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Original Article

Paediatrics Section

A Retrospective Study of Paediatric Dengue Cases in a Tertiary Care Hospital in Southern India

PADMANABHAN P ATHIRA[1], OZHIPARAMBIL A JAGAN[2], PADMA UMADEVI[3], KOMARAVOLU PRAGNATHA[4], P MENON VEENA[5]

ABSTRACT

Introduction: Dengue is an important arthropod-borne viral infection in humans and is the second most important re-emerging tropical disease. Children are particularly at risk of developing severe dengue and clinically identifying such cases are often a challenge.

Aim: To characterise the clinical and laboratory risk factors of dengue fever and its severity in children.

Materials and Methods: Retrospective evaluation of demographics, clinical, laboratory findings and outcome of suspected dengue fever in children admitted to the hospital between Jan 2015 - Feb 2017 was performed to identify risk factors of dengue fever and its severity.

Results: During the study period, a total of 211 children were clinically suspected on the admission as dengue fever, 34 of these were serologically confirmed dengue positive. A 74% (27/34) of these were primary dengue infections. The mean age of the dengue cohort was 7.6 years (±s.d. 4.8) with 59% (20/34) being boys. Based on 2009 WHO clinical criteria, 16 were identified as Dengue with warning Signs (DS), 7 as Dengue Without warning Signs (DWS) while 11 were identified as Severe Dengue (SD). Some of the frequently observed clinical features were fever (31/34), headache (5/34), thrombocytopenia (9/34), leukopenia (4/34) and rash (5/34). The mean WBC in children with severe dengue was 7.9 % (s.d.±5.0) with elevated monocytes 12.2 % (s.d.±3.5) compared to 11.3% (s.d.±5.8) and 6.6% (s.d.±2.0) in children with DS and DWS respectively. Transaminitis was more frequently observed in severe dengue.

Conclusion: Clinical and laboratory parameters of acute febrile illness in children can act as early prognosticators of dengue fever and its severity.

Keywords: Arthropod, Flavivirus, Fever, Haemoconcentration, Thrombocytopenia

INTRODUCTION

Dengue is regarded as the most important arthropod-borne viral infection in humans and is the second most important re-emerging tropical disease [1]. Dengue Virus (DENV) is a mosquito-borne single-stranded RNA virus belonging to the *family Flaviviridae*. Human transmission occurs from bites of infected mosquitoes, viz. *Aedes aegypti* (*A. aegypti*) and *Aedesalbopticus* (*A. albopticus*) [2]. Antigenically, there are four dengue serotypes identifies as DENV1, DENV2, DENV3 and DENV4 that are endemic throughout the tropical and subtropical regions of the world [3]. Dengue infections are increasing resulting in more illness and death and, in 2012 World Health Organization (WHO) reclassified dengue as 'the most important mosquito-borne viral disease in the world [4,5]. In 2007, the WHO reported about 20,000 deaths annually with 50-100 million infections occurring globally. Recent estimates, using cartographic approaches, however, indicates that this number has increased to 400 million [1,6]. Approximately 3.6 billion people are living in areas at risk of transmission (tropical and subtropical) around the globe [1,7,8]. Over the last 30 years, probably due to insufficient vector control, increased urbanization and air travel, the distribution of dengue and its vector has increased dramatically [9,10]. In July 2017, in India, the NVBDCP (National Vector Borne Disease Control & Prevention) reported about 28,702 cases of dengue with 46 deaths with dengue haemorrhagic fever noted as major cause of mortality in children [11].

Clinically, dengue can present as a mild asymptomatic fever that resolves rapidly or can manifest as a severe disease characterised by excessive bleeding and plasma leakage that eventually leads to shock and death. Some of the reported clinical signs and symptoms of dengue in children are fever, retro-orbital pain, myalgia, arthralgia, rash, petechiae, mucosal bleeding etc., [12,13]. The unpredictable nature of its severity and consequent fatality coupled with the lack of specific antivirals means that clinical management is largely based on providing timely and appropriate supportive treatment.

Children and elderly population often bear the main burden of morbidity and mortality of dengue [14,15]. In Asia, a greater heterogeneity is observed in the clinical presentation of dengue in children with the likelihood of developing severe disease frequent among children under 15 years of age than in the adults [16,17]. Clinical evolution of dengue infections is unpredictable and in the absence of specific antiviral agents, effective treatment remains predominantly symptomatic and supportive with emphasis on close monitoring of haematological parameters, warning signs of severe disease, fluid-replacement therapy and blood transfusions if needed. Therefore, early prognostication of potentially severe dengue cases, especially in children, will aid in the timely and appropriate management and thereby improve the outcome. Given the heterogeneous nature of the clinical presentation of dengue, identifying robust and sensitive clinical or laboratory predictors of dengue fever and its severity has not been easy. Retrospective, prospective as well as case-control studies have identified several clinical and laboratory predictive markers of dengue illness as well as dengue severity [10,16,18,19]. However, there are still no specific clinical or laboratory guidelines for early prognostication of dengue fever and/or its severity, especially in children.

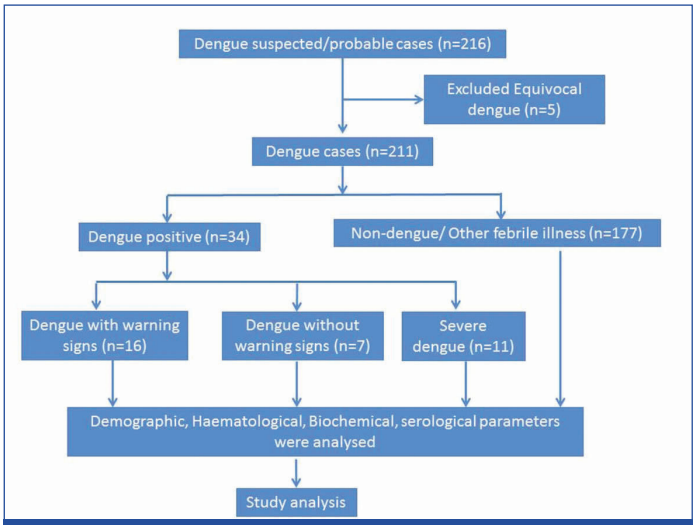
In this study, we aimed to retrospectively review and compare the clinical and laboratory findings that differentiate dengue fever from

non-dengue febrile illnesses and further analyse the clinical and laboratory variables associated with severe dengue.

MATERIALS AND METHODS

Study design: This was a cross-sectional, single-centre retrospective study carried out at Amrita Institute of Medical Science and Research Centre in Kochi, Kerala during January 2015 to February 2017. We reviewed the clinical, laboratory, treatment and outcome data of 216 children (<18 yrs of age) admitted to the hospital with fever and a suspected (probable) diagnosis of dengue.

Study population: The study cohort included children (<18 years of age) serologically diagnosed as dengue-positive at the time of admission using the dengue NS1 antigen and dengue IgM and IgG specific antibodies ELISAs (Panbio® Dengue Early Rapid, Alere™, Australia). According to the WHO recommendations (2009), all cases were classified clinically as severe dengue, DS and DWS ie, study sub-cohorts [Table/Fig-1]. Children with confirm dengue diagnosis (tested positive for either NS1 or IgM/IgG ELISA) were considered as dengue-positive group (dengue) with NS1 or IgM/IgG ELISA titre value of >22 Pan-Bio Units (PBU), while the rest were grouped as non-dengue fever/other febrile illness (<18 PBU) and equivocal dengue (18-22 PBU).



[Table/Fig-1]: Flow chart of the study.

During screening, we obtained detailed demographic, clinical, haematological, biochemical and laboratory data and treatment outcomes were evaluated for all cases included in this study. Additionally, biomarker ratios like Monocyte-Lymphocyte Ratio (MLR) and Neutrophil-Lymphocyte Ratio (NLR), Platelet Lymphocyte Ratio (PLR) were determined for each subject on the day of admission. The ratios are calculated by dividing the absolute counts of each cell type.

This retrospective study was approved by Institutional Review Board (IRB) at Amrita Institute of Medical Sciences and Research Centre.

STATISTICAL ANALYSIS

Univariate analysis was done on the various clinical parameters (symptoms, signs and full blood counts) using the Fisher's-exact test while laboratory parameters were evaluated as continuous variables and compared using either the Student's t-test or the Mann-Whitney U test as and when appropriate. Data analyses were done using Graph Pad software version 5 (Graph Pad, Chicago, IL, USA) with the level of significance set at a two-tailed p-value of <0.05.

RESULTS

A total of 216 'probable' dengue, children admitted to the general paediatrics and various paediatric subspecialty departments in our hospital from January 2015 to February 2017. Most of the children were admitted to General Paediatrics (87%), Patient distribution among the subspecialty departments was paediatric neurology (7.4%), paediatric rheumatology (3.7%), paediatric cardiology (1.3%) and paediatric surgery (0.9%). Dengue diagnosis was confirmed serologically in 34 children. Based on the WHO (2009) criteria for clinical case classification, 11 were classified as 'severe dengue'. Though overall no fatalities were observed in this study cohort, a significant difference in the mean duration of hospital stay was observed between the dengue and non-dengue febrile illness cases (4.9 days±s.d. 5.8 v/s 7.9 days s.d.±6.2; p=0.0073). Additionally, the clinical, haematological and biochemical laboratory values of the 211 dengue-like febrile illness cases were compared to identify features significantly associated with dengue fever.

Demographic characteristics of the study cohort: The demographic data of the study cohort are summarised in [Table/Fig-2]. The mean age of the children in the dengue fever subgroup was 7.6 years (s.d.±4.8) compared to 5.7 years (s.d.±4.4) in the non-dengue febrile cases. The study cohorts were predominantly children more than five-year-old with older age significantly associated with dengue fever. No significant association was observed between girls and boys in this age group, for dengue fever.

S No.	Demographics	Dengue N (%) N=34	Non-dengue N (%) N=177	Significance (p-value)
Age				
	Mean Age (in yrs)	7.6 (±4.8)	5.7 (±4.4)	0.01#
	Age groups			
	<1 yr	3	11	0.04
	1-5 yrs	11	90	
	5-11 yrs	9	52	
	11-14 yrs	11	24	
Gender				
	Female	14 (41)	83 (47)	0.54
	Male	20 (59)	94 (53)	

[Table/Fig-2]: Demographics of the study cohort.
Data are mean±(SD) and N (%). # Student's 't' test, $\chi 2$ test. yrs=years, level of significance <0.05

Clinical and laboratory features of the study cohort: A retrospective comparative review of 'on admission' clinical features presented by the study cohort is shown in [Table/Fig-3]. As expected, fever was the most common presentation and no significant difference in the fever days was observed between the dengue and non-dengue fever groups (7.6 s.d.±7.7 v/s 9.8 s.d.±10.5). We noted a significant association of leukopenia (p=0.0010) and thrombocytopenia (p=0.0003) with dengue fever. A systematic evaluation of the presenting vital signs showed a significant association of pulse pressure with dengue fever (p=0.003), with the mean pulse pressure reported in children with dengue fever being 92.8 mm Hg (s.d. ±17.4) compared to 103.9 mm Hg (s.d.±16.9) in the non-dengue group.

As shown in [Table/Fig-4], critical laboratory values were also evaluated in our study cohort and we found a statistically significant (p<0.04) increase in the monocyte counts among the paediatric cases of dengue fever compared to the non-dengue fever group. As expected, children with dengue fever had a mean platelet count significantly lower compared to that reported in children with febrile illness from non-dengue causes; (182.2 s.d.±158.1 v/s 277.1 s.d.±198.4; p=0.004). Haemoconcentration was also significantly altered between the two groups, Haematocrit (HCT) on admission

S No.	Signs and symptoms on presentation	Dengue N (%)	Non dengue N (%)	Signifi-cance (p-value)
		N=34	N=177	
1	Headache	5 (14.7)	15 (8.5)	0.26
2	Myalgia	3 (8.8)	13 (7.3)	0.77
3	Arthralgia	2 (5.8)	4 (2.2)	0.24
4	Rash	5 (14.7)	28 (15.8)	0.87
5	Abdominal Pain and Tenderness	2 (5.8)	10 (5.6)	0.96
6	Fever	31 (91.2)	157 (88.7)	0.67
7	Hepatomegaly	2 (5.8)	2 (5.8)	0.06
8	Thrombocytopenia	9 (26.4)	11 (6.2)	0.0003*
9	Leukopenia	4 (11.7)	2 (1.1)	0.0010*
10	Cold	1 (2.9)	4 (2.2)	0.59

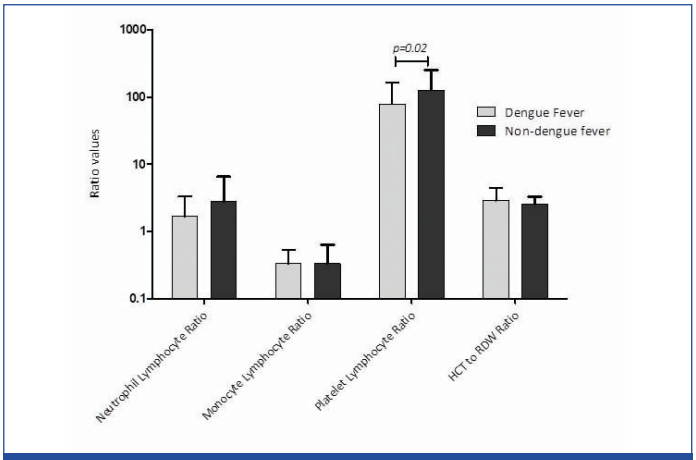
[Table/Fig-3]: Clinical characteristics of study cohort.
*Mean value are significant. $\chi 2$ test for calculating p-value, level of significance <0.05

were significantly elevated in dengue fever group {38.7 (±6.6) v/s 34.1 (±5.6); p=0.00002}. Among the biochemical parameters evaluated, transaminases (AST and ALT) were uniformly elevated in both groups and so was the prothrombin time. Significant differences were however observed in the aPTT values between the two groups, prolonged aPTT values were observed in children with dengue fever {45.3 (±20.2) v/s 36.3 (±7.9); p=0.03}. Plasma electrolytes levels in both groups of children remained within normal ranges.

S No.	Laboratory variables at admission	Dengue N=34 (Mean±SD)	Non dengue N =177 (Mean±SD)	Signifi-cance (p-value)
1	Pulse Pressure (mmHg)	92.8 (±17.4)	103.9 (±16.9)	0.003*
Haematology				
2	WBCs (K/µL)	9.47 (±6.9)	10.3 (±5.9)	0.45
3	Monocytes (%)	10.7 (±4.9)	8.7 (±4.7)	0.04
4	Lymphocytes (%)	39.9 (±17.2)	37.2 (±20.8)	0.24
5	Neutrophils (%)	46.7 (±17.5)	51.2 (±22.6)	0.14
6	RBCs (M/µL)	4.9 (±0.7)	4.6 (±2.4)	0.23
7	Platelets (K/µL)	182.2 (±158.1)	277.1 (±198.4)	0.004*
8	RDW (%)	14 (±2.5)	14.5 (±3.1)	0.37
9	HCT (%)	38.7 (±6.6)	34.1 (±5.6)	0.00002*
Liver Function Test				
10	ALT (IU/L)	143.8 (±482.3)	122.7 (±488.5)	0 .83
11	AST (IU/L)	233.6 (±574.9)	179.6 (±689.5)	0.68
12	ALP (IU/L)	169.1 (±83.2)	211.2 (±255.4)	0.36
Coagulation Tests				
13	INR (s)	1.3 (±0.6)	1.3 (±0.7)	0.93
14	PT (s)	17.7 (±6.2)	17.5 (±6.7)	0.95
15	APTT (s)	45.3 (±20.2)	36.3 (±7.9)	0.03
Electrolytes				
16	Sodium (mmol/L)	134.8 (±3.1)	134.7 (±3.8)	0.88
17	Potassium (mmol/L)	3.9 (±0.4)	4.0 (±0.5)	0.46

[Table/Fig-4]: Laboratory parameters of the study cohort.
Data are mean±(Standard deviation). *Mean value are significant. WBCs: White blood cells; RBCs: Red blood cells; RDW: Red blood cell distribution width; HCT: Haematocrit; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; INR: International normalized ratio; PT: Prothrombin time; APTT: Activated partial thromboplastin time.$\chi 2$ test for calculating p-value, level of significance <0.05

We evaluated the role of certain circulating inflammatory biomarkers like NLR (p=0.150), MLR (p = 0.638), Platelet-Lymphocyte Ratio (PLR) and haematocrit to RDW ratio (p = 0.268) in discriminating between dengue and non-dengue fever group. As shown in [Table/Fig-5], a comparatively lower mean PLR was recorded in children with dengue fever; (78.6±s.e.m.86.3 v/s 126.2±s.e.m.123.6; p=0.02). We also observed that 'on admission', a significantly higher proportion of dengue fever patients had NLR values < 2.0 (p=0.035) and MLR ≥ 0.20 (p=0.0095) compared to children suffering from non-dengue febrile illness [Table/Fig-6].



[Table/Fig-5]: Biomarkers of subclinical inflammation (Dengue fever vs Non-dengue fever).
p-value was calculated by Student's t-test, level of significance <0.05

Ratio	Ratio stratification	Non-dengue Fever	Dengue Fever	Significance ($\chi 2$ test)
NLR	<2.0	95	25	0.035
	≥2.0	82	9	
MLR	<0.20	67	5	0.0095*
	≥0.20	110	29	

[Table/Fig-6]: NLR and MLR ratio stratification (Dengue fever vs Non-dengue fever).
NLR: Neutrophil-Lymphocyte ratio; MLR: Monocyte-Lymphocyte ratio. *MLR is significant. p-value was calculated by Student's t-test, level of significance <0.05

Predictors of dengue severity: The clinical and laboratory findings among the dengue fever groups were evaluated to identify significant indicators of clinical severity. The clinical and laboratory values are represented in [Table/Fig-7]. Based on the WHO (2009) case classification criteria, 16 (47%) were clinically identified as DW, 7 (21%) as DWS and the rest 11 (32%) as 'severe dengue'. No significant differences were observed in age and gender with dengue severity in this cohort. Interestingly, a higher proportion (53%) of the paediatric cases were clinically identified to be in their convalescent phase of illness based on the fever duration and almost half (44%) of the patients in the critical phase of illness were clinically classified as 'severe' dengue. No significant association was found between the phase of illness and dengue severity. A majority of the of the dengue cases in the cohort (79%), were primary in nature as indicated by their IgM to IgG ratio values greater than 1.2 and in this subgroup, we did not identify infection status as a significant predictor of dengue severity.

Clinical and laboratory features of dengue fever group: A comparative review of the dengue positive subgroup revealed that headache (25%), myalgia (18.7%), fever (87.5%) and thrombocytopenia (25%) were commonly observed in children clinically classified as DW; rash (27.2%), fever (90.9%) and thrombocytopenia (36.3%) were prevalent among the 'severe dengue' patients. [Table/Fig-7].

Evaluation of the clinical laboratory findings among the dengue fever case is shown in [Table/Fig-8]. Systemic evaluation of vital signs like Blood pressure (BP), pulse pressure showed no significant association with dengue severity. Review of the haematological parameters revealed a significant (p=0.04) association of monocyte count with dengue severity with severe dengue children demonstrating elevated monocyte counts (12.2 s.d.±3.5) compared to that observed among the dengue children with and without warning signs (11.3 s.d.±5.8 and 6.6 s.d.±1.9 resp.).

S.No	Variables		Case Classification (WHO 2009 recommendations)			Significance (p-value)
			Dengue with warning signs N=16 (%)	Dengue without warning signs N=7 (%)	Severe Dengue N=11(%)	
Demographics						
1	Mean Age (yrs) (Mean±SD)		8.2 (±5.4)	6.7 (±5.2)	7.2 (±3.9)	0.75
2	Gender	Female	4	5	5	0.11
		Male	12	2	6	
Dengue infection characteristics						
3	Dengue Illness Phase	Febrile	3	1	3	0.68
		Critical	4	1	4	
		Conval-escent	9	5	4	
4	Infection Status	Primary	13	5	9	0.84
		Secondary	3	2	2	
Clinical Characteristics						
5	Headache		4 (25)	0	1(9.0)	(-)
6	Myalgia		3 (18.7)	0	0	(-)
7	Arthralgia		0	0	2 (1.8)	(-)
8	Rash		1 (6.2)	1 (14.2)	3 (27.2)	0.32
9	Abdominal Pain and Tenderness		1 (6.2)	1 (14.2)	0	(-)
10	Fever		14 (87.5)	7 (100)	10 (90.9)	0.96
11	Fever in days (Mean±SD)		8.2 (±10.7)	6.83 (±1.7)	7.1 (±4.0)	0.85
12	Hepatomegaly		1 (6.2)	0	0	(-)
13	Thrombocytopenia		4 (25)	1 (14.2)	4 (36.3)	0.58
14	Leukopenia		1 (6.2)	1 (14.2)	2 (1.8)	0.62
15	Cold		1 (6.2)	0	0	(-)

[Table/Fig-7]: Case classification of study cohorts bases on WHO 2009 classification.
WHO: World Health Organization; yrs: Years; SD: Standard deviation. p-value was calculated by Student's t-test, level of significance <0.05

Comparison of known biomarkers of subclinical inflammation like NLR, MLR, PLR and Haematocrit to RDW ratio has no significant association among study sub-cohorts as shown in the [Table/Fig-9].

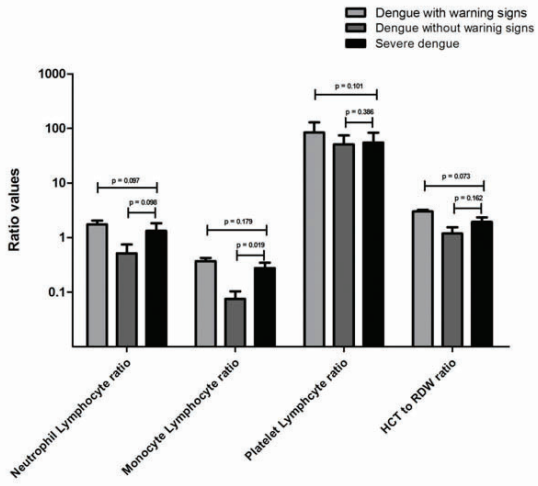
DISCUSSION

In children, early recognition of dengue fever and its severity in a dengue endemic and resource-limited region like Kerala, India would very helpful in reducing not only the mortality and morbidity of dengue illness but also the overall cost of hospitalization. In this study, we attempted to retrospectively review all children with febrile illness with a presumptive diagnosis of dengue fever and determine discriminators of dengue fever and its severity from other febrile illnesses. Our findings herein demonstrate that differential clinical and laboratory features can prognosticate dengue fever from other febrile illnesses.

Surprisingly, age was significantly associated with dengue fever with the mean age of children with dengue being higher (>5 yrs). This could possibly be explained as older children are more likely to be exposed to the environment and therefore more likely to experience mosquito bites. It may be noted however that the overall study cohort size was small and larger studies need to be done to validate the significant association of older age with dengue infections. The classical clinical presentation of dengue was not always observed in the children. In this study cohort, a higher proportion of the dengue fever patients presented with symptoms of headache (14.7%) and arthralgia (5.8%) compared

S. No	Laboratory variables on admission	Dengue Case Classification			Significance (p-value)
		Dengue with warning signs N=16 (Mean±SD)	Dengue without warning signs N=7 (Mean±SD)	Severe Dengue N= 11 (Mean±SD)	
Laboratory Values on Admission					
1	BP(S) (mmHg)	100.1 (±11.7)	102 (±2.8)	104.2 (±4.6)	0.74
2	BP(D) (mmHg)	66.9 (±11.8)	59 (±1.4)	67.2 (±4.4)	0.59
3	Pulse Pressure (mmHg)	96.5 (±20.4)	85.7 (±13.9)	88 (±7.3)	0.42
Haematology					
4	WBC (K/µL)	10.0 (±8.5)	10.5 (±5.9)	7.9 (±5.0)	0.67
5	Monocyte (%)	11.3 (±5.8)	6.6 (±1.9)	12.2 (±3.5)	0.04
6	Lymphocyte (%)	37.5 (±16.8)	46.7 (±16.1)	39.1 (±18.7)	0.50
7	Neutrophil (%)	49.0 (±16.7)	40.7 (±17.2)	47 (±19.6)	0.59
8	NLR	1.7 (±1.6)	1.1 (±1.1)	1.9 (±2.2)	0.61
9	MLR	0.3 (±0.2)	0.2 (±0.1)	0.4 (±0.2)	0.06
10	RBCs (M/µL)	5.0 (±0.8)	4.9 (±0.4)	4.7 (±0.7)	0.56
11	Platelet (K/µL)	138.1 (±112.1)	298.2 (±206.6)	172.5 (±159.3)	0.08
12	RDW (%)	13.7 (±2.0)	13.8 (±1.4)	14.4 (±3.6)	0.78
13	HCT (%)	40.4 (±7.2)	37.5 (±2.8)	36.9 (±7.2)	0.36
Liver Function Test					
14	ALT (IU/L)	79.3 (±150.3)	24.8 (±17.1)	306.6 (±832.3)	0.44
15	AST (IU/L)	222.8 (±512.9)	55.4 (±53.2)	340.2 (±794.8)	0.68
16	ALP (IU/L)	175.2 (±72.4)	181 (±124.3)	153.4 (±83.9)	0.77
Coagulation Test					
17	INR (s)	1.4 (±0.9)	1.1 (±4.7)	1.1 (±0.2)	(-)
18	PT (s)	19.2 (±8.7)	15.4	16.4 (±2.4)	(-)
29	APTT (s)	59.6 (±26.0)	31.9	35.4 (±2.2)	(-)
Electrolytes					
20	Sodium (mmol/L)	133.7 (±2.6)	137.4 (±5.2)	135.7 (±3.02)	0.13
21	Potassium (mmol/L)	3.98 (±0.6)	4 (±0.1)	3.9 (±0.2)	0.92

[Table/Fig-8]: Laboratory parameters of study sub cohorts.
yrs: Years; SD: Standard deviation; BP(S): Blood pressure systolic; BP(D): Blood pressure dystolic; WBCs: White blood cells; RBCs: Red blood cells; RDW: Red blood cell distribution width; HCT: Haematocrit; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; INR: International normalized ratio; PT: Prothrombin time; APTT: Activated partial thromboplastin time; NLR: Neutrophil-Lymphocyte ratio; MLR: Monocyte-Lymphocyte ratio. p-value was calculated by Student's t-test, level of significance <0.05



[Table/Fig-9]: Comparison of Biomarkers in subclinical inflammation among study sub cohorts.
p-value was calculated by Student's t-test, level of significance <0.05

to non-dengue cases while fever 10 (90.9) and rash 3 (27.2) were frequently observed in severe dengue cases. Similar findings were also reported by Majeed IA et al., in their study on 130 dengue patients and by Karoli R et al., [20,21]. Typical hallmark laboratory findings of dengue fever like leucopenia and thrombocytopenia showed significant association in our study too. Like reported elsewhere, Leucopenia was observed in 11.8% of dengue fever cases while thrombocytopenia was reported in 26.5% of the dengue fever group [19,22,23]. We also observed a significant increase in monocyte count in paediatric dengue patients and it was significantly associated with increased severity. Dengue virus has been shown to replicate in activated monocytic population but since we did not have data on viremia it is difficult to associate the observed monocytosis with increased viremia [24].

Usually, in severe cases like DHF and DSS, haemorrhagic manifestations with increased vascular permeability and fluid loss from vascular space into the chest and abdominal cavities are observed. These life-threatening symptoms usually occur in the critical or defervescence phase of illness were hypotension, weak pulse pressure (≤20 mm Hg) with cold, clammy skin is observed. In addition, coagulation abnormalities, haemostatic derangements and other vascular abnormalities also occur in this critical period. In our study cohort, haemoconcentration resulting from increased HCT (38.7 s.d.±6.6) was observed in dengue fever cases, however, no significant differences in the haematocrit values were observed in severe dengue cases. An increase in HCT values of more than 20% is usually reported in severe cases, however, since we did not have the baseline values of all the dengue positive cases we were unable to comprehensively evaluate the role of haemoconcentration in the severe dengue cases. Similarly, even though thrombocytopenia was significantly associated with dengue fever, no differential pattern was observed in the severe dengue cases. Similar findings were reported by Unnikrishnan R et al., thrombocytopenia (77.4%) was the major haematological abnormality followed by leukopenia (52.8%) and anaemia (13.2%) [25]. Similarly, aPTT (45.3±20.2) were significantly increased in dengue fever patients but were not necessarily associated with severity. Increased vascular leakage and but in dengue subcohorts no significant difference was reported.

Hepatic dysfunctions are also commonly observed in dengue cases with severe dengue characterised by elevated liver enzyme levels [26,27]. The liver enzymes like AST and ALT were uniformly elevated among the paediatric dengue patients. Evaluation of circulating inflammation biomarkers like NLR, MLR, showed no significant differences in the mean values of these markers between dengue and non-dengue and severe dengue cases. However, application of cut-off values of ≥ 2.00 for NLR and ≥0.20 for MLR revealed a significant association of NLR values <2.00 and MLR values ≥0.20 with dengue fever. Mortality was not observed in the present study. While similar studies by Adrian Ong et al., in their studyon 3186 cases of Dengue Fever (DF)/haemorrhagic dengue fever (DHF), 5.4% case-fatality was observed of which three cases had serological evidence of primary dengue infection [28] and 2.9% mortality rate was observed among 699 patients in a study conducted by Almas A et al., [29].

LIMITATION

One of the major limitations of this study is the number of confirmed dengue cases included for the comparative review. As a single-centre tertiary care setting, there could be a high possibility of selection bias in the study population and the results presented here need to be reviewed in this context. Larger prospective studies will be needed to further validate the findings observed in this cohort.

CONCLUSION

Our study findings highlight the heterogeneous clinical presentations of dengue fever in children and identify routine clinical and laboratory parameters like leucopenia, thrombocytopenia and elevated NLR and MLR significantly discriminating dengue from other febrile illness.

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PARTICULARS OF CONTRIBUTORS:
1. Student, Department of Pharmacology, Amrita School of Pharmacy, Amrita University, Kochi, Kerala, India.
2. Lecturer, Department of Clinical Virology, Amrita Institute of Medical Sciences, Amrita University, Kochi, Kerala, India.
3. Associate Professor, Department of Pharmacology, Amrita School of Pharmacy, Amrita University, Kochi, Kerala, India.
4. Pediatric Consultant, Department of Pediatric, Amrita Institute of Medical Sciences, Amrita University, Kochi, Kerala, India.
5. Professor, Department of Clinical Virology, Amrita Institute of Medical Sciences, Amrita University, Kochi, Kerala, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. P Menon Veena,
Professor, Department of Clinical Virology, Amrita Institute of Medical Sciences, AIMS Ponekkara, Kochi-682041, Kerala, India.
E-mail: vpmenon26@gmail.com

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