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Demographic and clinical features of suspected dengue and dengue haemorrhagic fever in the Northern Province of Sri Lanka, a region afflicted by an internal conflict for more than 30 years—a retrospective analysis

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SUMMARY

Objectives: The aim of this study was to determine the demographic, clinical, and notification data of suspected dengue fever (DF) and dengue hemorrhagic fever (DHF) cases admitted to Jaffna Teaching Hospital, Sri Lanka.
Methods: The data were collected from bed head tickets of all patients presenting with clinically suspected DF/DHF from October 2009 to September 2010.
Results: A total of 1085 clinically suspected DF/DHF cases were identified, with high numbers occurring during December 2009 to March 2010. The majority of the reported patients were females (n = 550, 50.7%) and approximately three-quarters of the patients (n = 797, 73.5%) were adults. All had fever, but fever spikes were noted in only 129 cases (11.9%; 95% confidence interval (CI) 10.1–13.9%). Over 50% of cases had vomiting (95% CI 47.5–53.5%). Haemorrhages were noted in 266 (24.5%), with gum bleeding in 99 patients (37.2%). Low white blood cell and platelet counts were noted in 27.1% and 85.6% of cases, respectively. Of the 1085 cases, only 24 (2.2%) were screened for dengue IgM/IgG and only 458 cases (42.2%) were notified to the Epidemiology Unit, Ministry of Health, Sri Lanka.
Conclusions: The absence of laboratory diagnosis and poor notification to the Epidemiology Unit were the major drawbacks noted.

1. Introduction

Dengue virus (DENV) infection has been affecting humans for many years, with an estimated 50 million DENV infections occurring every year globally. On average, one million dengue fever (DF) and dengue hemorrhagic fever (DHF) cases have been reported annually in more than 100 countries in the tropical and subtropical regions of the world.[1] Dengue cases across the dengue endemic regions including the Americas, Southeast Asia, and the Western Pacific exceeded 1.2 million in 2008 and 2.3 million in 2010 based on official data submitted by the member states. Over the last 2 to 3 years, overall reported cases of dengue have continued to increase at an alarming rate, and there has been an expansion of the endemic regions.[2] Moreover, the spread of *Aedes* species mosquitoes and their adaptation to a changing climate, population growth, unplanned urbanization, evolving dengue viruses, and the lack of laboratory diagnostic facilities in several

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dengue endemic countries have not only contributed to the increase in dengue cases, but have also caused difficulties in managing the cases in those countries effectively.[3,4]

DF/DHF is a mosquito-borne *Flavivirus* infection. DENV-infected individuals experience a spectrum of clinical manifestations, which include an acute self-limiting flu-like illness to a severe disease with haemoconcentration (20% increase in haematocrit) and evidence of plasma leakage, such as pleural effusion and ascites; the latter is termed DHF. Clinically DF is mid-way between mild DENV infection and DHF and is characterized by headache, myalgia, arthralgia, retro-orbital pain, and occasionally a maculopapular rash. In some patients, DHF might progress to hypovolemic shock and this is termed dengue shock syndrome (DSS).

DF/DHF is an increasingly important public health problem in Sri Lanka. Unlike malaria, which is prevalent in the agrarian suburban areas of the island, DF/DHF is prevalent mostly in the urban areas of cities. The four serotypes of DENV have been co-circulating in Sri Lanka for more than 30 years and their distribution has not changed drastically, despite the emergence of new subtypes within a serotype.[3] Although the Sri Lankan population had been exposed to DENV for a long time, severe forms of DENV infection (DHF/DSS) were rare before 1989.[5] Studies have shown the existence of more than one DENV serotype in many parts of the country,[3] but the status of the different DENV serotypes and their presence in the Northern Province is not known, as the area was affected by war and was unsettled for more than 30 years. There was a report of an island-wide epidemic of DF associated with DENV serotypes 1 and 2 from 1965 to 1968 that caused DHF in 66 patients and 15 deaths.[6] Serotypes DENV-1 and DENV-2 were isolated from the outbreaks in 1965 and 1966[7] and the Northern Province was not affected by this epidemic.

Data from a study conducted between 2003 and 2006 indicated the circulation of DENV-1 serotype in the Western Province of Sri Lanka.[8] In 2009, Sri Lanka experienced the largest epidemic of DF/DHF (35 008 reported cases and 346 deaths; 170 cases/100 000 population); a study conducted in Colombo determined the cause of this outbreak to be a new strain of DENV-1.[9] However further investigations are necessary to determine the dynamics of the DENV DF/DHF outbreak of 2009 in the North Province of Sri Lanka. DENV nucleic acid detection by RT-PCR in patients with DF/DHF from August 2010 to December 2010 showed the predominance of DENV-1, accounting for more than 95% of cases in the Western Province of Sri Lanka;[10] the virus type was similar

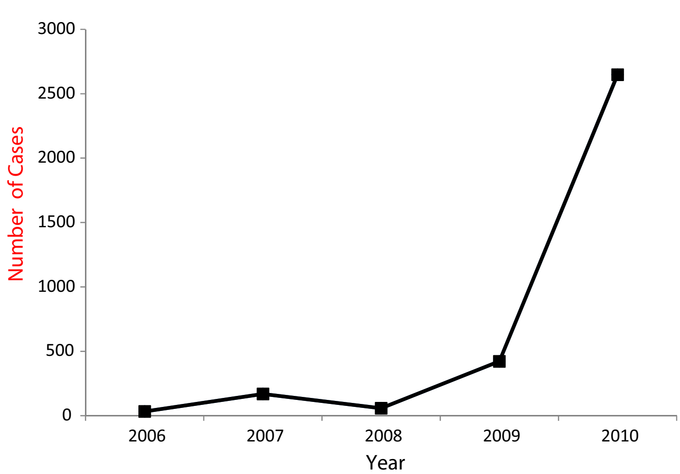

Figure 1. Notification of clinically suspected DF/DHF cases from Jaffna District, 2006–2010.

to that observed by the Epidemiology Unit of the country for the stated period, suggesting a serotype shift in the larger DF/DHF outbreaks in the last 2–3 years in Sri Lanka.

In general, over 1000 DF/DHF cases have been reported in Sri Lanka every year, mostly from the South, West, and Central provinces of the island. However, with the cessation of the 30-year conflict in the Northern Province, there has been a rapid increase in DF/DHF cases in the North (capital Jaffna) starting from the bigger island-wide outbreak in 2009 (Figure 1). Although a lot has been done to understand the circulating types of DENV in resource-limited areas like the Northern Province, we conducted this study to determine certain aspects of the epidemiology and clinical features of clinically suspected DF/DHF in patients admitted to Jaffna Teaching Hospital (JTH). We also sought to assess the accuracy of the case notification process to the Epidemiology Unit of the Ministry of Health, Sri Lanka.

2. Materials and methods

2.1. Study setting

Ethical clearance for the study was obtained from the Faculty of Medicine, University of Peradeniya, Sri Lanka. This was a retrospective study that analyzed the available data from JTH, which is the largest leading state hospital governed by the Central Government of Sri Lanka and is the only teaching hospital in the Northern Province of Sri Lanka. Altogether 2767 patients were admitted with a clinical diagnosis of DF/DHF between October 2009 and September 2010. However, complete data were available for only 1085 patients.

Data were extracted from patient notes to collect socio-demographic factors, clinical characteristics of the presenting illness, laboratory investigations, probable diagnosis, management, and the outcome of the illness. If not indicated in the individual case notes, certain signs and symptoms of DF/DHF were considered to be absent in that particular patient. The white blood cell count (WBC), platelet count, haemoglobin (Hb), packed cell volume (PCV), blood urea (BU), sodium, potassium, and dengue IgM/IgG were obtained from the laboratory reports. If reports were not available for a particular parameter, we assumed that the patient was not investigated for that parameter.

2.2. Notification data

Notification information for the patients with DF/DHF was obtained from the notification register maintained by the infection control unit of the hospital.

2.3. Data analysis

Data were analyzed using SPSS version 17 (SPSS Inc., Chicago, IL, USA); the Chi-square test and Fisher's exact test were used to explain associations. Odd ratios (OR) were used wherever applicable, and *p*-values of <0.05 were considered significant.

3. Results

A total of 1085 DF/DHF cases (with complete records) were identified for the period October 2009 to September 2010. A seasonal association was observed, with the highest number of DF/DHF cases occurring during January 2010. Five hundred and fifty (50.7%) of the reported cases were females. There were significantly more adult suspected DF/DHF cases than child cases ($n = 797$, 73.5%; $p < 0.001$). Although all patients with DF/DHF had fever, fever spikes were noted on admission in only 129 cases (11.9%; 95% confidence interval (CI) 10.1–13.9%). On average, fever

Table 1
Summary of clinical and laboratory profiles of adult DF/DHF cases in the current and previous studies

Symptoms	Present study		Kularatne et al.[13]	Malavige et al.[16]
	Area: Northern	95% CI	Area: Central	Area: Western
Number studied	797		348	108
Headache (%)	60.8	57.4–64.2	74.8	NS
Vomiting (%)	50.6	47.1–54.0	NS	64
Myalgia (%)	30.9	27.7–34.1	73.2	76
Flushing (%)	29.9	26.8–33.1	35	42
Bleeding manifestations (%)	28.1	25.1–31.3	6.8	42
Arthralgia (%)	14.6	12.2–17.1	NS	57
Retro-orbital pain (%)	9.9	8.0–12.1	NS	NS
Ascites/pleural effusions (%)	12.2	9.2–15.1	3	45
Hepatomegaly (%)	19.9	17.3–22.8	NS	0.02

DF, dengue fever; DHF, dengue haemorrhagic fever; CI, confidence interval; NS, not stated.

Table 2
Summary of clinical and laboratory profiles of child DF/DHF cases in the current and previous studies

Symptoms	Present study		Malavige et al.[19]
	Area: Northern	95% CI	Area: Western
Number studied	288		108
Headache (%)	35	29.7–40.7	NS
Vomiting (%)	48.9	43.2–54.7	64
Myalgia (%)	13.8	10.2–18.3	76
Flushing (%)	13.8	10.2–18.3	42
Bleeding manifestations (%)	15.2	11.5–19.8	42
Arthralgia (%)	5.2	3.1–8.3	57
Fever spike (%)	11.9	8.4–15.9	NS
Retro-orbital pain (%)	2.4	1.1–4.7	NS
Ascites (%)	2.8	1.3–5.2	45
Pleural effusions (%)	3.8	2.0–6.5	66.3
Hepatomegaly (%)	43.7	38.1–49.5	0.02
WBC $<4 \times 10^9$/l	21.5	17.1–26.6	15.3
Prolonged CRT	8.3	5.5–12.0	29.8
Platelets $<100 \times 10^9$/l	88.5	84.5–91.8	70.1

DF, dengue fever; DHF, dengue haemorrhagic fever; CI, confidence interval; NS, not stated; WBC, white blood cell count; CRT, capillary refilling time.

lasted for 4.5 days after admission (range 1–20 days). Most of the cases were admitted to hospital 8 days after the onset of symptoms (mean 7.93, median 8, range 1–24 days). The youngest case was aged 1 year and the oldest was aged 83 years; the mean age was 22.1 years. Clinicians in the Northern Province categorized suspected DF/DHF cases into three categories as follows: (1) DF, (2) DHF, and (3) DENV infection. In that respect, 601 patients were diagnosed with DF, 132 with DHF, and 352 patients were diagnosed with a DENV infection; the latter was considered mild compared to DF and DHF.

In the adult cohort, headache (60.8%), vomiting (50.6%), myalgia (30.9%), and a flushed appearance (29.9%) were the main clinical features. Similar clinical features such as vomiting (49.8%), headache (35%), myalgia (13.8%), and a flushed appearance (13.8%) were noted in children. Overall 266 (24.5%) patients had haemorrhages, of whom 224 were adults. Hepatomegaly was more common in children (43.7%) than adults (19.9%) (Tables 1 and 2). In both age categories (children and adults, n = 266), gum bleeding (37.2%) was the major haemorrhagic manifestation, followed by melena, petechiae/purpura, haematemesis, and haemoptysis.

A low WBC ($<4 \times 10^9$) and platelet count were noted in 294 (27.1%) and 929 (85.6%) patients, respectively. Approximately 7% of the patients had a platelet count of $<20 \times 10^9$/L. A prolonged capillary refilling time (CRT) was noted in 11.7% of the patients. Hypotension and tachycardia were noted in 19% and 27.1%, respectively. Of the 1085 suspected DF/DHF cases, only 24 (2.2%) were screened for dengue IgM/IgG antibodies. Of these, 13 were positive for dengue IgM only, five patients had both dengue IgM and IgG, and four only had dengue IgG. Of the 1085 DF/DHF cases based on the complete records, only 458 (42.2%) were notified to the Epidemiology Unit.

4. Discussion

Before 2009, DF/DHF was not a major public health problem in Jaffna District and around 50 cases per year were notified to the Epidemiology Unit of The Ministry of Health, Sri Lanka. However, the Western, Southern, Central, and North Central provinces of Sri Lanka have had high numbers of reported DF/DHF cases with high morbidity and mortality since the late 1980s.

From 2008 to 2010, there was a sudden increase in DF/DHF cases in Jaffna District (Figure 1). The numbers of reported DF/DHF cases in 2008, 2009, and 2010 were 58, 422, and 2648, respectively. Due to the unsettled conditions that prevailed in the Northern Province of Sri Lanka until 2009, there was no movement of people from other parts of the island to the North Province and vice versa. With the complete opening of the major entry route to Jaffna in 2009, after the end of war, there was a sudden movement of people in both directions, but the rate of movement has been highest from other parts of the island to Jaffna. It appears that the movement of people has contributed to the significantly higher number of DF/DHF cases following the cessation of war.

Although *Aedes* species mosquitoes have been reported in Jaffna for a long time, only a few cases of DF/DHF were reported until 2009. This might be due to the absence or low level of circulation of DENV in Jaffna prior to the mass movement of people to the peninsula following the end of conflict, despite the presence of *Aedes* species mosquitoes. The establishment and spread of DENV infections with the movement of people is a well documented phenomenon in the expansion of DF/DHF in many regions of the world.[4,11] In the study area, poor reporting might have contributed to the low number of cases until 2008 (n = ~50). However, the increase of >2000 cases in 2009/2010 cannot be explained by delays in reporting. Conversely, even if we consider only the 458 (42.2% of the admitted cases with complete reports) cases reported to the Epidemiology Unit of the Ministry of Health, this number is still much higher than those reported prior to 2009.

Considering the influence of torrential rainfall patterns in the area, a high number of DF/DHF cases (n = 809, 74.6%) were reported between December 2009 and March 2010 (Figure 2), coinciding with the monsoon rains in Jaffna District (Figure 2). Rainfall in Jaffna occurs mainly from October to November by inter-monsoonal rain and then from October to February by North East monsoonal rain (Meteorology Department, Jaffna) and thus the outbreak coincided with the inter-monsoonal and North East monsoonal rains; this would have facilitated a conducive environment for mosquito breeding and DENV transmission and spread. A similar phenomenon of a high number of DF/DHF cases

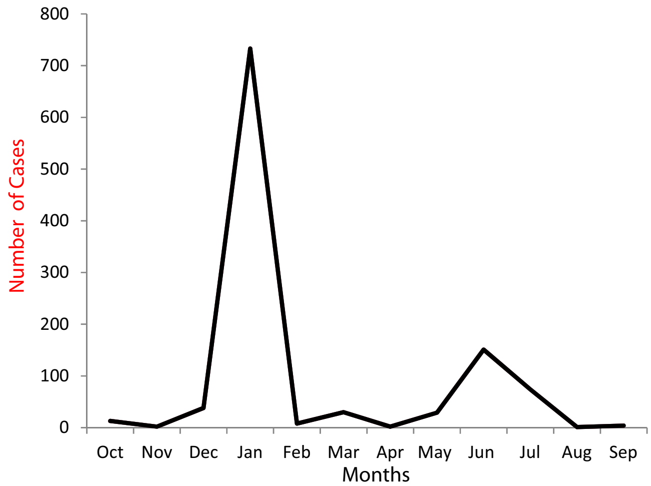

Figure 2. Seasonal variation and the distribution of clinically suspected DF/DHF cases.

coinciding with the torrential rainfall pattern has been shown in India and the Philippines.[12,13]

Based on the demographic data, females were found to be affected by DF/DHF slightly more than males in the adult and paediatric cohorts, but this difference was not statistically significant ($p > 0.5$). Similar findings have been reported in the Philippines[13] and Sri Lanka;[14] females have been shown to be affected more than males. In contrast, other previous studies have shown a higher prevalence of DF/DHF in males in India,[12] Singapore,[15] and certain areas of Sri Lanka.[15,16] Nevertheless, the finding of the current study of more females being affected with DF/DHF than males was not statistically significant and is not consistent with some previous studies conducted in Sri Lanka. In the study area, most adult females engage in outdoor activities such as cleaning the house premises, gardening, and collecting firewood from adjacent areas, hence these women may be exposed to daytime biting mosquitoes.

The mean age of dengue-affected cases in this study was 22.1 years; this finding of adults being affected by DF/DHF is in agreement with the data obtained from recent Sri Lankan studies. In the past DF/DHF was primarily a paediatric disease in Sri Lanka, however there has been a shift in the affected age in the last 8 years (mean 22–25 years).[3,14,16] Adults of both genders, either going to office jobs or working in the house premises or paddy fields might be exposed to daytime biting mosquitoes. In contrast to adults, infants mainly stay inside the houses during the daytime and thus are protected from these mosquitoes. The staff of schools in Jaffna District are well educated in taking measures to prevent dengue mosquito breeding, hence the school children rarely acquire the infection during the daytime. These reasons might explain the higher number of cases among adults than children in the study area. On the other hand adults may have immunity to a particular type of DENV and these adults when infected with a second type of DENV would become symptomatic, in contrast to children with primary infections, again contributing to the increase in DF/DHF cases in adults.

Based on the current study in adults (n = 797), fever and headache were the predominant clinical features, followed by vomiting, myalgia, haemorrhages, and a flushed appearance (Table 1). A similar clinical profile has been reported in patients from the Central Province of Sri Lanka in a small group of patients (n = 348).[14] On the other hand, myalgia, vomiting, arthralgia, and a flushed appearance have been reported among DF/DHF patients in the Western Province; however these patients did not have headache but did have diarrhoea.[17] The current study population and the cohort of a previous study[14] did not have diarrhoea as a clinical manifestation, although diarrhoea has been observed in patients in Singapore and Taiwan.[18,19] The presence of diarrhoea in certain study cohorts and its absence in other study cohorts might be due to inter-observer variations and a lack of consistency in self-reported morbidities by certain patients.

In paediatric patients, vomiting, headache, myalgia, and a flushed appearance were the common clinical manifestations in the current study; these have been noted with high frequencies in a different study[20] (Table 2). In another study, headache and myalgia/arthralgia were not noted in children;[16] this might be due to difficulties in expressing certain complaints by children in certain populations. In the present study cohort, pleural effusions and ascites were not common in children, but high frequencies of pleural effusions and ascites have been noted in a previous study.[20]

In the current study, hepatomegaly was found in 26.5% (n = 287) of patients – 43.7% of children and 19.9% of adults. Hepatomegaly has been reported to be common in adults[17] and absent in children[20] in previous studies; however hepatomegaly was absent in both children and adults in one previous study.[14] Inter-observer variation might be one of the reasons for these discrepancies in the clinical findings. Moreover, the immune status of the affected population to dengue viruses and the genetic makeup of the infecting dengue virus might also have had an influence on the variation in clinical manifestations.

Although bleeding manifestations were high in adults, gum bleeding was the most common in both children and adults, followed by melena, petechiae/purpura, haematemesis, and haemoptysis. In previous studies, the petechiae type of haemorrhage was found in several patients, with other bleeding manifestations occurring at similar rates to the current study in children and adults.[17,20] Thrombocytopenia was the major non-specific laboratory finding that was used in the assessment of leakage and bleeding in the current study, as also assessed by other investigators.[18,21] Furthermore, 21.5% of adults and 19.4% of children were given blood products or fresh frozen plasma to minimize leakage and bleeding, and mortality rates of 0.5% and 1% were noted in children and adults, respectively, in the current study.

Out of 1085 cases, 24 were screened for dengue IgM/IgG antibodies by rapid assays. There were no specific criteria applied with regard to the selection of patients for testing. Only those patients who could afford the cost of the assay in private sector laboratories had testing for dengue IgM/IgG antibodies. As this was the first large outbreak in Jaffna District, the health authorities were not prepared in terms of laboratory diagnosis. The dengue IgM/IgG positive rates (18/24) indicate the accuracy of the clinical diagnosis to be approximately 75%. The lack of laboratory diagnosis is a serious issue in Jaffna District. The clinical diagnosis might be accurate when done by an experienced clinician, but we have no laboratory-specific data to support the clinical diagnosis. Considering that DF/DHF is endemic in Sri Lanka and that there is a prevalence of dengue vectors on the island, clinical suspicion might be sufficient to support the majority of DF/DHF case diagnoses during an outbreak.[21] On the other hand, the lack of laboratory diagnostic methods to confirm the clinical suspicion might affect the prompt management of patients and the management of the complications of DF. Early laboratory diagnosis would be useful, as DF/DHF may be clinically similar to other bacterial and viral infections.[22] Equally, in a country with several other infections like typhoid, typhus, leptospirosis, and chikungunya, laboratory confirmation will help to assess the DF/DHF burden to take measures to manage and control DF/DHF.

Notification of DF/DHF to the Health Epidemiology Unit is mandatory, however more than half of the DF/DHF cases were not notified based on the findings of the present study. In the absence of a specific treatment or vaccine, vector control is the only method for the prevention and control of DF/DHF and vector control can be accelerated by the authorities through proper notification. Thus the JTH authorities should take necessary action to ensure proper DF/DHF notification to the Epidemiology Unit, Ministry of Health, Sri Lanka.

In conclusion, the suspected DF/DHF cases clearly showed a seasonal variation in the distribution of cases. Females were more affected than males by DF/DHF in Jaffna in the 2009/2010 outbreak. Most of the clinical features observed were in agreement with the clinical findings described by others, but vomiting was an important feature observed at a high frequency in the current study. The absence of laboratory diagnosis was the major drawback noted in this study, and most of the cases were admitted almost a week after the onset of symptoms. The delays in hospital admission show the inadequate knowledge of the public on DF/DHF and probably the poor level of clinical suspicion of the primary contact doctors in the peripheral hospitals. Hence, proper training of primary contact doctors on the clinical diagnosis of DF/DHF would allow patients to attend early medical assessment at a larger hospital like JTH for admission and proper monitoring in order to prevent progression to the complications of DF/DHF. On the other hand, increasing the availability of prompt virological and antibody based diagnostic tests in the state sector laboratories in the area would help to confirm the clinical suspicion, leading to more rapid hospital care for patients who might be prone to the complications of DF/DHF. Moreover, educating the public on dengue warning signs and emphasizing the importance of seeking medical help promptly would also contribute to the prevention of the complications of DF/DHF.

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Ethics: The study was conducted using protocols approved by the Ethics Review Committee of the Faculty of Medicine, University of Peradeniya, Sri Lanka.

Conflict of interest: None declared by the authors.

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