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"A STUDY ON CLINICAL CORRELATION AND OUTCOME WITH HEPATIC DYSFUNCTION IN CHILDREN WITH DENGUE FEVER IN A TERTIARY CARE HOSPITAL"

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ABSTRACT This study was conducted to know about the clinical correlation and outcome of hepatic dysfunction in children with dengue fever. We conducted Prospective observational study by including Dengue NS1 Ag and/or IgM positive children. After detailed clinical examination and haematological investigation children were categorized into 3 groups as (a) DNWS: dengue fever with no warning signs (b) DWWS: dengue fever with warning signs (c) SDF: severe dengue fever. Severity of hepatic dysfunction were statistically analysed and compared between different categories of dengue fever severity. We included total 100 children with dengue fever in our study. Prevalence of hepatic dysfunction in our study was 34%. Proportion of hepatic dysfunction patients with severe disease were 58.8% as against 4.5% without hepatic dysfunction. Distribution according to signs revealed that altered sensorium, seizures, hypotension, bradycardia, hepatomegaly were seen predominantly in patients with hepatic dysfunction. 100% of dengue patients with hepatic dysfunction were admitted for more than 14 days and 45.71% were admitted for 7-14 days showing the statistically significant association of hepatic dysfunction and duration of hospital stay. All 3 i.e. 100% of dengue deaths were associated with hepatic dysfunction.

KEYWORDS : hepatic dysfunction, DWNS(Dengue with no warning signs), DWWS(Dengue with warning signs), Severe dengue, hepatomegaly.

INTRDUCTION:

Dengue or break bone fever has gradually evolved as one of the important causes of febrile illness in the tropical and subtropical region[1,2] which is an arboviral infection with the largest worldwide incidence.[3] Host factors including the relentless urbanization with poor hygiene, dilapidated health systems to increasing international travel, fuel the spread of this disease geographically and increase the disease burden of tropics significantly.[1,2,3] Dengue infections are known to present with a diverse clinical spectrum, ranging from asymptomatic illness to fatal outcome. Unusual manifestations have become more common. These include encephalitis, Guillian-Barre Syndrome, dengue hepatitis, myocarditis and acute respiratory distress syndrome. Hepatic dysfunction varies from mild injury with elevation of transaminase activity, hepatomegaly to severe damage with jaundice and fulminant hepatic failure. The degree of liver dysfunction in children with dengue infection varies from mild injury with elevation of transaminase activity, hepatomegaly (tender/non-tender) to severe injury with jaundice and fulminant hepatic failure.[9] Since dengue fever is known for its hematological complications, this present study is being done to correlate the same with its clinical outcomes. Early recognition and prompt initiation of appropriate supportive treatment can decrease the morbidity and mortality. Most data reported on abnormal liver functions in dengue are retrospective. Therefore this crosssectional study with new data was undertaken to assess the spectrum of hepatic involvement in children with Dengue infection at a tertiary care centre.

Objectives:

- To study the hepatic dysfunction in children with dengue infection
- To study the clinical correlation like clinical features, laboratory parameters, morbidity and mortality.
- To study the clinical correlation and outcome with hepatic dysfunction in children with dengue infection.

MATERIALS AND METHODS:

We conducted Prospective Observtional Study where Dengue NS1 Ag and IgM positive were included. After obtaining informed consent, a pre structured proforma was used to record the relevant information from each subject. After detailed clinical examination and haematological investigation children were categorized into 3 groups as (a) DNWS: dengue fever with no warning signs (b)DWWS: dengue fever with warning signs (c)SDF: severe dengue fever. Severity of hepatic dysfunction were statistically analysed and compared between different categories of dengue fever severity.

RESULTS:

Table 1: Distribution according to age

		Frequency	Percent
Age group in years	<1	10	10.0
	2 to 5	31	31.0
	6 to 10	49	49.0
	Total	100	100.0

We included total 100 children with dengue fever in our study. Majority of them were from 6-10 years i.e. 49% followed by 10% from less than 1 years and 31% from 2-5 years age group.

Table 2: Distribution according to gender

		Frequency	Percent
 Gender	Male	61	61.0
	Female	39	39.0
	Total	100	100.0

61% were males and 39% were females.

Table 3: Distribution according to dengue severity grade

	No. of patients
DNWS	42
DWWS	35
SD	23
Total	100

Distribution according to dengue severity grade revealed that majority i.e. 42% had DNWS, 35% had DWWS and 23% had SD.

Table 4: Distribution according to age group and hepatic dysfunction

		Hepatic dysfunction				Total		p
		Yes		No			Total %	
		No	%	No	%			
Age group in years	1 month to 1 years	6	60	4	40	10	100	0.04, Significant
	1 to 5 years	9	29.03	22	70.97	31	100	
	6 to 14 years	19	38.77	30	61.22	49	100	
	Total	34		66		100		

Prevalence of hepatic dysfunction in our study was 34%. There were 10 patients with age 1month to 1year out of which 60% had hepatic dysfunction which is significantly high. There were 31 patients

between 1 to 5 years and in that 29.03% had hepatic dysfunction and 70.97% did not. There were 49 patients between 6 to 12 years of which 61.22% did not have hepatic dysfuction. We observed statistically significant association between age and hepatic dysfunction in our study (p<0.05).

Table 4: Distribution according to age group

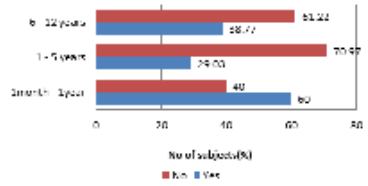

Table 5: Distribution according to dengue severity and hepatic dysfunction

		Hepatic dysfunction				Total	Total (%)	P
		Yes		No				
		No	%	No	%			
Dengue grade	DNWS	4	9.52	38	90.47	42	100	0.0001, Highly significant
	DWWS	10	28.57	25	71.42	35	100	
	SD	20	86.95	3	13.04	23	100	
	Total	34		66		100		

Proportion of hepatic dysfunction patients with severe disease were 86.95% as against 13.04% without hepatic dysfunction. Proportion of hepatic dysfunction patients with DWWS were 28.57% as against 71.42% without hepatic dysfunction. Proportion of hepatic dysfunction patients with DNWS were 9.52% as against 90.47% without hepatic dysfunction. We observed statistically significant association between severity of dengue disease and hepatic dysfunction in our study (p<0.05).

Table 6: Distribution according to symptoms in hepatic dysfunction

Symptoms	Hepatic dysfunction				Total	p	Inference
	Yes (n-34)		No (n-66)				
	No	%	No	%			
Fever	34	100.0	66	100.0	100	--	---
Headache	32	94.1	50	75.8	82	0.02	Significant
Arthralgia	25	73.5	46	69.7	71	0.68	Not significant
Loose stools	29	85.3	23	34.8	52	0.0001	Highly significant
Myalgia	30	88.2	63	95.5	93	0.18	Not significant
Persistent Vomiting	34	100.0	2	3.0	36	0.0001	Highly significant
Pain in abdomen	34	100.0	34	51.5	68	0.0001	Highly significant
Skin bleed	20	58.8	6	9.1	26	0.0001	Highly significant
Mucosal bleed	16	47.1	1	1.5	17	0.0001	Highly significant

Table 7: Distribution of patients with bleeding manifestations(skin and mucosal)

Platelet count	<20000/micL	20000-50000/micL	Total	P value
Total	13	17	30	0.019, Significant
Pts with hepatic dysfunction (%)	7(53%)	13(76%)	20	
Pts without hepatic dysfunction (%)	6(47%)	4(24%)	10	

There were total 30 patients with bleeding manifestations. Of the total 30, 13 patients had platelet count <20,000/micL. Out of those 13 patients, 53% patients had hepatic dysfunction as against 47% without hepatic dysfunction which is not much significant. But there were 17 patients with platelet count 20,000 to 50,000/micL and 76% patients with hepatic dysfunction as compared to 24% without hepatic dysfunction, showing significant association (p<0.05). It means in patients with hepatic dysfunction, there was significant bleeding even when the platelet count were not significantly reduced.

Table 8: Distribution according to signs in hepatic dysfunction

Signs	Hepatic dysfunction				Total	p	Inference
	Yes (n-34)		No (n-66)				
	No	%	No	%			
Altered sensorium	15	44.1	5	7.6	20	0.0001	Highly significant
Seizures	8	23.5	3	4.5	11	0.04	Significant
Ascitis	14	41.2	1	1.5	15	0.0001	Highly significant
Pleural effusion	30	88.2	6	9.1	36	0.0001	Highly significant
Heatomegaly	34	100.0	8	12.1	42	0.0001	Highly significant
Hypotension	34	100.0	27	40.9	61	0.0001	Highly significant
Bradycardia	31	91.2	10	15.2	41	0.0001	Highly significant

Table 9: Distribution according to Liver function tests in hepatic dysfunction

		Hepatic dysfunction				Total	P
		SGOT		SGPT			
		No	%	No	%		
Dengue grade	DNWS	2	5.88	2	6.89	4	0.042, Highly significant
	DWWS	12	35.29	9	31.09	21	
	SD	20	58.82	18	62.06	38	
	Total	34	100	29	100	63	

Elevated levels of SGOT were seen in 58.82% of SD cases followed by 35.29% DWWS and 5.88% of DNWS cases. Elevated levels of SGPT were seen in 62.06% of SD cases followed by 31.09% DWWS and 6.89% of DNWS cases. This difference in the number of cases with respect to dengue severity grade was found to be statistically significant (p<0.05).

Table 10: Distribution according to WBC in hepatic dysfunction

		Hepatic dysfunction				Total	Total (%)	P
		Yes		No				
		No	%	No	%			
WBC(/micL)	<4000	29	32.22	61	67.77	90	100	0.084, not significant
	4000-11000	5	62.5	3	37.5	8	100	
	>11000	00	00	2	100	2		
	Total	34		66		100		

WBC was found to be reduced in 32% dengue patients with hepatic dysfunction with no significant association of WBC and hepatic dysfunction (p>0.05)

Table 11: Distribution according to platelets in hepatic dysfunction

		Hepatic dysfunction				Total	Total (%)	P
		Yes		No				
		No	%	No	%			
Platelets (/micL)	>1.5L	00	00	2	100	2	100	0.41, not significant
	1-1.5L	00	00	10	100	10	100	
	50000-1L	8	36.36	14	63.63	22	100	
	20000-50000	16	44.44	20	55.55	36	100	
	<20000	10	33.33	20	66.66	30	100	
	Total	34		66		100		

All 100% dengue cases were found to be having reduced platelets below 1 lakhs with no significant association of WBC and hepatic dysfunction (p>0.05)

Table 12: Distribution according to IVC status in hepatic dysfunction

		Hepatic dysfunction				Total	Total (%)	P=0.001, significant
		Yes		No				
		No	%	No	%			
IVC	Collapsed	30	53.57	26	46.42	56	100	
	Normal	4	9.09	40	90.90	44	100	
	Total	34		66		100		

IVC was found to be collapsed in 53% dengue patients with hepatic dysfunction as against 47% patients without hepatic dysfunction showing the statistically significant association dengue, hepatic dysfunction with IVC (p<0.05).

Table 13: Distribution according to use of blood products in hepatic dysfunction

		Hepatic dysfunction				Total	P= 0.0007, Highly significant
		Yes		No			
		No	%	No	%		
Received blood products	Yes	29	85.29	27	40.90	56	
	No	6	17.64	38	57.57	44	
	Total	34	100	66	100	100	

85.29% dengue patients with hepatic dysfunction required blood products (platelets and FFP) showing the statistically significant association of hepatic dysfunction and use of blood products ($p<0.05$).

Table 14: Distribution according to duration of hospital stay in hepatic dysfunction

		Hepatic dysfunction				Total	Total (%)	P
		Yes		No				
		No	%	No	%			
Duration of hospital stay	<7 days	4	7.69	48	92.30	52	100	0.01, Highly significant
	7-14 days	16	45.71	19	54.28	35	100	
	>14 days	13	100	00	00	13	100	
	Total	34		66		100		

100% of dengue patients with hepatic dysfunction were admitted for more than 14 days and 45.71% were admitted for 7-14 days showing the statistically significant association of hepatic dysfunction and duration of hospital stay ($p<0.05$).

Table 15: Distribution according to outcome in hepatic dysfunction

		Hepatic dysfunction				Total	Total (%)	P=0.018, significant
		Yes		No				
		No	%	No	%			
Outcome	Discharge	31	31.95	66	68.04	97	100	
	Death	03	100	00	00	03	100	
	Total	34		66		100		

There were total 3 deaths and all of them had hepatic dysfunction which is 100%. 68.04% patients who were discharged did not have hepatic dysfunction and remaining 31.95% had hepatic dysfunction. Hence statistically significant association of hepatic dysfunction on outcome has been found($p<0.05$).

DISCUSSION:

- **Prevalence of hepatic dysfunction**

Siddappa FD et al97 reported that out of the 52 cases, hepatic dysfunction was present in 35 (67.30%) patients. Most common criteria met in the study to define hepatic dysfunction was elevated liver enzymes 32 (61.53%), followed by hepatomegaly 21 (40.48%), INR≥1.5 in8 (15.38%) children. Jaundice was present in 1 (1.92%) child. None of the patients had acute hepatic failure or hepatic encephalopathy. Hepatomegaly was present in 21 (40.38%) cases. All patients with severe dengue had hepatomegaly. Whereas 68.75% of dengue with warning signs and 35.71% of dengue without warning signs patients had hepatomegaly. This association of hepatomegaly with disease severity was statistically significant ($p = 0.0262$).

Mishra S. et al[96] reported that 58.76% of the cases had normal leukocyte count, while leucopoenia was seen in 25.77% and leukocytosis in 15.46% of the cases. Among the liver enzymes, SGOT was elevated in a larger proportion (47.42%) of patients when compared to alanine aminotransferase (SGPT) which was 30.92%. Elevation in SGOT was significantly seen in those with severe dengue (76.92%, *P* value: 0.0346) rather than nonsevere dengue (42.85%). SGPT was very high (>1000 IU/L) in 3 patients whereas SGOT was very high (>1000 IU/L) in 5 patients. All these patients with high liver enzymes had other severities also. Out of them one child that had very high titre of both liver enzymes succumbed despite admission to the intensive care unit. Parameters like prothrombin time (PT) and activated partial thromboplastin time (aPTT) were abnormal in 23 (23.7%) patients. In 10 (76.9%) cases of severe dengue PT/aPTT levels came out to be abnormal. 27.83% presented with thrombocytopenia (platelet < 100000). 69.23% of severe dengue cases had thrombocytopenia whereas only 21.42% of nonsevere dengue cases had thrombocytopenia. Thrombocytopenia was seen to be more relevant in those with severe dengue. One of the important findings of dengue is raised haematocrit which was seen in 34.02% of the cases and it was statistically not significant.

CONCLUSION:

1. Prevalence of hepatic dysfunction in our study was 34%.
2. We observed higher rate of hepatic dysfunction patients with severe disease were 58.8% in our study.
3. Number of patients with signs and symptoms were significantly more in hepatic dysfunction
4. All liver parameters were significantly elevated in patients with hepatic dysfunction in our study.
5. There was a significant positive association of hepatic dysfunction and death of patients with dengue infection.

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