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Clinical and Biochemical Characteristics of Dengue Infections in Children From Sri Lanka

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Abstract

Introduction: Analyzing dengue disease patterns from different parts of the world should help us formulate more evidence based treatment guidelines and appropriately allocate limited healthcare resources. Therefore, we described the disease characteristics of hospitalised pediatric patients with dengue infections from Sri Lanka during the 2017 dengue epidemic.

Methods: Clinical and biochemical characteristics of pediatric dengue patients treated at a secondary care hospital in Sri Lanka from 1 June 2017 to 31 August 2017 were analyzed. Our findings were compared with previous pediatric dengue studies in Asia.

Results: A total of 305 patients (number of males = 184(60%); mean age = 8.6 years) were analyzed. DF (Dengue Fever)—245 (80.3%), DHF (Dengue Hemorrhagic fever)—I:52 (17%), DHF—II:7 (2.3%), and DHF—III:1 (0.3%). Significant associations were found between DHF and abdominal symptoms/signs and overt bleeding manifestations ($P < .001$). Time of onset of the critical phase was variable (Day 3: 12%, Day 4-5: 78%, Day 6: 5%, and Day 7: 5%). Platelet and white-cell counts (WBC) were significantly lower in DHF than DF; liver enzyme derangement was mild and was similar in the DHF and DF subgroups. None had cardiac, renal, or neurological manifestations and all recovered uneventfully.

Conclusion: In Sri Lankan pediatric dengue patients, we found abdominal symptoms and signs, decreased WBC and platelet counts and bleeding manifestations were to be significantly associated with DHF. Liver enzyme derangement did not predict DHF. The time of onset of the critical phase was difficult to predict due to the considerable variations noted.

Keywords

dengue virus infections, children, Sri Lanka, dengue epidemic, dengue fever

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Introduction

Dengue viral infections are common in children and cause high morbidity and increased financial burden to the health system.[1] Around 500,000 people with Dengue Hemorrhagic Fever (DHF) need hospitalization each year, the majority being children aged less than 5 years.[1] Reports from different parts of the world suggest a changing pattern in the incidence of dengue infections and associated organ involvement such as respiratory, cardiac, gastrointestinal, hepatic, renal and neurological.[2-9]

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In Sri Lanka, dengue epidemics occur regularly and cause considerable financial burden to the health care sector and economy of the country.[10,11] Although children are commonly affected by dengue, published data on dengue infections in children living in Sri Lanka are limited.[12-14] Following the study by Malavige et al, no study in Sri Lanka has described the patterns of dengue infections specifically in the pediatric population.[12] In 2017, Sri Lanka faced its largest dengue epidemic, requiring reallocation of resources and specialized dengue treatment units to combat the large epidemic.[15-17] Systematically collected demographic and clinical data during such dengue epidemics is essential for evidence based practice. Lack of such information will lead health policy makers and clinicians to rely on personal experience and knowledge as opposed to tangible evidence when basing their decisions related to allocation of resources and individual patient management. Therefore, we conducted a follow up study to identify patterns of clinical, demographic and biochemical findings of hospitalized pediatric dengue patients during the Sri Lankan dengue epidemic in 2017 and compared our findings with similar pediatric dengue data in Sri Lanka and other regional Asian countries.

Materials and Methods

All children with fever who were admitted to the 2 pediatric wards at a secondary care hospital in Sri Lanka (Base Hospital Panadura) from 1 June 2017 to 31 August 2017 and who fulfilled a locally revised criteria based on the 1997-WHO dengue case classifications were recruited (see Supplementary File). Ethical clearance was received from the National Hospital of Sri Lanka-ethical review committee (No: AAJ/ETH/COM/2017-21) and institutional approval was obtained from the director of the hospital. Informed written consents were obtained before inclusion to the study. Categorization of patients into DF or DHF was based on the 1997 and 2009 WHO case definitions.[18,19] The clinical, demographic and biochemical findings were collected from the clinical records using a standardized questionnaire. In those with severe infections, hematological parameters such as white blood cell (WBC), hematocrit and platelet counts were recorded 8 hourly. Biochemical parameters such as serum creatinine, liver enzymes and serum electrolytes were performed till discharge on a daily basis. In stable patients with mild infections, we collected hematological parameters daily and biochemical parameters every other day. Ultrasonographic assessments were initiated from day 3 onwards, or if the platelets were less than $100{,}000 \times 10^3/\mu L$. Ultrasonographic assessment was routinely performed twice daily until a clinical improvement was detected with a concomitant rise in platelet counts. If patients had any features of fluid leakage with or without shock, they were classified as having DHF irrespective of bleeding manifestations. DHF was sub-classified into 4 grades (grade I, grade II, grade III, and grade IV) as described in the 2007 WHO dengue case definitions. The critical phase was defined as the period of fluid leakage in DHF associated with defervescence and rise in hematocrit.

Data were analyzed using SPSS (version 17) and data were described as frequency and percentages. Possible predictive or associated factors in relation to DHF were described using the Pearson Chi square test and Student's *T* test. A p value less than 0.05 was deemed statistically significant. Furthermore, subgroup analyses were performed between DF and DHF patients and also DHF-I and DHF-II/DHF-III.

Results

A total of 305 children who were diagnosed with dengue viral infections were studied. The majority were male—184(60.3%). The mean age was 8.6(Standard deviation [SD] = 3.3) years and 154 (50.5%) got admitted on the 3rd and 4th days of their illnesses. The mean duration of symptoms at presentation was 3.9(SD: 1.4) days and the mean duration of hospitalization was 3.8 (SD: 1.3) days (for DF: 3.5 (SD: 1.2) and DHF: 4.9 (SD: 1.3), $P < .001$). Fever was present in all patients during the onset of the infection (mean duration of fever: 4.0 days, SD: 1.4). Symptoms, such as headache 55% (n = 168), body aches 52.5% (n = 160), vomiting 43.1% (n = 131), abdominal pain 21.6% (n = 66), nausea 21.3% (n = 65), and diarrhea 15.4% (n = 47) were commonly associated with dengue. Bleeding manifestations were present in 2.6% (n = 8) and was more prevalent in DHF patients (5.1% vs 2%, $P = .18$) but the difference noted was not statistically significant. Around 38% (n = 116) and 6.9% (n = 21) had tenderness over the right hypochondrium and epigastrium, respectively. Around 80% of patients had DF (DF-245 (80.3%), DHF grade I-52 (17%), DHF grade II-7 (2.3%), and DHF grade III–1 (0.3%)). Clinically detectable ascites and pleural effusion were present among 71.6% (n = 43) and 26.7% (n = 16) of the DHF patients. Table 1 shows the comparison between the clinical features of DF and DHF. Compared with DF patients, a significantly greater proportion of DHF patients had abdominal symptoms (vomiting 64.4% vs 38%, diarrhea 27.1% vs 12.6%, and abdominal pain 32.2% vs 19.1%, $P < .001$). Furthermore, right hypochondrial tenderness was significantly higher in the DHF group compared to DF (84.7% vs 26.8%, $P < .001$). According to the 2009 dengue case classifications, 245

Table 1. Clinical Characteristics of DF and DHF.

		Total		DF		DHF		Odds ratio (95% CI)	*P* value
		N	%	N	%	N	%		
Gender	Male	184	60.3	146	59.6	38	63.3%	1.1 (0.7-1.8)	0.60
	Female	121	39.7	99	40.4	22	36.7%		
Age		8.6 ± SD3.2		8.6 ± SD3.3		8.7 ± SD2.9		—	0.92
Headache	Yes	168	55.1	127	51.8	41	68.3	1.8 (1.1-2.9)	0.02
	No	137	44.9	118	48.2	19	31.7		
Body aches	Yes	160	52.5	122	49.8	38	63.3	1.6 (0.9-2.5)	0.60
	No	145	47.5	123	50.2	22	36.7		
Vomiting	Yes	131	43.0	93	38.1	38	63.3	2.3 (1.4-3.7)	<0.001
	No	174	57.0	152	61.9	22	36.7		
Right hypochondrial tenderness	Yes	116	38.0	65	26.5	51	85.0	9.2 (4.7-18.0)	<0.001
	No	189	62.0	180	73.5	9	15.0		
Abdominal pain	Yes	66	21.6	47	19.2	19	31.7	1.7 (1.1-2.7)	0.035
	No	239	78.4	198	80.8	41	68.3		
Nausea	Yes	65	21.3	53	21.6	12	20.0	0.9 (0.5-1.6)	0.78
	No	240	78.7	192	78.4	48	80.0		
Diarrhea	Yes	47	15.4	31	12.7	16	26.7	2.0 (1.2-3.2)	0.007
	No	258	84.6	214	87.3	44	73.3		
Epigastric tenderness	Yes	21	6.9	17	6.9	4	6.7	0.9 (0.4-2.4)	0.94
	No	284	93.1	228	93.1	56	93.3		
Bleeding manifestations	Yes	8	2.6	5	2.0	3	5.0	1.9 (0.8-5.0)	0.2
	No	297	97.4	240	98.0	57	95.0		
Retro orbital pain	Yes	7	2.3	4	1.6	3	5.0	2.2 (0.9-5.4)	0.12
	No	298	97.7	241	98.4	57	95.0		

Table 2. WHO Classification 1997 vs 2009.

		Dengue				Severe dengue			
		With warning signs		Without warning signs		Yes		No	
		N	%	N	%	N	%	N	%
DF/DHF	DF	185	75.5	60	100.0	0	0.0%	245	81.1
	DHF-I	52	21.2	0	0.0	0	0.0%	52	17.2
	DHF-II	7	2.9	0	0.0	2	66.7%	5	1.7
	DHF-III	1	0.4	0	0.0	1	33.3%	0	0.0
DF/DHF overall	DF	185	75.5	60	100.0	0	0.0%	245	81.1
	DHF	60	24.5	0	0.0	3	100.0%	57	18.9

children had warning signs and 3 patients had severe dengue. The comparison between the 1997 and 2009 dengue case classifications is given in Table 2.

Among the DHF patients, the onset of the critical phase was noted following a mean duration of illness of 4.6 days (SD 0.9). The majority of children went into the critical phase on day 4 and day 5 (Day 4%-28.3%, n = 17 and Day 5%-50.0%, n = 30). However, 7 patients (11.9%) went into the critical phase on day 3. Furthermore, three patients each went into critical phase on day 6 and day 7 of the illness. Around 52% (n = 159) required crystalloids and 5.2% (n = 16) required colloids (boluses of dextran). Only two patients (0.7%) required blood transfusion.

Among DHF patients, a significantly lower WBC and platelet counts were noted as expected (Table 3). The lowest platelet count was less than $25{,}000 \times 10^3/\mu L$ among 45% of DHF patients, compared to 2.0% of DF patients. The lowest platelet count of less than $50{,}000 \times 10^3/\mu L$ was seen among 76.7% of DHF patients. The mean platelet count at the beginning of critical phase was $94 \times 10^3/\mu L$. The mean white cell count at the

Table 3. Laboratory Findings of DF and DHF.

	DF		DHF		
	N	%	N	%	*P* value
Lowest platelet count (Mean ± SD)/μL	104 ± SD46		39 ± SD28		<.001
<25000	5	2.0	27	45.0%	<.001
25 000–50 000	14	5.7%	19	31.7%	
50 000–75 000	39	15.9%	6	10.0%	
75 000–100 000	62	25.3%	6	10.0%	
>100 000	125	51.0%	2	3.3%	
Lowest WBC (Mean ± SD) × 10^9/L	3.5 ± SD1.6		3.7 ± SD1.7		.68
<2	31	12.7%	10	16.7%	.003
2–4	143	58.4%	34	56.7%	
>4	71	29.0%	16	26.7%	
Highest AST (Mean ± SD) IU/L	85.4 ± SD51.4		93.5 ± SD45.3		.33
mild	149	60.9%	42	69.5%	.96
moderate	7	2.8%	2	3.4%	
Severe	0	0	0	0	
Highest ALT (Mean ± SD) IU/L	53.1 ± SD42.1		52.3 ± SD43.3		.91
mild	108	44.3%	25	40.7%	.87
moderate	8	3.3%	2	3.4%	
severe	0	0	0	0	
Serum creatinine (Mean ± SD) mmol/L	41.3 ± SD16.5		40.7 ± SD15.1		.90
Serum sodium (Mean ± SD) mEq/L	135 ± SD2.5		133.5 ± SD3.3		.001
Serum potassium (Mean ± SD) mEq/L	4.0 ± SD.44		3.9 ± SD.5		.31

beginning of critical phase was 4.7 × 10^9/L. More importantly, the onset of critical phase was detected while the platelet count was more than 100,000/μL in around 32% of patients.

Liver enzyme derangements were subclassified as mild, moderate and marked.[20] Mild (less than 5-fold rise), moderate (5-10 fold rise) and marked (greater than 10-fold rise) derangement of aspartate transaminase (AST) were noted in 62.6% (n = 191), 3.0% (n = 9), and none, respectively. Whereas mild, moderate and marked derangement of alanine transaminase (ALT) were present in 43.6% (n = 133), 3.3% (n = 10), and none, respectively. There was no significant different in the proportion of patients with liver enzyme derangement among the DHF and DF subgroups (Table 3). None of the patients developed renal or cardiac involvement and there were no neurological complications. None required intensive care unit (ICU) treatment and all patients had an uncomplicated recovery.

Discussion

In 2017, Sri Lanka experienced its largest dengue epidemic, with an overwhelming number of dengue patients being managed in secondary and tertiary care hospitals.[15] We found that the onset of the critical phase was unpredictable due to the considerable variations noted. Although, most patients went into critical phase on the 4th and 5th days of the illness, approximately 12% went into critical phase on day 3. Thus, patients should be monitored to detect features of fluid leakage from the third day of illness irrespective of the platelet count.

Around 10% (n = 6) of children went into critical phases on the 6th day or later, which usually corresponds to the time of discharge after recovering from uncomplicated dengue infections. Thus, the treating physicians should take careful decision when discharging patients with suspected dengue infections and there should be acceptable evidence to suggest clinical recovery.

In this study, around 81% had DF and 19% had DHF. Furthermore, a considerable proportion with dengue fever had abdominal signs and symptoms which were vomiting (43%), tenderness over the right hypochondrium (38%) diarrhea (15%) and abdominal pain (22%). Moreover, the abdominal symptoms and signs were more associated with DHF compared with DF ($P < .001$). In certain instances, the abdominal complaints were one of the predominant symptoms during admission. Therefore, the clinical presentation may mimic an acute abdomen which is usually treated in a surgical unit. Furthermore, inadequate resuscitation or over resuscitation in this context and delay in detecting fluid leakage may result in detrimental outcomes. Similar studies have also shown dengue patients with significant

Table 4. Comparison With Similar Studies in Sri Lanka.

Author (year)	Present study (2017)	Sirisena (2014)	Murugananthan (2014)	Messer (2012)	Malavige (2006)	Lucas (2000)
Country	Sri Lanka	Sri Lanka	Sri Lanka	Sri Lanka	Sri Lanka	Sri Lanka
Study design	Retrospective	Cross sectional pilot study	Retrospective study	N/A	Prospective study	Retrospective study
Sample size	305 children	147 (254 with adult cases)	288 (1085 with adult cases)	65 (357 with adult cases)	104 children	177 children
Male %	60.30%	62.6%	49.3%	57.7%	41.3%	N/A
Female %	39.70%	37.4%	50.7%	42.3%	58.7%	N/A
Mean duration of fever (days)	3.9	N/A	4.5	N/A	N/A	N/A
DF	80.70%	68.9%	55.4%	79.8%	17.3%	19.2%
DHF	19.30%	30.3%	12.2%	31.4%	82.7%	80.8%
Cardiac	None	N/A	N/A	N/A	2.9%	N/A
Neurological	None	N/A	N/A	N/A	6.7%	6.2%
Renal	None	N/A	N/A	N/A	N/A	N/A
Hepatic	Mild = 62.6%, moderate = 3%	1.2%	26.2%	7.7%	N/A	78.0%
Headache	55.10%	90.2%	54.0%	50.8%	71.2%	16.4%
Bodyache	52.50%	79.1%	26.4%	53.8%	N/A	15.3%
Nausea	21.30%	N/A	N/A	N/A	N/A	N/A
Vomiting	43.10%	N/A	50.1%	42.5%	74.0%	82.5%
Diarrhea	15.40%	N/A	N/A	N/A	17.3%	N/A
Abdominal pain	21.60%	N/A	N/A	29.8%	N/A	43.5%
Bleeding manifestations	2.60%	18.9%	24.7%	N/A	38.5%	42.9%
Right hypochandrial tenderness	38.00%	N/A	N/A	N/A	N/A	57.1%
Epigastric tenderness	6.90%	N/A	N/A	N/A	N/A	N/A
Platelet count	Count $< 25 \times 10^9$/L = 10.5%; Count $< 100 \times 10^9$/L = 58.4%;	Count $< 100 \times 10^9$/L = 65.4; Count $< 20 \times 10^9$/L = 2.4%	N/A	Count $< 100 \times 10^9$/L = 53.6%	Count $< 100 \times 10^9$/L = 70.2%, count $< 20 \times 10^9$/L = 9.6%	Count $< 100 \times 10^9$/L = 39.0%
WBC count	Count $< 4 \times 10^6$/L = 71.5%	Count $< 4 \times 10^6$/L = 76.0%	N/A	N/A	Count $< 4 \times 10^9$/L = 15.4%	N/A
Mortality	None	1	Percentage = 0.9% (absolute count N/A)	N/A	0	2

Note. N/A: not available.

Table 5. Comparison with Similar Studies in South Asia.

Author (Year)	Present study(2017)	Banerjee (2018)	Ramachandran (2016)	Pai Jakribettu (2015)	Kumar (2010)	Kamath (2006)	Ratageri (2005)	Shah (2004)	Narayanan (2002)	Sajid (2012)	Ahmed (2008)	Alam (2010)	Pervin (2004)	Ahmed (2001)
Country	Sri Lanka	India	India	India	India	India	India	India	India	Pakistan	Pakistan	Bangladesh	Bangladesh	Bangladesh
Study design	Retrospective	Prospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Prospective	Prospective	Prospective	Prospective	Prospective	Prospective	Prospective
Sample size	305	200	69	69	359 adults (≥15) and 107 pediatric (<15) cases	109 DHF III-IV/ DSS cases	23	39	59	35	35	54	97	72
Male%	60.30%	58.00%	62.3%	69.57%	64.6%	50.46%	48%	N/A	52.54%	57.14%	54.29%	50.00%	N/A	58.33%
Female%	39.70%	42.00%	37.7%	30.43%	35.4%	49.54%	52%	N/A	47.46%	42.86%	45.71%	50.00%	N/A	41.67%
Mean duration of fever (days)	3.9	N/A	N/A	N/A	6-10days	N/A	N/A	7.7	4.9	N/A	N/A	4.9	N/A	8.2
DF	80.70%	N/A	N/A	N/A	83.9%	N/A	17%	2.6%	72.88%	N/A	31.43%	40%	N/A	36.11%
DHF	19.30%	N/A	N/A	N/A	8.8%	100.00%	83%	97.4%	27.12%	N/A	68.57%	59.3%	18.56%	63.89%
Cardiac	None	N/A	N/A	N/A	N/A	4.59%	N/A	N/A	Bradycardia = 10.17%	N/A	N/A	N/A	N/A	N/A
Neurological	None	N/A	N/A	N/A	Altered sensorium = 10.3%	22.02%	22%	48.7%	23.73%	N/A	2.86%	N/A	N/A	N/A
Renal	None	N/A	39.1%	N/A	Renal failure = 0.2%	4.59%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Hepatic	Mild = 62.6%, Moderate = 3%	N/A	50.7%	4.35%	53.2%	36.70%	87%	97.4%	52.54%	54.29%	37.14%	31.48%	13.40%	50.00%
Headache	55.10%	55.50%	N/A	52.17%	47.6%	N/A	22%	N/A	28.81%	N/A	40.00%	31.48%	82.47%	77.78%
Bodyache	52.50%	63.00%	N/A	100.00%	64.6%	N/A	N/A	N/A	54.24%	5.71%	34.29%	46.30%	84.54%	76.39%
Nausea	21.30%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Vomiting	43.10%	N/A	63.8%	42.03%	47.6%	N/A	82%	86.6%	83.05%	34.29%	68.57%	N/A	36.08%	12.50%
Diarrhea	15.40%	N/A	N/A	8.69%	13.9%	N/A	13%	48.7%	N/A	17.14%	N/A	9.26%	N/A	19.44%
Abdominal pain	21.60%	N/A	71.0%	11.59%	37.5%	N/A	61%	N/A	23.73%	51.43%	68.57%	59.26%	6.19%	N/A
Bleeding manifestations	2.60%	13.00%	Mucosal bleeding = 39.1%	N/A	Petechiae 67.2%, ecchymosis 6.2%, gum bleeding 5.2%, hematuria 4.9%, melena 4.7%, hematemesis 3%, and epistaxis 2.6%	N/A	N/A	53.8%	66.10%	5.71%	62.86%	59.26%	N/A	86.11%
Right hypochondrial tenderness	38.00%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Epigastric tenderness	6.90%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Platelet count	Count < 25 × 10^9/L = 10.5%; Count < 100 × 10^9/L = 58.4%	N/A	Count < 100 × 10^9/L = 82.6%	N/A	N/A	N/A	Count < 100 × 10^9/L = 82%	"Thrombocy topenia" = 92.3%	Count < 100 × 10^9/L = 72.88%; Count < 50 × 10^9/L = 20.34%	Count < 50 × 10^9/L = 11.43%	Count < 150 × 10^9/L = 85.71%	Count < 50 × 10^9/L = 68.52%; Count < 20 × 10^9/L = 9.26%	Count < 100 × 10^9/L = 22.68%	Count < 100 × 10^9/L = 37.5%
WBC count	Count < 4 × 10^6/L = 71.5%	N/A	N/A	N/A	N/A	N/A	Count < 5 × 10^6/L = 26%	N/A	Lymphocyte count > 50% = 30.51%	Count < 4 × 10^6/L = 14.29%	Count < 4 × 10^6/L = 42.86%; Neutrophils > 60% = 20.00%	Count < 4 × 10^6/L = 9.26%	N/A	Leucopenia = 12.5%
Mortality	None	N = 3	N = 4	N = 2	N = 11	N = 9	N = 0	N = 3	N = 2	N = 0	N = 1	6%	N/A	N = 5

Note. N/A: not available.

Table 6. Comparison with Similar Studies in Southeast Asia.

Author (Year)	Present study (2017)	Hanafusa (2008)	Wichmann (2004)	Sawasdivorn (2001)	Kalayanarooj (1997)	Lam (2017)	Thu (2012)	Phuong (2004)	Chairulfatah (1995)
Country	Sri Lanka	Thailand	Thailand	Thailand	Thailand	Vietnam	Vietnam	Vietnam	Indonesia
Study design	Retrospective	Retrospective	Retrospective	Retrospective	Prospective	Prospective, observational study	Prospective	Prospective	Prospective
Sample size	305	147	60 adults and 287 pediatric cases	45	60	2301 pediatric cases (5 - 15years)	647 adults and 881 pediatric cases	712	128 DHF cases
Male%	60.30%	51.70%	50.7%	58.33%	53.33%	59.0%	55.4%	52.53%	N/A
Female%	39.70%	48.30%	49.3%	41.67%	46.67%	41.0%	44.6%	47.47%	N/A
Mean duration of fever (days)	3.9	N/A	5.4	N/A	N/A	N/A	N/A	N/A	N/A
DF	80.70%	53.74%	36.9%	100.00%	53.33%	N/A	61.1%	43.82%	0%
DHF	19.30%	46.26%	63.1%	0.00%	46.67%	N/A	38.9%	44.80%	100%
Cardiac	None	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Neurological	None	10.88%	0.9%	N/A	N/A	N/A	0.7%	N/A	3%
Renal	None	N/A	N/A	N/A	N/A	N/A	0.2%	N/A	N/A
Hepatic	Mild = 62.6%, moderate = 3%	82.05%	40.3%	N/A	N/A	10.0%	38.2%	36.52%	47%
Headache	55.10%	51.02%	15.0%	80.48%	77.19%	N/A	63.2%	37.68%	N/A
Bodyache	52.50%	12.24%	8.4%	41.46%	N/A	N/A	N/A	9.90%	N/A
Nausea	21.30%	N/A	57.0%	N/A	67.80%	N/A	N/A	N/A	N/A
Vomiting	43.10%	72.79%	59.0%	N/A	70.00%	36.0%	52.1%	64.33%	56%
Diarrhea	15.40%	N/A	N/A	N/A	N/A	N/A	N/A	9.70%	4%
Abdominal pain	21.60%	68.03%	N/A	N/A	33.90%	20.0%	36.9%	62.31%	N/A
Bleeding manifestations	2.60%	N/A	35.7%	100.00%	13.33%	42.0%	69.7%	15.31%	N/A
right hypochondrial tenderness	38.00%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Epigastric tenderness	6.90%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	62%
Platelet count	Count $< 25 \times 10^9$/L = 10.5%; Count $< 100 \times 10^9$/L = 58.4%;	N/A	N/A	N/A	N/A	N/A	N/A	Count $< 100 \times 10^9$/L = 80.59%	Count $< 100 \times 10^9$/L = 15.3%
WBC count	Count $< 4 \times 10^6$/L = 71.5%	N/A	N/A	Count $< 5 \times 10^6$/L = 62.22%	N/A	N/A	N/A	N/A	N/A
Mortality	None	N = 0	N = 1	N/A	N/A	N/A	N = 8	N = 0	3%

Note. N/A: not available.

gastro-intestinal manifestations.[21,22] Therefore, a patient with predominant gastrointestinal symptoms in a dengue endemic area, especially during an epidemic should alert the healthcare personnel to consider the possibility of dengue.

The bleeding manifestation observed in our study was considerably low compared to previous studies.[21-23] In our study, only 2.6% of patients had overt bleeding manifestations. However, analyzing the changes in the hematocrit levels (comparing the hematocrit level following clinical recovery and another stable recording during the course of the illness) revealed that 8% (n=24) of the dengue patients showed a drop in the hematocrit level of more than 5%. Though, this analysis is a crude assessment, the possibility of concealed bleeding is a possibility.

Several studies have described a considerable rise in liver enzymes such as AST and ALT in DHF cases than DF, with higher rise in AST more than ALT. Moreover, a surge in aminotransferases, predominantly AST has been described in association with the severity of the illness.[24,25] In the present study, we did not detect any significant difference in the AST/ALT in the DHF cohort compared to DF group (Table 3).

Table 4[12,13,26-28] summarizes the data presented in similar pediatric dengue publications from Sri Lanka. The distribution of gender was comparable. The prevalence of DHF was comparatively lower in our study. Proportion of patients with abdominal symptoms such as abdominal pain and vomiting was similar. High percentage had liver impairment but the majority were mild. Moderate liver impairment was only seen in 3%. Lower WBC and platelet cell counts were described in our study. However, the bleeding manifestations described in the present study were considerably lower compared to previous Sri Lankan studies. Table 5[29-41] compared the findings of our study with similar studies from South Asia. The distribution of gender was comparable. The proportion of DHF to DF was seen to vary between studies where some studies had lower proportion of DHF similar to our study. The proportion of patients with lower platelet count was higher in other studies. Table 6[23,42-48] shows the comparison of our data with previous pediatric dengue publications from Southeast Asia. The proportion of DHF to DF, and liver involvement were variable. Compared to South Asian and South East Asian studies, the gastrointestinal symptoms including abdominal pain and vomiting were lower in our study and furthermore, the prevalence of bleeding manifestations was considerably lower.

We did a parallel study on adult dengue patients and during comparison with this adult cohort (n=1167), we noted several differences.[49] The proportion of DHF was significantly lower among the children (19.3% vs 33.6%, $P<.001$). A Sri Lankan study by Malavige et al in 2006 noted that children had a higher tendency for fluid leakage than the adults. However, the pattern observed in the current epidemic was different.[12,21] Children had more gastrointestinal symptoms and signs such as vomiting (43.1% vs 19.7%, $P<.001$), tenderness in the right hypochondrium (38.0% vs 26.0%, $P<$x.001) and abdominal pain (21.6% vs 15.0%, $P=.005$), compared to adults.

Conclusion

We have comprehensively analyzed the clinical and biochemical characteristics among a group of hospitalized pediatric dengue patients during a large Sri Lankan dengue epidemic. We found that abdominal symptoms and signs, low WBC and low platelet counts to be significantly associated with DHF. Liver enzyme derangement did not predict DHF. Considerable variations were noted in relation to the onset of the critical phase. Furthermore, we noted several differences in the pattern of dengue infections in children compared with previous publications from Sri Lanka. Moreover, considerable differences in the clinical and biochemical measurements were seen when compared with hospitalized adult dengue patients during the same epidemic.

Appendix

List of Abbreviations

DF dengue fever
DHF dengue hemorrhagic fever
WHO World health Organization
SD standard deviation
WBC white blood cell
AST aspartate transaminase
ALT alanine transaminase

Authors' Contributions

UJ: contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring itegrity and accuracy.
MM: contributed to conception and design; contributed to acquisition; drafted manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring itegrity and accuracy.
DH: contributed to conception and design; contributed to acquisition; drafted manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring itegrity and accuracy.

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PY: contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring itegrity and accuracy.
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SLS: contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring itegrity and accuracy.

Declaration of Conflicting Interests

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Ethics Approval and Informed Consent

Ethical approval was obtained from Ethical Review Committee of National of Sri Lanka to conduct the study (No: AAJ/ETH/COM/2017-21). Informed written consent was obtained from parents/guardians and assent from children where appropriate before including in the study.

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Availability of Data and Materials

The datasets and materials generated and analyzed during the current study are available from the corresponding author on reasonable request.

Supplemental Material

Supplemental material for this article is available online.

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