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Study of Clinical Spectrum, Laboratory Profile and Outcome in Dengue Virus-Infected Children Admitted In P.B.M. Children Hospital, Bikaner Rajasthan

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Introduction

Aim : To study the epidemiology, clinical features and outcome of admitted children suffering from dengue infection.

Material and Methods : This prospective study was conducted in Department of Paediatrics, Sardar Patel Medical College, Bikaner from October 2016 to September 2017. Patients who were fulfilling our inclusion and exclusion criteria. Cases were managed as per standard treatment protocol put forward by WHO (2009).

Results : In our series, out of total 100 cases, 32 had DFNWS, 62 had DFWS and 6 had Severe dengue. Total 62% cases were males and 38% cases were females and male to female ratio was 1.63:1. Majority of our children belonged to urban area (73%) while only 27% belonged to rural area. Fever was the most common manifestation of dengue infection and was present in 100% children, next common manifestations was vomiting in 71% children, myalgia 67%, headache 59%, pain abdomen 53%, positive tourniquet 43%, rash 29%, retro-orbital pain 12%, lethargy 7% and shock only 3% cases. Hepatomegaly 50%, positive tourniquet test 43% and bleeding manifestations were present in 39% children. Edema was the most common sign in 22% children, followed by ascites (17%), and pleural effusion (12%). In laboratory profile, thrombocytopenia was found in 71% of children and elevated liver enzymes were found in 33% of children.

Conclusion: 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.

Keywords: DFNWS, DFWS, Myalgia, Hepatomegaly.

Background

Dengue virus was isolated in India for the first time in 1945. The first evidence of occurrence of dengue fever in the country was reported in 1956 from Vellore district in Tamil Nadu. The first dengue hemorrhagic fever outbreak occurred in Calcutta (West Bengal)[1,2] and since then more and more new states have been reporting the disease which mostly strikes in epidemic proportions often inflicting heavy morbidity and mortality. Several fatal forms of the disease, i.e., dengue hemorrhagic fever, dengue shock syndrome have been reported in India from time to time in Kolkata, Delhi and Chennai[3]. Infection with dengue virus (DENV) causes a spectrum of clinical manifestations ranging from mild dengue fever (DF) to potentially lethal dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS)[4]. DF is generally self-limiting, but its symptoms can be debilitating and cause considerable incapacitating morbidity, which have a significant health

and economic toll in the society. In a small percentage of patients, DF evolves to the more severe forms of DHF and DSS, which are characterized by abnormal hemostasis, vascular leakage and liver damage. There is currently no specific antiviral therapy or vaccine available for DF or DHF/DSS. Furthermore, the underlying molecular mechanisms of DENV pathogenesis are still unclear. Therefore, the pathological differences between the severe DHF/DSS and the mild, self-limiting; DF suggests differential virus-host interactions in the susceptibility to the disease. Both viral and host immune factors seem to be involved, but the role of each is not fully understood[5].

Several factors have traditionally limited the usefulness of these studies in biomarker development. Firstly, the highly variable nature of patient cohorts (e.g. paediatric versus adults; ethnicity) used makes it difficult to compare the results of these various studies. Secondly, most studies have examined 'case versus control' type of sample population instead of longitudinal studies to distinguish 'predictors' from 'indicators'. Finally, a lack of follow-up in larger population base to test the prognostic potential of proposed markers limits their clinical application. The early dengue infection and outcome (EDEN) study in Singapore prospectively recruits and follows-up adult dengue patients in Singapore through early febrile, defervescence as well as convalescence stages[6] of the disease. This makes this longitudinal study highly suited for the identification of prognostic markers of severe dengue disease. The current study aims to provide 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.

Material & Methods

This prospective study was conducted in Department of Paediatrics, Sardar Patel Medical College, Bikaner from October 2016 to September 2017. Total 121 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; 8 were positive for malaria parasite, 5 had urinary tract infection, 3 had enteric fever and 2 were positive for chikungunya; and guardian of 3 children refused for written consent, so excluded from current study. Thus, 100 admitted children were enrolled in this study for further analysis.

Inclusion Criteria

- Children <16 years who were serologically positive with dengue illness were included.
- Malaria infection was rule out by microscopy examination and RDT.
- Those willing to provide written informed consent and comply with protocol requirement.

Exclusion Criteria

- Other concomitant illness like malaria, enteric fever, chikungunya etc. judged by history and physical examination.
- Subjects unwilling to consent for the study.

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.

Statistical Analysis

Collected data were transferred into SPSS version 17.0 and were analyzed with the help of frequency tables,

percentage and appropriate statistical test wherever applicable.

Management

Cases were managed as per standard treatment protocol put forward by WHO (2009).

Results

Total 121 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; 8 were positive for malaria parasite, 5 had urinary tract infection, 3 had enteric fever and 2 were positive for chikungunya; and guardian of 3 children refused for written consent, so excluded from current study. Thus, 100 admitted children were enrolled in this study for further analysis.

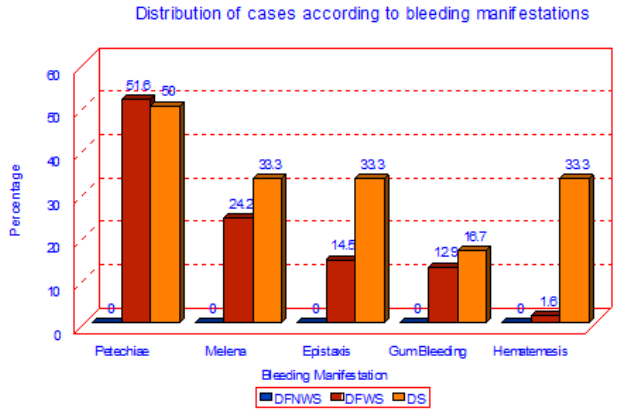
Table 1: Clinico-laboratory profile of dengue in relation to severity of dengue fever

Presenting Complaints	Severity of Dengue Fever						Total	
	DFNWS		DFWS		SD			
	No.	%	No.	%	No.	%	No.	%
Fever	32	100	62	100	6	100	100	100
Vomiting	21	65.6	46	74.2	4	66.7	71	71.0
Headache	17	53.1	40	64.5	2	33.3	59	59.0
Pain Abdomen	5	15.6	46	74.2	2	33.3	53	53.0
Myalgia	23	71.9	41	66.1	3	50.0	67	67.0
Retro-Orbital Pain	1	3.1	9	14.5	2	33.3	12	12.0
Rash	2	6.2	26	41.9	1	16.7	29	29.0
Lethargy	0	-	4	6.5	3	50.0	7	7.0
Shock	0	-	0	-	3	50.0	3	3.0
Hepatomegaly	7	21.9	38	61.3	5	83.3	50	50.0
Positive Torniquet test	10	31.3	29	46.8	4	66.7	43	43.0
Bleeding Manifestations	0	-	33	53.2	6	100	39	39.0
Ascites	0	-	11	17.7	6	100	17	17.0
Pleural Effusion	0	-	7	11.3	5	83.3	12	12.0
Edema	2	6.3	17	27.4	3	50.0	22	22.0
Thrombocytopenia	6	18.8	59	95.2	6	100.0	71	71.0
Elevated liver Enzymes	1	3.1	28	45.2	4	66.7	33	33.0

According to presenting complaints, fever was the most common manifestation of dengue infection and was present in 100% children, next common manifestations was vomiting in 71% children, myalgia in 67%, headache in 59%, pain abdomen in 53%, positive tourniquet in 43%, rash in 29%, retro-orbital pain in 12%, lethargy in 7% and shock in only 3% cases. Hepatomegaly in 50%, positive tourniquet test in 43% and bleeding manifestations were present in 39% children. According to extravasation of plasma, edema was the most common sign in 22% children, followed by ascites (17%), and pleural effusion (12%). In laboratory profile, thrombocytopenia was found in 71% of children and elevated liver enzymes were found in 33% of children.

Table 2 : Distribution of cases according to bleeding manifestation

Bleeding Manifestation	DFNWS (n=32)	DFWS (n=62)	SD (n=6)	Total
Petechiae	0	32(51.6)	3 (50)	35
Melena	0	15(24.2)	2(33.3)	17
Epistaxis	0	9(14.5)	2(33.3)	11
Gum Bleeding	0	8(12.9)	1(16.7)	9
Hematemesis	0	1(1.6)	2(33.3)	3



According to bleeding manifestations, no patients of DFNWS group had any type of bleeding manifestation while in DFWS children, 51.6%, 24.2%, 14.5%, 9% and 1.6% cases had petechiae, melena, epistaxis, gum bleeding and hematemesis respectively while in SD group, 3 cases had petechiae, 2 patients each had melena, epistaxis and hematemesis while only 1 patient had gum bleeding.

Table 3: Statistical analysis of Haemoglobin at different days.

Hb (on day)	Dengue Severity						F	P
	DFNWS		DFWS		SD			
	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev		
1	8.28	1.44	9.81	1.53	10.80	2.48	12.740	<0.001
2	8.02	1.29	9.47	1.52	10.95	3.76	12.160	<0.001
3	7.92	1.09	9.19	1.38	10.67	2.54	14.379	<0.001
4	8.31	1.39	9.61	1.46	10.12	3.30	8.091	0.001

According to above table, when we compared dengue severity with haemoglobin, mean haemoglobin on day 1, in DFNWS group was 8.28±1.44gm%, in DFWS it was 9.81±1.53gm% and in SD 10.80±2.48 gm%. On applying ANOVA test, the difference was found statistically highly significant (p<0.001)> on day 2nd, mean haemoglobin in DFNWS group was 8.02±1.29gm%, in DFWS it was 9.47±1.52gm% and in SD 10.95±3.76 gm% and this difference was found statistically highly significant (p<0.001). On day 3rd, mean haemoglobin in DFNWS group was 7.92±1.09gm%, in DFWS it was 9.19±1.38gm% and in SD 10.67±3.30 gm% and this difference was found statistically highly significant (p<0.001).On 4th day, mean haemoglobin in DFNWS group was 8.31±1.39gm%, in DFWS it was 9.61±1.46gm% and in SD 10.12±3.30 gm% and this difference was found statistically highly significant (p<0.001).

Table 4:Statistical analysis of Haematocrit at different days

Haematocrit (on day)	Dengue Severity						F	P
	DFNWS		DFWS		SD			
	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev		
1	33.26	4.45	36.22	5.11	36.40	9.46	3.537	0.033
2	31.37	4.07	33.83	6.28	35.88	11.62	2.353	0.101
3	29.98	3.99	32.34	4.25	33.60	7.43	3.682	0029
4	32.10	4.19	33.71	6.37	31.66	9.33	0.944	0.393

In our study, we compared haematocrit with severity of dengue. Mean haematocrit on day 1 in DFNWS group was 33.26±4.45, in DFWS it was 36.22±5.11 thousand and in SD it was 36.40±9.46. On applying ANOVA test, the difference was found statistically significant (p<0.05).

On day 2nd, mean haematocrit in DFNWS group was 31.37±4.07, in DFWS it was 33.83±6.28 and in SD group it was 35.88±11.62 and this difference was statistically insignificant (p>0.05).

On day 3rd, mean haematocrit in DFNWS group was 29.98±3.99, in DFWS it was 23.50±4.25 and in SD group it was 33.60±7.43 and this difference also found statistically significant (p<0.05).

On day 4th, mean haematocrit in DFNWS group was 32.10±4.19, in DFWS it was 33.71±6.37and in SD group it was 31.66±9.3 thousand and this difference was found statistically insignificant (p>0.05).

Table 5: Statistical analysis of Total Leucocyte Count at different days.

TLC (in thousands) (on day)	Dengue Severity						F	P
	DFNWS		DFWS		DS			
	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev		
1	5.10	2.04	4.06	1.42	2.88	1.42	6.613	0.002
2	4.65	1.48	4.78	3.92	3.20	1.45	0.654	0.522
3	4.64	1.41	4.56	1.60	4.02	1.43	0.417	0.660
4	5.85	6.75	4.76	2.12	4.16	1.79	0.859	0.427

In our study, we compared TLC with severity of dengue. Mean TLC on day 1 in DFNWS group was 5.10±2.04 thousand, in DFWS it was 4.06±1.42 thousand and in SD it was 2.88±1.42 thousand. On applying ANOVA test, the difference was found statistically significant (p<0.01).

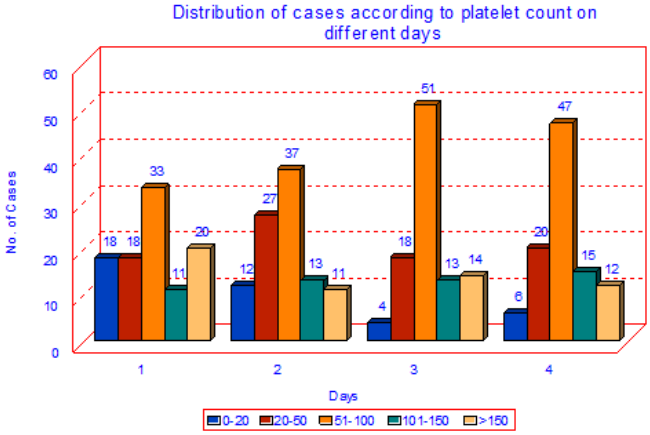
On day 2nd, mean TLC in DFNWS group was 4.65±1.48 thousand, in DFWS it was 4.78±3.92 and in SD group it was 3.20±1.45 thousand and this difference was statistically insignificant (p>0.05).

On day 3rd, mean TLC in DFNWS group was 4.64±1.41 thousand, in DFWS it was 4.56±1.60 and in SD group it was 4.02±1.43 thousand and this difference also found statistically insignificant (p>0.05).

On day 4th, mean TLC in DFNWS group was 5.85±6.75 thousand, in DFWS it was 4.76±2.12 and in SD group it was 4.16±1.79 thousand and this difference was found statistically insignificant (p>0.05).

Table 6:Statistical analysis of Platelet Count at different days.

Platelet count (in thousands) (on day)	Dengue Severity						F	P
	DFNWS		DFWS		SD			
	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev		
1	184.84	88.71	58.64	47.16	31.21	49.40	45.069	<0.001
2	147.06	68.41	47.55	22.21	37.67	27.97	59.528	<0.001
3	146.83	72.22	63.55	25.94	44.00	14.04	27.926	<0.001
4	150.66	72.42	56.68	23.47	60.97	23.78	46.478	<0.001



In our study, we compared platelet count with severity of dengue. Mean Platelet count on day 1 in DFNWS group was 184.84±88.71 thousand, in DFWS it was 58.64±47.16 thousand and in SD it was 31.21±49.40 thousand. On applying ANOVA test, the difference was found statistically highly significant (p<0.001).

On day 2nd, mean platelet count in DFNWS group was 147.06±68.41 thousand, in DFWS it was 47.55±22.21 and in SD group it was 37.67±27.97 thousand and this difference was statistically highly significant (p<0.001).

On day 3rd, mean platelet count in DFNWS group was 146.83±72.22 thousand, in DFWS it was 63.55±25.94 and in SD group it was 44.00±14.04 thousand and this difference also found statistically highly significant (p<0.001).

On day 4th, mean platelet count in DFNWS group was 150.66±72.42 thousand, in DFWS it was 56.68±23.47 and in SD group it was 60.97±23.78 thousand and this difference highly significant (p<0.001).

Table 7: Statistical analysis of different parameters

Parameters	Dengue Severity						F	P
	DFNWS		DFWS		SD			
	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev		
Haemoglobin (Hb)	8.13	1.19	9.52	1.36	10.26	2.88	11.951	<0.001
Haematocrit (HCT)	31.68	3.70	34.03	4.72	34.38	8.88	2.765	0.068
Platelet count (Thousand)	157.35	70.59	56.61	20.38	43.46	24.05	60.235	<0.001
Total Leucocyte Count (TLC) (Thousand)	5.06	2.01	4.54	1.65	3.57	1.30	2.138	0.123
Blood Urea (mg/dl)	28.03	5.03	30.97	5.54	30.17	9.22	2.850	0.063
S. Creatinine (mg/dl)	0.60	0.13	0.71	0.21	0.73	0.44	3.068	0.051
SGOT (IU/L)	34.93	14.70	57.05	69.66	477.33	613.95	23.117	<0.001
SGPT (IU/L)	34.07	13.47	53.19	56.08	70.00	958.11	24.841	<0.001
Sodium (mEq/L)	138.65	2.88	135.50	4.84	130.67	5.16	10.837	<0.001
Potassium (mEq/L)	4.27	0.42	4.17	0.37	3.67	0.54	5.784	0.004

Above table shows overall mean of different parameters. Overall mean Hb in DFNWS group was 8.13±1.19gm%, in DFWS group it was 9.52±1.36 and in SD group it was 10.26±2.88 and the difference between overall Hb and Dengue severity was found statistically highly significant (p<0.001).

Overall mean haematocrit in DFNWS group was 31.68±3.70, in DFWS it was 34.03±4.72 and in DS group it was 34.38±8.88 and the difference was found statistically insignificant while mean platelet count in DFNWS group was 157.35±70.59, in DFWS group 56.61±20.38 and in SD group it was 43.46±24.05 and this difference was found statistically highly significant (p<0.001). Overall mean TLC in DFNWS group was 5.06±2.01, in DFWS it was 4.54±1.65 and in SD group it was 3.57±1.30 and this difference was also found statistically insignificant (p>0.05).

When we compared different parameters with dengue severity, 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 a significant difference ($p<0.001$) and potassium had a significant difference ($p<0.01$).

Table 8: Distribution of cases according to platelet count on different days.

Days	Platelet Count (in thousands)				
	0-20	20-50	51-100	101-150	>150
1	18	18	33	11	20
2	12	27	37	13	11
3	4	18	51	13	14
4	6	20	47	15	12

Table 12 shows distribution of children according to platelet count on different days. On day one 18 children each had their platelet count between 0-20 and 20-50 thousand while 33, 11 and 20 children had their platelet count between 51-100, 101-150 and >150 thousand respectively.

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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