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A Study of Clinical Profile in Correlation with Laboratory Investigations and Radiological Findings in Dengue Fever and Dengue Like Illness in Children Up to 12 Years of Age at A Tertiary Care Hospital in Central India - A Hospital Based Prospective Study

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Abstract

Background: Dengue is an important arboviral infection in tropical countries. Children suffering from dengue fever (DF) shows a large variation in clinical features and laboratory parameters. Hence the present study was undertaken to assess the clinical profile in correlation with laboratory investigations and radiological findings in DF and dengue like illness (DLI) in children up to 12 years of age.

Method: A total 364 patients of age <12 years admitted in pediatric wards with fever, abdominal pain, rash and DLI were studied during the study period from 1st January 2020 to 31st December 2020.

Results: Maximum children (50.27%) had mild DF followed by moderate (30.49%) and severe DF (19.23%). In all clinical spectrum of disease, fever was the predominant complaint and hepatomegaly was commonest sign. Tourniquet test was positive in 40.38% of cases, more in DHF-SH group (97.91%). Overall mean value of platelet count was 46534±32148.73 cells/cumm. The maximum number of cases having platelet count in the range of <20000 cells/cumm in DHF-SH and DHF-III & IV groups. Serum albumin was more in DHF-SH and DHF-III & IV group, ($p<0.001$). The mean SGOT was more in SOI group, DHF-III & IV, DHF-SH, DF+WS and DHF-I & II which was statistically significant ($p<0.05$) whereas mean SGPT was more in SOI group than other groups. Pleural effusion was the most common chest x-ray (31.31%) and USG finding (39.83%).

Conclusion: Mild dengue fever was the most common presentation. On investigation deranged LFT, RFT, pleural effusion, thickened gall bladder wall, hepatomegaly on ultrasound abdomen, pleural effusion on chest radiogram were associated with complicated forms of disease.

Keywords: Dengue fever; Dengue like illness; Hepatomegaly; Tourniquet test; Platelet count; Chest x-ray

Introduction

Dengue is a mosquito borne infection caused by flavivirus and prevalent for more than a century in tropical countries. Global incidence of dengue fever has increased dramatically in the recent decades [1]. According to WHO, about 50–100 million new infections are estimated to occur annually in more than hundred endemic countries, with an intense increase in the number of countries reporting the disease [2]. A very large proportion (≈ 90%) of them are children aged less than five years and 90 percent of DHF are children less than 15 years of age [3]. Also, in India, epidemics are becoming more frequent. Involvement of younger age group and increasing in the frequency of epidemics are indicators of higher incidence of infection. Classical dengue fever is an acute febrile illness but in a small

percentage of Dengue infection, a more severe form of disease known as DHF occurs. Early recognition and meticulous management are very important to save precious lives from this killer disease [1].

Moreover, dengue fever is a self-limited though debilitating illness characterized by fever, headache, gastrointestinal disturbances, body pains and rash. More severe dengue is marked by increased vascular permeability, thrombocytopenia, and hemorrhagic manifestations; in severe cases fluid leakage into the interstitial spaces results in shock, which without appropriate treatment may lead to death, particularly in children. Insights into the pathogenesis of severe dengue, particularly mechanisms of thrombocytopenia are limited [4]. In addition, the lack of necessary laboratory facilities, particularly in remote, rural areas, may cause difficultly in discriminating dengue infection from OFI [5]. Thrombocytopenia and bleeding are common complications of dengue fever. In general platelet count is a poor predictor of bleeding manifestations [6].

Every year the epidemiology and clinical manifestations are changing with dengue fever. So, the trending changes in the epidemiology of dengue has leads to problems with the use of the existing WHO classification. According to new WHO guidelines on Dengue by using a set of clinical and/or laboratory parameters, one sees a clear-cut difference between patients with severe dengue, moderate and mild dengue [1,7]. There are very few studies based on the revised new dengue classification. Hence the present study was undertaken to assess various clinical manifestations, atypical presentation and complications of Dengue fever and to find the association between the clinical findings with laboratory investigations and radiological findings as per new classification of dengue.

Materials and Methods

After obtaining Institutional Ethics Committee approval and written informed consent from each participant's parents, this prospective observational study was conducted in the Department of Pediatrics at Tertiary Care Centre in central India during a period of one year from 1 January 2020 to 31 December 2020. A total 364 children below 12 years of age with fever of 2-7 days who fit into the clinical case definition for probable dengue with or without warning signs and severe dengue according to the new case classification given by WHO Dengue Clinical Case Management guidelines 2009 were included in the study. Children with febrile illness of >2wks duration, patients with any identified specific infection like Malaria, Typhoid, UTI, hematological malignancies which may lead to similar manifestations and those not willing to give consent were excluded from the study.

A detailed clinical history of each patient was taken followed by detailed physical examination as per pre-designed proforma. Detailed history included the fever, headache, bodyache, hematemesis, malena, hematuria and epistaxis, breathing difficulty, convulsions, swelling, puffy face, and decreased frequency of passing urine. Birth history, family history was noted. Detailed clinical examination at the time of admission- The parameters checked were temperature, pulse rate, respiratory rate, blood pressure, capillary refill time, hepatomegaly, splenomegaly, lymphadenopathy, oedema, petechiae and altered level of consciousness. Tourniquet test was done by inflating a blood pressure cuff to a point midway between systolic and diastolic pressure for 5 minutes. The test was considered positive when 20 or more petechiae appeared per square inch on the arm 1.5inch below cubital fossa. Investigations including complete blood count with platelet count, peripheral smear study, urine routine microscopy, blood urea, serum creatinine, liver enzymes and serum bilirubin, X ray chest, MP rapid card test, Dengue (NS1, IgG, IgM), Widal test, USG abdomen and thorax were done. All details were entered in predesigned proforma and results were analysed.

Statistical Analysis

The data were analysed by using SPSS software version 20. For descriptive statistics like proportions, mean and standard deviation were used whereas inferential statistics like chi square test, Independent T test were used. P-value less than 0.05 was taken as significant level.

Observations and Results

Out of total 364 cases studied, 183 (50.27%) children had mild dengue fever, 111 (30.50%) children had moderate dengue fever and 70 (19.23%) had severe dengue fever. The clinical spectrum of cases is shown in table 1

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Table 1: Clinical Spectrum of Cases

Diagnosis		**No.**	**%**
Mild Dengue fever	(Fever without complication and organ involvement)	183	50.27
Moderate Dengue fever	Dengue in high-risk group	05	1.37
	DF with warning signs/symptoms	80	21.98
	DHF- I & II (Minor bleeds)	26	7.14
Severe Dengue fever	DHF with significant hemorrhage	48	13.18
	DHF with shock (DHF III & IV-DSS)	18	4.94
	Severe organ involvement (expanded dengue syndrome)	04	1.09
Total		364	100

The highest number of cases were found in age group of 4 to 6 years (28.57%), ranged from 1 month to 12 years. In all subgroups also there were more affected age group was 4 to 6 years. But it was statistically not significant (P=0.732). Infants comprised 1.09% of total study group and all were in dengue in high-risk group. The males were affected slightly more than females in total and also in all clinical spectrum of diseases but it was not statistically significant with p value of 0.68, (Table 2).

Table 2: Age and sex distribution of patients according to clinical spectrum

Diagnosis	**Age distribution of patients (years)**					**Gender distribution**	
	<1	**1-3**	**4-6**	**7-9**	**10-12**	**Male**	**Female**
Mild DF	00	26	54	52	51	121	62
Dengue in high-risk group	05	00	00	00	00	03	02
DF with warning signs	00	18	22	21	19	58	22
DHF- I & II	00	04	08	07	07	17	09
DHF with significant hemorrhage	00	12	11	13	12	31	17
DHF- III & IV	00	01	07	06	04	10	08
Severe organ involvement	00	00	02	01	01	03	01
Total (no.)	05	61	104	100	94	243	121

All the children (100%) presented with fever as the predominant complaint and also in all clinical spectrum of disease fever was the predominant complaint. The overall mean duration of fever was 6.23 and there was no much variation among subgroups, which was not statistically significant. The skin bleeds were the most common manifestation, among which flushing was commonest noted in 167 cases (45.87%) followed by Petechiae-ecchymosis (31.31%) and Macular rash (22.52%). The bleeding manifestations were more in DHF + significant Hemorrhage group (40.38%) followed by DF + warning signs (25.54%) and DHF- I & II group (23.90%). Other symptoms like cold and cough were more in Mild DF group, (Table 3).

Table 3: Clinical manifestations of Dengue fever

Clinical	**Clinical spectrum**

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manifestations	Mild DF (n-183)	Dengue in high risk (n=05)	DF + warning signs (n=80)	DHF- I & II (n=26)	DHF + significant Hemorrhage (n=48)	DHF- III & IV (n=18)	Severe organ involvement (n=4)
Systemic Symptoms							
Fever	183	05	80	26	48	18	04
Mean duration of fever	5.90	5.88	6.01	6.23	6.20	6.31	6.43
Myalgia	10	00	09	04	06	06	03
Arthralgia	09	00	07	05	02	03	01
Headache	00	00	20	13	15	07	02
Edema	00	03	04	05	09	08	02
Abdominal symptoms							
Vomiting	15	04	38	22	35	17	01
Diarrhea	14	01	05	06	08	07	00
Abdominal pain	00	00	42	21	30	16	04
Abdominal distension	02	00	00	00	00	09	03
Bleeding symptoms							
Flushing	57	01	35	21	34	16	03
Macular rash	00	00	25	22	21	10	04
Petechiae-ecchymosis	00	00	33	24	40	15	02
Melena	00	02	00	00	27	13	02
Hematuria	00	00	00	11	24	11	03
Hematemesis	00	00	00	01	00	01	00
Epistaxis	00	00	00	08	01	00	01
Other symptoms							
Cold	07	01	01	03	05	03	01
Cough	20	01	18	10	05	06	04
Convulsion	00	00	00	00	00	00	02

From the figure 1, it was observed that in all the clinical spectrum the most common sign was hepatomegaly (33.2%). Hepatomegaly was highest in DHF- III & IV group (16/18= 88.88%) followed by in DHF with significant hemorrhage group (41/48= 85.41%) and DHF I and II group (20/26=76.92%). This distribution of signs according to clinical spectrum of disease was statistically significant with p value of 0.0132.

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Figure 1: Distribution of signs according to clinical spectrum

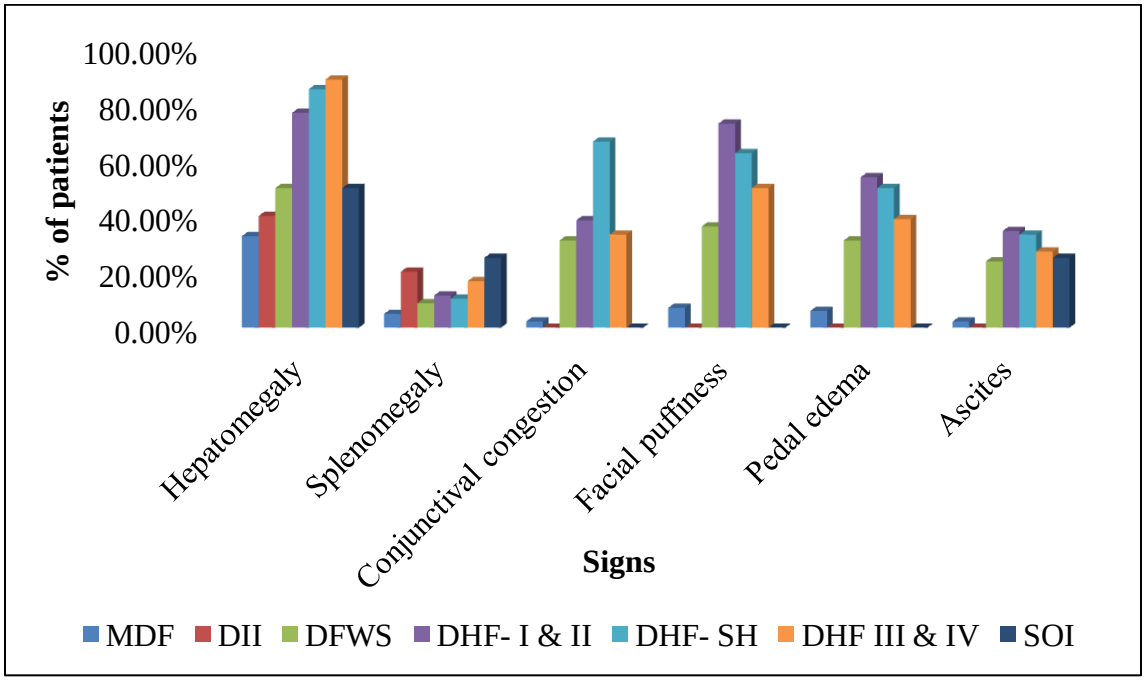
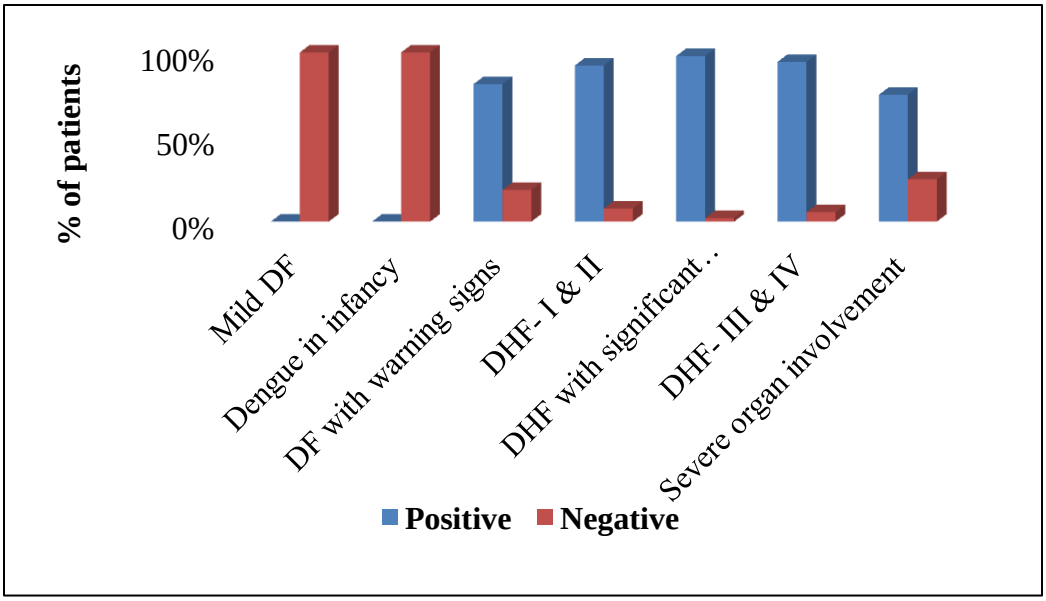


Figure 2 show the analysis of tourniquet test results according to clinical spectrum. The tourniquet test was positive in 40.38% of cases, more in DHF with significant hemorrhage group (97.91%) and DHF- I & II group (92.30%). Characteristically it was found to be positive in only 44.44% of DHF- III & IV group.

Figure 2: Analysis of tourniquet test results according to clinical spectrum



Overall mean value of platelet count was 46534±32148.73 cells/cu mm. The maximum number of cases having platelet count in the range of <20000 cells/cumm in DHF- SH and DHF- III & IV groups. The total mean hemoglobin, hematocrit level, leukocyte count (LC) and total mean of prothrombin time (PT) was 11.833±2.456 gm%, 37.564%, 6643.7 cells/cu mm and 13.9 sec respectively.

The comparison of mean blood urea was statistically insignificant with p value of 0.773. The total mean value of serum creatinine was 0.785 mg/dl, ranged from 0.4 – 1.8 mg/dl. The total mean value of serum albumin was 3.174 gm%. Serum albumin of <3.4 gm% was seen in 61.26% (223 children) of children, more in DHF- SH and

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DHF- III & IV group. It was statistically significant ($p<0.001$). The mean SGOT was more in SOI group, DHF- III & IV, DHF- SH, DF + WS and DHF- I & II which was statistically significant ($p<0.05$). The mean SGPT was more in SOI group than other groups, (Table 4).

Table 4: Distribution of patients according laboratory parameters

Labor. parameters (Means)	Clinical spectrum						
	MDF	**DII**	**DF+WS**	**DHF-I & II**	**DHF-SH**	**DHF- III & IV**	**SOI**
Platelets x 1000	118.5	115.3	31	28.5	23	21	21
Haemoglobin g%	11.11	10.33	10.84	9.65	9.88	10.01	9.75
Hematocrit (%)	36.64	36.84	39.74	38.68	37.24	36.84	36.14
LC (cells/cu)	3473.12	3798.45	3642.32	6554.45	5873.12	4798.45	4742.30
PT (in seconds)	13.1	13.2	13.1	13.6	16.3	16.1	14.1
B. Urea (mg/dl)	15	42.754	37.68	44.085	48.31	47.702	56.682
S. Creatinine mg/dl	0.5	0.5	0.7	0.9	1.1	1.2	1.5
S. Albumin (g/dl)	3.388	3.113	3.016	2.736	2.410	2.137	2.011
SGOT	38.2	34.4	66.2	83.43	91.58	107.46	750
SGPT	33.4	34.5	54.4	57.54	89.56	99.03	286
Na	135.10	130.44	134.58	135.56	131.75	131.98	131.87
K	4.22	4.13	3.86	3.35	3.37	3.34	3.55

It was observed that dengue Ag was positive in 196 cases (53.84%), IgM was positive in 259 cases (71.15%) and IgG was positive in 134 cases (36.81%) in this study. Dengue IgM positivity was more in all clinical spectrum groups of disease as depicted in figure 3.

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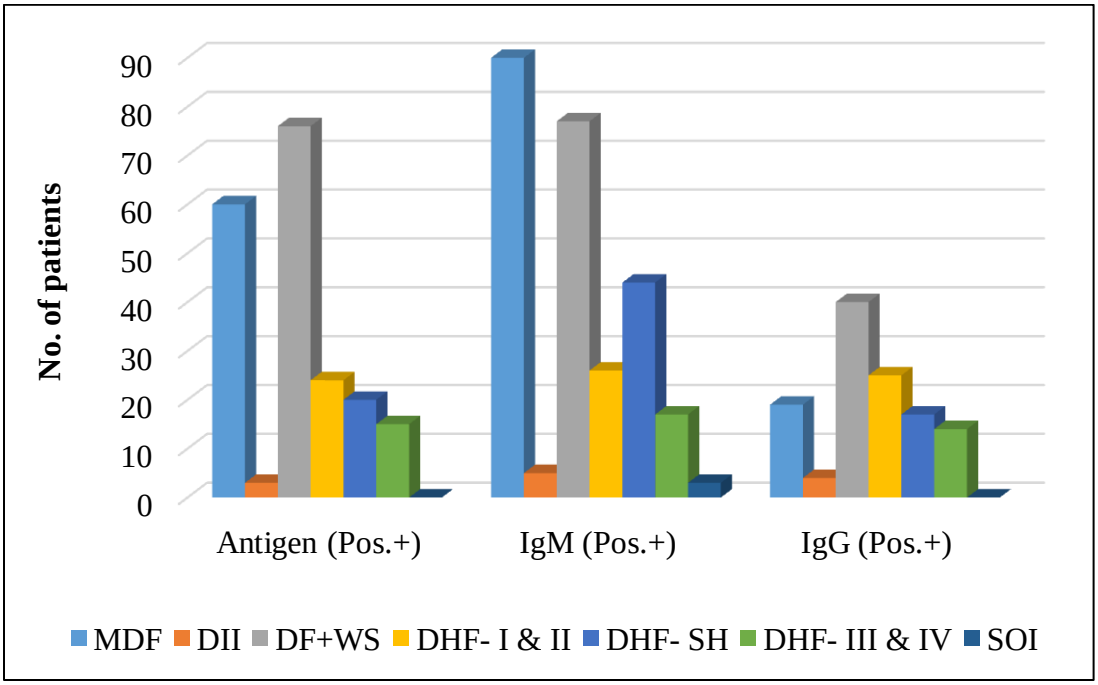
Figure 3: Dengue serology according to clinical spectrum of cases



Chest x-ray was done in all the 364 cases, in 114 children (31.31%) there was pleural effusion and, in the DF + WS, MDF and DHF- SH group the number of cases were more compare to other groups group, ($\chi 2 = 22.570$, $P<0.001$) It was statistically significant.

It was observed that pleural effusion was the most common USG finding 145 (39.83%) followed by gall bladder wall thickening 138 (37.91%), ascites 126 (34.61%), acalculous cholecystitis 79 (21.70%), splenomegaly 78 (21.42%) and hepatomegaly 61(16.75%), (Table 5).

Table 5: Distribution of children according radiological findings

Test component	Clinical spectrum						
	MDF (n=183)	DII (n=5)	DF + WS (n=80)	DHF- I & II (n=26)	DHF- SH (n=48)	DHF- III & IV (n=18)	SOI (n=4)
Chest X-ray							
Normal	153	02	43	19	20	11	02
Effusion	30	03	37	07	28	07	02
USG findings							
Normal	83	03	44	11	21	10	00
Pleural effusion	67	01	34	10	24	07	02
Gall bladder wall thickening	61	02	33	14	19	07	02
Ascites	60	00	30	12	18	06	00
Acalculous cholecystitis	22	01	28	13	10	04	01

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Hepatomegaly	10	02	26	11	08	03	01
Splenomegaly	14	01	27	09	15	08	04

Discussion

In the present study, out of 364 children, 50.27% children had mild DF, 30.49% had moderate DF and 19.23%, severe DF. However, those in the moderate dengue were split into three subgroups- Dengue in High-risk group (1.37%), DF with warning signs (21.97%) and DHF- I & II (Minor bleeds) (7.14%). Whereas severe dengue also split into three subgroup- DHF with significant hemorrhage (13.18%), DHF with shock (DHF III & IV-DSS) (4.94%) and severe organ involvement group (expanded dengue syndrome) (1.09%). The present study correlated with the previous studies [8-10] and the differences in the clinical spectrum of disease in all these studies, may be due to increasing endemicity, environmental factors and changing virulence of the viruses.

The maximum number of cases were found in age group of 4 to 6 years (28.57%), Also, in all subgroups there were more affected age group was 4 to 6 years, (P=0.732). Infants comprised 1.09% of total study group and all were in dengue in high-risk group. Infants are lesser in present study when comparing with Kabilan et al [10] and Aggarwal et al [11]. However, other studies [12, 13] reported the predominant age group was between 6-10 years. In the present study, males were affected slightly more than females in total and also in subgroups, (p=0.68). It may be due to increased outdoor activities of male children. Similar finding reported in the previous studies [11, 14].

All the children (100%) presented with fever as the predominant complaint followed by vomiting (36.20%) and abdominal pain (31%). Also in all clinical spectrum of disease fever was the predominant complaint followed by vomiting, abdominal pain. Abdominal pain was significantly more common in DF + warning signs group (42 patients). The overall mean duration of fever was 6.23 and there was no much variation among subgroups, which was not statistically significant. These findings are comparable with the study done by Nagaveni P et al [13] and Antony J et al [15]. In DHF III and IV mean duration of fever was 6.31 days which is comparable with the study conducted by Narayanan et al [14]. The skin bleeds were the most common manifestation, among which flushing was commonest noted in 167 cases (45.87%) followed by Petechiae-ecchymosis (31.31%) and Macular rash (22.52%). The bleeding manifestations were more in DHF + significant Hemorrhage group (40.38%) followed by DF + warning signs (25.54%) and DHF- I & II group (23.90%). Apart from flushing and petechiae, which usually associated with bleeding manifestations, Hematemesis and epistaxis were the predominant modes of bleeding and hematemesis was the most common bleeding manifestation reported in other Indian studies. These findings are correlated with the previous studies [16, 17]. In all the clinical spectrum the most common sign was hepatomegaly (33.2%), followed by facial puffiness (28%), conjunctival congestion (19.80%) and pedal edema (19.2%). Hepatomegaly was highest in DHF- III & IV group (16/18= 88.88%) followed by in DHF with significant hemorrhage group (41/48= 85.41%) and DHF I and II group (20/26=76.92%). These findings are comparable with the study done by Aggarwal et al [11], Narayanan et al [14], Mishra S. et al [18] and Reddy GM et al [19].

Tourniquet test was positive in 40.38% of cases, more in DHF with significant hemorrhage group (97.91%) and DHF- I & II group (92.30%). Characteristically it was found to be positive in only 44.44% of DHF- III & IV group. This distribution was statistically significant p<0.001. However, other studies [11, 14, 20] have noted varying results in this test. Tourniquet test is not a reliable test for diagnosis as observed in many other Indian studies [20, 21].

Platelets counts carry one of the most important keys for diagnosis. In present study overall mean value of platelet count was 46534±32148.73 cells/cu mm. The WHO criteria of low platelet count of < 1, 00,000 cells/cu mm was seen in most of the cases 306(84.06%). With maximum number of cases having platelet count in the range of <20000 cells/cumm in DHF- SH and DHF- III & IV groups. Thus, there is correlation between the counts and the disease severity. These results correlated with the

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other studies [11, 22]. The platelet counts at the admission was neither an indicator of prognosis nor of bleeding tendencies or progression of the disease. This suggest that other factors like platelet dysfunction or disseminated intravascular coagulation may have role in bleeding in dengue fever cases. However, studies which include only DHF cases shows correlation between low platelet count and bleeding manifestations [11]. The studies by Narayanan et al [14] and Gomber et al [20] have documented the same opinion. The total mean hemoglobin, hematocrit level, leukocyte count and total mean of prothrombin time was 11.833±2.456 gm%, 37.564%, 6643.7 cells/cu mm and 13.9 sec respectively. There was no significant statistical correlation between hematocrit and severity of disease among the clinical subgroups of dengue. However, the range of total leukocyte count varied from 1400 – 22000 cells/cumm with a mean count of 6643.7 cells/cu mm. 132 (36.26%) patients had leucopenia i.e., <5000 cells/cu mm which almost correlates with the Butt N et al study [23]. PT is a sensitive indicator of synthetic function of liver. Few studies have documented utility of PTT as a diagnostic indicator. In present study, PT was normal in 30 cases (8.24%). The prothrombin time ranged from 12.0-18 sec with a total mean of 13.9 sec. The total mean value of serum albumin was 3.174 gm%. Serum albumin of <3.4 gm% was seen in 61.26% (223 children) of children, more in DHF- SH and DHF- III & IV group. It is statistically significant ($p<0.001$). The present study findings concurred with the previous studies and we found that thrombocytopenia was the most commonly associated finding [14, 20]. The mean SGOT was more in SOI group, DHF- III & IV, DHF- SH, DF + WS and DHF- I & II which was statistically significant ($p<0.05$). The mean SGPT was more in SOI group than other groups. It was also seen in Kalyanarooj et al [9] and Aggarwal et al study [11].

Chest x-ray was done in all the 364 cases, in 114 children (31.31%) there was pleural effusion and, in the DF+WS, MDF and DHF- SH group the number of cases were more compare to other groups group, ($\chi 2 = 22.570$, $P<0.001$) It was statistically significant. WHO has mentioned pleural effusion, especially on right side, as a consistent finding of dengue. According to WHO, pleural effusion is a supporting evidence of plasma leakage, the distinguishing feature of DHF. It also mentions that extent of pleural effusion correlates with the severity of the disease and bilateral pleural effusion is common in shock. Pleural effusion was the most common USG finding 145 (39.83%) followed by gall bladder wall thickening 138 (37.91%) and ascites 126 (34.61%). These findings are correlated with the study done by Venkata Sai PM et al [24] and Kalenahalli J et al [25].

Conclusion

In the present study mild dengue fever i.e., fever without complication and organ involvement was the most common presentation followed by other complicated forms such as DF with warning signs/symptoms and DHF with significant hemorrhage. On investigation deranged liver function test, renal function test, pleural effusion, thickened gall bladder wall, hepatomegaly on ultrasound abdomen, pleural effusion on chest radiogram were associated with complicated forms of disease. Much more awareness, vigilance and research in the diagnostic modalities is further needed to avoid unnecessary panic and platelet transfusions.

Limitations

1. Viral antibody titers were not done to diagnose primary and secondary dengue precisely.
2. Serotypes were not done. So, the predominant serotype was not identified.
3. Treatment modalities like type of fluid used, need for inotrope support, ventilator support, need for blood products were not studied.

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