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ASSESSMENT OF CLINICAL PHENOTYPE WITH FOCUS ON MUSCLE INVOLVEMENT IN PAEDIATRIC PATIENTS WITH DENGUE FEVER

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ABSTRACT

Background: Dengue fever is a major public health problem with morbidity and mortality and the recent epidemic showed variable clinical presentations with unpredictable clinical progression and outcome. Increasing work is being done to identify a biomarker that may predict the various clinical phenotype or complications.

Materials and Methods: This was a prospective study conducted in the department of Pediatrics in a tertiary care hospital. Patients with clinically suspected dengue fever underwent dengue serology tests. Patients were followed till 48 hours post defervescence of

fever or settling of any other ongoing concern. Data analysis was done using Windows SPSS software version 20 and P value less than 0.05 was considered statistically significant.

Results: A total of 200 patients were enrolled in the study. Maximum number of cases (48%) was in the age group of 11 to 15 years. Commonest symptom was fever in 100% cases. NS1 antigen was positive in 96% cases. Severe dengue patients were significantly more in age group of 6 to 10 years (58.2%) Children with dengue with warning signs had significantly raised levels of SGOT, SGPT and CPK.

Conclusion: Biochemical markers may help to identify and appropriately manage the high risk children of dengue fever with warning signs thus reducing morbidity and mortality due to dengue fever.

Keywords: dengue, biochemical markers, muscle involvement

INTRODUCTION

Dengue fever is the most aggressively spreading mosquito borne viral disease with an estimated thirty fold increase in incidence over the last five decades with an unpredictable clinical course and outcome. Dengue fever is a major public health problem with morbidity and mortality and the recent epidemic showed variable clinical presentations with unpredicted clinical progression and outcome (1). In India the first case of Dengue fever was reported in Vellore (1956) and the first case of Dengue Haemorrhagic fever in Calcutta (1963) (2). The incidence of dengue in India has been estimated to be 7.5 to 32.5 million per year (3) and it is one of the leading causes for hospitalization and mortality in India (3).

According to the World Health Organization (WHO) there has been a rise in reporting of dengue cases for the past five decades (2).

An estimated 500,000 people with severe dengue infection require hospitalization every year and 90% of them are children less than 5 years of age. Without proper treatment, Case Fatality Rate in severe dengue is more than 20% and with timely management it can be reduced to less than 1%. Patients can present with varied symptoms which can be mild to life threatening. Myalgia is a commonly described symptom but frank muscle weakness or rhabdomyolysis are rare. Involvement of muscle in patients with dengue infection can present with myalgias, myositis, rhabdomyolysis and hypokalemic paralysis. Mostly affected muscles are back and proximal limb muscles. Myalgia is reported in around 93% of dengue patients (4). The exact pathogenesis of myalgia in dengue infection is not known. Probably at the time of viremia diffuse viral invasion of muscles and the further inflammatory changes in muscles resulting in muscle pain. The myalgias are often transient and self limiting. Increasing work is being done to identify a biomarker that may predict the various clinical phenotype or complications. Hence this prospective study was undertaken to evaluate clinical profile and outcome of dengue fever in children who presented to Pediatric ward with dengue infection at a tertiary care hospital in Rajasthan.

Material and Methods

This was a prospective study conducted in the department of Pediatrics in a tertiary care hospital. The sample size was all the subjects admitted from the time period of January 2020 to July 2021. All children between ages 3 months and less than 18 years with Dengue NS1 Antigen positive or IgM positive with or without IgG positive were included in the study. All cases with any congenital musculo-skeletal anomalies like Duchene Muscular Dystrophy, cases with known connective tissue disease or liver disease and cases who received intramuscular injection within last two weeks were excluded from the study. Patients with clinically suspected dengue fever were administered dengue serology tests. Patients identified with dengue NS1 antigen or Dengue IgM positive were grouped according to WHO criteria as having dengue fever, dengue with warning signs and severe dengue. Screening of children was done using a 'Dengue Day 1 Test'. Patients' positive for NS1 antigen or IgM were informed and requested for consent for the study. All relevant investigations were done as per the clinical course of the illness. Biochemical parameters like SGOT, SGPT, CPK were assessed at admission, at day 7 and day 14 of illness. The admitted patients were managed as per standard protocols of the admitting physician while the OPDs were followed up every other day till recovery with the patient being free to visit earlier if necessary. A child was considered to have clinically recovered if the child was free from fever for more than 24 hours with subjective improvement in clinical condition and was hemodynamically stable.

Statistical analysis

The data was coded and entered in Microsoft Excel Spreadsheet. Analysis was done using Windows SPSS software version 20 (IBM SPSS Statistic Inc Chicago Illinois USA) which included student's t-test. Quantitative data were expressed in mean percentage and standard deviation while qualitative data were in percentage. Chi square test or Fischer's exact test were used whenever two or more than two groups were used whenever two or more than two groups were used to compare. Statistically significant P value was considered as less than 0.05.

Results

A total of 200 patients were enrolled in the study with 70% (140) males and 30% (60) females. Maximum number of cases 96 (48%) were in the age group of 11 to 15 years followed by 30% in the group of 6-10 years. Commonest symptom was fever in 100% cases followed by Pain abdomen (50%), Vomiting (49%), Myalgia (35%) and decreased appetite (32%).

NS1 positive, IgM Positive and IgG Positive were found to be 96%, 34% and 7% respectively. 53% cases were Dengue fever with warning signs, 38.5% with Dengue fever and 8.5% with severe dengue. Severe dengue patients were significantly more in age group of 6 to 10 years (58.82%).

NS1 antigen was significantly positive in severe dengue (88.24%), 100% in dengue fever and 94.34% in dengue fever with warning signs. (p=0.036S). IgG antibody was significantly more positive in severe dengue (23.53%) (P=0.02S). Myalgia was present in 41.18% in

severe dengue, 38.68% in Dengue fever with warning signs and less (29.78%) in dengue fever. Table 1.

In the present study, 37.47% of children with dengue with warning signs had marked increase in CPK levels which is significant (P=0.001S). In the current study, amongst the children with dengue with warning signs, 50.94% had significant elevation of serum AST (SGOT) (P=0.006S) similar to serum ALT (SGPT) t 31.3% with dengue fever with warning signs (p=0.002S).Table2.

Discussion

This prospective study 'Assessment of clinical phenotype with focus on muscle involvement in pediatric patients with Dengue fever' was conducted in children who presented to out-patient department or ward in department of pediatrics, in a tertiary care hospital in Jaipur with dengue infection. This study was conducted with aim to assess the clinical and biochemical profile of pediatric patients with dengue fever and to correlate the disease severity with SGOT, SGPT and CPK as biochemical markers.

In our study, maximum number of cases (48.5%) were in the age group of 11to 15 years followed by 30% in 6-10 years group, 12% in 1-5 years age group, 6% in >15 years age group and 4% in < 12 months age group which was a similar finding in many other studies like Pothapregada S et al (5) where the mean age (standard deviation) of the presentation was 6.9±3.3 years and 6-12 years was the most commonly affected age group. Ramana Sastry C.P.V et al (6) found almost 50% were among 6-8 years age group. Kumari M et al (7) observed that maximum cases were seen in age group >6 years (51%) and the least affected group were 1-3 years of age. Children > 6years are more involved because of the diurnal adaptation of Aedes mosquito in stored water.

In our findings male and female were observed to be 70% and 30% respectively which was similar to a study by Kumari M et al (7).

In our study there were 53% (106) cases of Dengue fever with warning signs (DFW). Dengue fever and severe dengue were seen to be 38.5% and 8.5% respectively. Non-severe dengue included both dengue fever and dengue fever with warning signs and severe dengue included dengue haemorrhagic fever and/or dengue shock syndrome which was in consonance with the study done by Pothapregada S et al (5).

In our study 100% cases presented with fever, followed by Pain abdomen in 50%, Vomiting in 49%, Myalgia in 35% and decreased appetite in 32% which was similar to a study by Pai Jakribettu et al (8) and Garg RK et al (9). Pothapregada S et al (5) also observed that the commonest clinical manifestation was fever in 94.6% of their cases.

In our study NS1 positive, IgM positive and IgG positive were found to be 96%, 34% and 7% respectively. Pothapregada S et al (5) observed that NS1 antigen was positive in 84.2% cases and dengue IgG was positive in 15.7%.

Severe dengue patients were significantly more in the age group of 6-10 years (58.2%) as compared to dengue fever with warning signs and dengue fever. Mayalgia was present in 41.18% cases in severe dengue. Although myalgia is commomnly manifested in dengue fever, myositis is unusual. This possible mechanism for myositis is the release of cytokines which are myotoxic, mainly tumor necrosis factor (TNF alpha) hence injuring the affected muscles (10). These patients need to be detected on time as there is a risk of progressing to

renal failure (11). In children with myositis, dengue fever should be considered as a prime differential diagnosis.

Our study showed that the liver function tests were deranged, SGOT was markedly increased than SGPT in almost all of the dengue patients and it was 3-4 times higher in dengue haemorrhagic fever. 37.47% of children with dengue with warning signs had marked increase in CPK levels which is significant in comparison to children with dengue fever. In the current study, amongst the children with dengue with warning signs, 50.94% had significant elevation of SGOT in children in comparison to children with dengue fever. These findings were similar to studies by Amrita Roy et al (12) and Kulothungan Ravishankar et al (13). According to Shubhankar Mishra et al (14) elevation of SGOT is more associated with severity of infection than SGPT which coincides with our study. Very high levels of SGOT and SGPT indicate severity of the disease as well as morbidity and mortality.

Conclusion

Our study suggested that elevated SGOT and SGPT can predict a more severe form of dengue infection. Hence these Biochemical markers may be useful in identification and close monitoring of potentially sick children with dengue infection and could be indicators of early tissue injury in the acute phase of dengue infection. Dengue virus causes hypoxia, shock or liver damage which have all been suggested to be pathogenic mechanisms for the occurrence of transaminitis. Biochemical markers may help to identify and appropriately manage the high risk children when compared with a large number of children with dengue fever with warning signs, thereby reducing morbidity and mortality due to dengue fever. Application of these results may help optimize resource allocation, leading to a more opportune and effective care of these patients with dengue in disease endemic areas.

Limitations

Most of the patients were lost to follow up because of good outcome and absence of chronicity. Due to corona pandemic patients enrolled in the study were much less than anticipated.

Recommendations

Rising trend of elevated transaminases should be used as predictor of entrance into critical phase. So further studies are recommended to corroborated our evidences and establish standards.

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TABLE 1: Demographic and clinical profile

Variables	GROUP	NUMBER	PERCENTAGE%
AGE	>15 YEARS	12	6
	11-15 YEARS	96	48
	6-10 YEARS	60	30
	1-5 YEARS	24	12
	< 12 MONTHS	8	4
SEX	MALE	140	70
	FEMALE	60	30
INVESTIGATION	NS1 POSITIVE	192	96
	IgM POSITIVE	68	34
	IgG POSITIVE	14	7
CLASSIFICATION OF DENGUE	DENGUE WITH WARNING SIGNS	106	53
	DENGUE FEVER	77	38.5
	SEVERE DENGUE	17	8.5
SYMPTOMS	FEVER	200	100
	PAIN ABDOMEN	100	50
	VOMITING	98	49
	MYALGIA	70	35
	DECREASED APPETITE	64	32

TABLE 2: Biochemical profile

INVESTIGATION	**DENGUE FEVER**		**DENGUE WITH WARNING SIGNS**		**SEVERE DENGUE**		**p-value**
	NUMBER	**PERCENTAGE**	**NUMBER**	**PERCENTAGE**	**NUMBER**	**PERCENTAGE**	
NS1							
Positive	77	100	100	94.34	15	88.24	0.036 **S**
Negative	0	0	6	5.66	2	11.76	
CPK							
< 300	47	61.04	59	55.66	8	47.06	0.001**S**
300-600	15	19.48	7	6.6	6	35.29	
>600	15	19.48	40	37.74	3	17.65	
SGOT							
<100	30	38.96	25	23.58	4	23.53	0.006**S**
100-200	29	37.66	27	25.47	6	35.29	
>200	18	23.38	54	50.94	7	41.18	
SGPT							
<100	52	67.53	44	41.51	10	58.82	0.002**S**
100-200	16	20.78	29	27.36	1	5.88	
>200	9	11.69	33	31.13	6	35.29	