality rate in present study was 1.25%. Kumar et al (2017)[23] found case fatality rate 7%, while Dhooria et al[3]found 3.7%. Early diagnosis and improved case management of DFWS and SD is required to bring down case fatality below 1%.

CONCLUSION

In the present study highest number of case were found in age group 10-15 years with male predominance. Dengue fever with warning signs was the most common presentation in admitted children. Hepatomegaly was

most common physical finding and petechiae were most common bleeding manifestation. Liver dysfunction was predominant with severe dengue illness. In laboratory findings leucopenia appeared earlier than thrombocytopenia in our study. Current WHO guideline (2009) helps in early identification of high risk children according to warning sign so that prompt treatment is given timely.

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