A Retrospective Study of the 1996 DEN-1 Epidemic in Trinidad: Demographic and Clinical Features

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Abstract
A retrospective analysis of the 1996 DEN-1 epidemic in Trinidad was undertaken to better understand the clinical and demographic expression of dengue infection in the island during one of the larger epidemics in the past 10 years and following the reintroduction of DEN-1 into the island in 1991 after a gap of 14 years. A total of 393 laboratory-confirmed cases were identified. Of these, notes for 157 patients were available for analysis. The epidemic was island-wide, though most cases occurred in the most densely populated county of St. George. There was a slight predominance of females (51.6%) among the cases, and while all age groups were affected, older children and adults comprised the majority. South Asians among the population predominated. Overall, 27 clinical symptoms were reported. The most common were: fever (98.7%), generalized pain (96.2%) and anorexia (63.1%). Rash, arthralgia, retro-orbital pain and haemorrhage (all mentioned in the WHO clinical description for dengue fever) were reported in <50% of cases. Gastrointestinal symptoms were also very common and occurred in over two-thirds of cases at presentation. Bleeding manifestations were reported in 30% of patients and commonly involved the gastrointestinal tract. Features of DHF were noted in only six (4%) patients and there was one fatality. Deficiencies in documented clinical and laboratory monitoring of patients, coupled with a lack of population-specific laboratory reference ranges, may contribute to under-diagnosis of DHF in Trinidad.

Keywords: Dengue, DHF, demographic analysis, clinical analysis, Trinidad.

Introduction
The dengue viruses (DEN), of the Flaviviridae family, are mosquito-transmitted viruses that can cause dengue fever (DF). DF is an acute febrile illness characterized by intense headaches, retro-orbital pain, myalgia, arthralgia, anorexia and rash. Additionally, in a minority of cases, a severe and potentially fatal form of dengue infection known as dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS) is manifested, primarily through increased vascular permeability and shock. Dengue exists as four distinct serotypes, DEN-1-4. Infection with one serotype gives life-long immunity for that virus but not to the others. Data suggest that secondary infection with a

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We present here a retrospective analysis of the 1996 DEN-1 epidemic in Trinidad. This study was done, firstly, to observe the clinical and demographic expression of the dengue infection in the Trinidad population during one of the largest epidemics of the past 10 years. In particular, we wished to assess the ethnic distribution of the disease since there had been previous anecdotal reports of a more severe disease in persons of South Asian ancestry. Secondly, the study was done to gain an understanding of the clinical and laboratory infrastructure for dengue in Trinidad and Tobago as part of the development of our ongoing dengue-related clinical research in the island.

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typing of dengue viruses in support of viral surveillance programmes\textsuperscript{42}.

A total of 1,200 samples from symptomatic suspected dengue cases in Trinidad and Tobago were sent to CAREC in 1996 for laboratory confirmation, of which 393 were found positive. We identified these confirmed cases of dengue infection and the medical institutions from which the samples had originated. The demographic, clinical and laboratory information related to each sample was collected from the respective medical records of each patient.

Data were entered into a computerized Excel database (Microsoft\textsuperscript{\textregistered} Excel 2000) and analysed according to demographic groupings such as ethnicity, county of residence, age and gender and by frequencies of clinical symptoms. The incidence rates per 10,000 persons were calculated using the 1990 census data\textsuperscript{13}. Proportional data were tested using the Chi square test and statistical significance was established at $P<0.05$. All statistical analyses of the demographic and clinical data were done using SigmaStat\textsuperscript{\textregistered} Statistical Software for Windows Version 2.03 (Copyright\textsuperscript{\textregistered} 1992-1997 SPSS Inc.). Ethical approval for this project was obtained from the Ethics Committee of the Faculty of Medical Sciences, University of the West Indies, St. Augustine.

\section*{Results}

The names of the 393 laboratory-confirmed dengue patients were obtained from the CAREC database for 1996. Of these, 258 (66\%) could be traced to the source institution or the treating doctor. Clinical records were obtained for a total of 157 patients (40\%). Information was incomplete in 60 (15\%) of these cases. The following is an analysis of the clinical and demographic data available from the records of the 157 dengue-confirmed cases.

\subsection*{Geographical and temporal distribution of dengue virus infections}

One hundred and fifty-four patients' addresses were available. The estimated county-specific incidence rates (per 10,000 population) based on these addresses ranged from 0.60 to 1.87, with the extreme values occurring in the rural counties of Nariva/Mayaro and St. Andrews/St. David respectively (Figure 1). The highest proportion of these 154 confirmed cases (46\%) occurred in the most densely populated county of St. George, in which the capital, Port-of-Spain, is situated. There was no significant difference in the rates of infection among all the counties ($P=0.513$; power of test with $\alpha=0.05:0.301$).

A review of the admission dates to health care facilities for 136 dengue-confirmed patients showed that there was a gradual increase in the number of cases from April to June, followed by a large rise in July (29 cases) to a maximum in the month of August (51 cases). In 1996, the rainfall pattern (Figure 2) consisted of a large increase in the rainfall (171.7 mm) between April and May, followed by peak precipitation in June (333.1 mm). A comparison of dengue admissions with the monthly precipitation suggests a direct relationship between the rainfall and the number of cases reported, with a two-month lag between the peak rainfall and the peak number of admissions.
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Figure 1. Map of Trinidad showing county-specific incidence rates (per 10,000 persons) for dengue infections in 1996 (values in lower half of boxes) based on addresses from 154 confirmed cases. Values in the upper half of boxes show the proportion of the 157 cases found in each county. County divisions are according to the Regional Health Authorities of Trinidad & Tobago.

![Map of Trinidad](image1)

Figure 2. Monthly admissions of 136 laboratory confirmed dengue cases and precipitation levels for the year 1996. Rainfall data obtained from the records of the Trinidad & Tobago Meteorological Office, Piarco, Trinidad.

![Monthly admissions and rainfall graph](image2)
Incidence rates of dengue infections in relation to gender, age and ethnicity

Gender and age data were available for all 157 cases. There was a slight female predominance of 51.6%.

The highest proportion of the cases occurred in the 30-34-year age group (15.9% of the cases), followed by 59 and 10-14-year olds (14.0% and 14.6% respectively) (Figure 3). The differences among the groups were found to be highly significant ($P<0.001$; power of test with $\alpha=0.05$: 0.998). The estimated incidence rate in children ($\leq 15$ yrs) was not significantly different from that in adults ($>15$ yrs). An analysis of the estimated incidence rates by county showed that there was variation in the age groups with the highest incidence rates for each county. In three counties, the highest estimated incidence rates occurred in persons 40 years and over; Caroni (50-59 yrs) (2.9%), Victoria (40-49 yrs) (2.09%) and St. Andrews/St. David (40-49 yrs) (3.65%). However, estimated highest incidence rates were observed in younger patients in the counties of St George (0-9 yrs) (1.89%) and St. Patrick (10-19 yrs) (2.46%).

Figure 3. Age distribution of 157 confirmed dengue cases
Self-reported ethnicity was available for 136 patients. Of these, 50% were South Asians, 35% were Africans, 11% were mixed, and 4% were Chinese and Europeans. As seen in Figure 4, a comparison of the incidence rates by ethnicity for the whole sample and by county showed that the incidence rates of dengue infection were the greatest among South Asians for the group as a whole and in three of the four counties. A statistically significant difference was achieved in the county, St. Patrick, where the number of South Asian patients was higher than the African patients ($P=0.005$; power of test with $\alpha=0.05$: 0.807), and in the whole group where the incidence rate for South Asians was significantly higher than the mixed population ($P=0.016$; power of test with $\alpha=0.05$: 0.70).

**Figure 4.** Incidence rates (per 10 000 persons) for 136 confirmed dengue infection patients by ethnicity for whole population and individual counties. County Victoria was excluded since ethnicity was reported in <50% of cases in that county.

Summary of clinical and haemorrhagic manifestations

Overall, 24 clinical symptoms were reported in the medical records retrieved. The frequency of these symptoms at presentation is shown in Figure 5. Multiple symptoms at the time of admission were generally reported. In this cohort, gastrointestinal (GIT) complaints (nausea, vomiting, diarrhoea and anorexia) were commonly reported (66.2%). Symptoms highlighted in black indicate the symptoms listed in the WHO clinical description of dengue fever\(^ { [14] }\). Four of these symptoms, arthralgia, retro-orbital (R/O) pain, rash and haemorrhage, were recorded in <50% of cases.
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Figure 5. Frequency distribution of clinical symptoms at presentation in 157 dengue confirmed patients. Symptoms highlighted in black are part of the WHO clinical description of dengue fever

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>100</td>
</tr>
<tr>
<td>Pain</td>
<td>99</td>
</tr>
<tr>
<td>Anorexia</td>
<td>99</td>
</tr>
<tr>
<td>Myalgia</td>
<td>98</td>
</tr>
<tr>
<td>Headaches</td>
<td>95</td>
</tr>
<tr>
<td>Vomiting</td>
<td>90</td>
</tr>
<tr>
<td>Dehydration</td>
<td>56</td>
</tr>
<tr>
<td>Upper resp.</td>
<td>52</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>50</td>
</tr>
<tr>
<td>R/O pain</td>
<td>50</td>
</tr>
<tr>
<td>Chills</td>
<td>45</td>
</tr>
<tr>
<td>Rash</td>
<td>42</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>38</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>34</td>
</tr>
<tr>
<td>Adenopathy</td>
<td>25</td>
</tr>
<tr>
<td>Conjunctivits</td>
<td>25</td>
</tr>
<tr>
<td>Dizziness</td>
<td>20</td>
</tr>
<tr>
<td>Petechiae</td>
<td>17</td>
</tr>
<tr>
<td>Malaise</td>
<td>15</td>
</tr>
<tr>
<td>Rhinorrhoea</td>
<td>14</td>
</tr>
<tr>
<td>Itching</td>
<td>11</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>7</td>
</tr>
<tr>
<td>Short breath</td>
<td>6</td>
</tr>
<tr>
<td>Photophobia</td>
<td>4</td>
</tr>
</tbody>
</table>

In 34 patients (21.7%), haemorrhagic manifestations (HM) other than petechiae were reported. The reported haemorrhagic symptoms and their frequency of occurrence are illustrated in Figure 6. More than one form of bleeding was noted in some patients. In keeping with the high frequency of gastrointestinal complaints reported, GIT bleeding including bloody stool and rectal bleeding occurred in 50% of the patients.

Six cases (approximately 4% of the 157 cases) could be defined as of DHF based on the WHO criteria for the diagnosis of DHF/DSS\[14\]. Of these, five were female; five were South Asians and one was mixed; four were children and one case (29-year old, South Asian female) died.
Figure 6. **Type and frequency of haemorrhagic symptoms among 34 dengue confirmed patients who presented with haemorrhagic manifestations. Symptom highlighted in black is part of the WHO clinical description for DHF**

- Gastrointestinal bleeding, 29.4%
- Gingival bleeding, 29.4%
- Bloody stool, 17.7%
- Urinary tract bleeding, 14.7%
- Nasal bleeding, 11.8%
- Not specified, 5.9%
- Heavy menstrual flow, 5.9%
- Rectal bleeding, 2.9%
- Bloodstained sputum, 2.9%

**Discussion**

We reviewed the clinical and demographic features of 157 dengue-confirmed patients from a DEN-1 epidemic in Trinidad. This epidemic followed the reintroduction of this serotype into the island in 1991 after an absence of 14 years and the first documentation of DHF in the island in 1993. Approximately 1,200 samples from suspected symptomatic patients were sent for laboratory confirmation and, of these, 393 (approx. 33%) proved to be positive. Clinical and demographic data reported here are from 40% of the confirmed cases from that outbreak. The outbreak was island-wide with the estimated incidence rates being the highest in rural communities, though most cases occurred in the most densely populated county of St. George. There was a slight predominance of females and the infection occurred in all age groups. The estimated incidence rates were generally higher in patients of South Asian ethnicity. Gastrointestinal symptoms were the most common clinical manifestations at presentation. Haemorrhagic manifestations, when present, also commonly involved GIT. Six patients met the clinical and laboratory criteria for DHF and, of these, one died.

However, the 157 (40%) available records closely reflected the distribution of patients from public and private hospitals, private doctors and health centres seen for the 258 names that were traced to their respective sample sources. In the sample of 258 patients, public hospitals accounted for...
71%, private hospitals 16.7%, and health centres and general practitioners 6.2% each. In the sample of 157 patients for whom medical records were obtained, public hospitals accounted for 67%, private hospitals 17.2%, health centres 6.4% and general practitioners 10%. Over 80% of the patients were seen in hospitals.

The majority of cases (46%) in the sample lived in the most densely populated county in Trinidad, St. George's where 36.5% of the total population of Trinidad resides and where the Capital, Port-of-Spain (POS), and its environs are located. Dengue, as a mosquito-borne infection, would be expected to spread rapidly in populous areas, so the presence of a large proportion of patients in and around POS is consistent with the experience elsewhere of dengue infection as an urban phenomenon. Interestingly, our estimates of county-specific dengue incidence (based on the sample of 157 patients) yielded rates that did not differ significantly between rural and urban counties in Trinidad. This suggests that despite the variation in population density, DEN-1 infection was fairly evenly spread across the island. The island of Trinidad is merely 4,828 km² and the similarity of the incidence rates across the island may reflect a combination of a DEN-1 naïve population and easy accessibility to all parts of the island.

The DEN-1 1996 epidemic occurred in the rainy season with most admissions taking place in July and August, 1-2 months after the peak rainfall for that year in June. Rainfall is considered to be a risk factor for the development of dengue outbreaks, especially where there is improper storage of water or the presence of receptacles in the domestic environment such as discarded plastic containers in which water can collect. The main mosquito vector for dengue viruses in the Caribbean and Latin America is Aedes aegypti, which breeds primarily in relatively clean, stagnant domestic water containers. Local research has shown that important breeding sites for Aedes in Trinidad and Tobago include outdoor drums, water tanks, tyres and small discarded bottles and cans, which get filled easily with stagnant fresh water during the rainy season. The lag between the peak rainfall and the number of confirmed dengue cases might reflect the period of the mosquito-vector population expansion.

All age groups were affected but over 63% of them were adults (>15 years, the cut off age for paediatric patients in Trinidad). Since DEN-1 had been reintroduced in Trinidad in 1991, it is expected that children aged 5 years or less would constitute a susceptible population. Infection in this group would be primary in which the majority would be asymptomatic. This may account for children aged 0-4 years comprising only 8% of the sample. Despite the 1992/93 DEN-1 outbreak in which over 3,060 cases were reported, there were still many adults in 1996 who were susceptible to DEN-1. In total, there were 3,588 reported cases that year. However, based on the CAREC experience, only 33% of the clinically suspected dengue cases at that time were actually confirmed by laboratory tests, suggesting thereby that even during that outbreak, many cases with clinical features consistent with dengue may in fact not have been of dengue infection. Clinical symptoms of dengue are known to overlap with many other infections such as measles, hepatitis A, rubella and leptospirosis.
The high proportion of cases in the 30-34, 5-9 and 10-14-year age groups suggests the possibility of spread between children and parents. In Trinidad and Tobago, 25% of the heads of households are 30-39 years of age with an average of 1.99 children per household. Trinidadian women often start their families in late teenage or early twenties, so parents aged 30-34 years will have children in the age groups 5-9 or 10-14 years.

The racial composition of this sample differs from that reported for the general population, which is composed of South Asians (40.3%), Africans (39.6%), mixed (18.4%) and the rest (1.6%) of other racial groups. Thus, there is an overrepresentation of South Asians (50%) in our sample with fewer persons of African origin (35%) and of mixed race (11%). Since hospitalized patients account for 84% of the study population, it may reflect an increased number of South Asians being hospitalized for dengue infection as compared with other racial groups. Teelucksingh has previously reported a higher incidence of more severe dengue infection and mortality in South Asian people (colloquially referred to as East Indians) in Trinidad.

These data cannot exclude differences in the environmental factors that might also increase the exposure of South Asian people to more mosquito bites. South Asians have traditionally been the predominant racial group in agriculture and animal rearing in Trinidad. In rural communities on the island there is relatively poor piped water supply, resulting in more water storage, thus providing ideal domestic breeding sites for Aedes aegypti. Therefore, farmers in rural areas of Trinidad may be at an increased risk of mosquito bites and consequent dengue infection. The tendency towards an increased incidence in South Asians is interesting and merits further analysis with larger cohorts of dengue-confirmed cases.

The range of symptoms reported in the 157 Trinadian dengue-confirmed patients is similar to those described for patients with acute dengue in other parts of the world. Recent-onset fever and generalized body pains occurred in almost all patients. Headache, anorexia and myalgia, which often occur in the prodrome, were noted in 60% or more of the cases. Gastrointestinal and upper respiratory symptoms were also common complaints at presentation. Gastrointestinal symptoms have been described as predominant clinical manifestations in epidemics in which there is an adult-susceptible population. The 1996 epidemic was almost wholly due to DEN-1 and the bulk of the study population comprised older children and adults.

The symptoms of classic dengue as described by WHO occurred in fewer than expected numbers of patients. For example, retro-orbital pain and arthralgia were reported in 32% of patients and rash only noted in 27%. While this may be due to a true low prevalence of these symptoms in the study population, the cultural expression of symptomatology may also contribute to a falsely low detection of these symptoms. For example, in Trinidad, all pains in the head region, including orbital pain, are commonly referred to as "headache". Similarly, joint pains may often be included in "muscle" pain or be part of a more generalized "body pains". The rash, which is usually transient, may be easily missed and even more so in dark-skin complexions.

Haemorrhagic manifestations, including petechiae, were noted in 51 (32.5%) patients. This is consistent with other reports.
of the prevalence of haemorrhage in dengue fever\[18\]. In keeping with the global experience, the bleeding manifestations occurred at many sites. Despite the bleeding manifestations in almost a third of the patients, the WHO criteria for DHF were fulfilled only by 6 (4%) patients\[14\]. Of these, five were female and one was male, five were South Asian and one was of mixed ethnicity and four were children and two were adults. One patient, a 29-year-old female of South Asian ethnicity died. The female gender and children were more prone to the development of DHF/DSS in dengue-endemic areas\[3\]. While the 1996 epidemic was predominantly DEN-1, DEN-2 was already endemic in the island\[12\]. Further, the predominance of persons of South Asian ancestry in this group was also consistent with the observation that certain races were more susceptible to DHF/DSS than others.

The number of cases of DHF/DSS may have been underestimated. One of the essential WHO criteria for establishing the diagnosis of DHF/DSS is the proof of increased vascular leakage such as an increase of at least 20% in average haematocrit for age and sex; a drop in haematocrit of 20% or more following treatment, or clinical evidence of the same such as pleural effusion, ascites or hypoproteinaemia\[14\]. However, since the plasma leakage can be transient and only evident by laboratory testing in milder forms of DHF cases (e.g. Grade 1 and 2 DHF), it is possible to miss patients with these forms of DHF if clinical monitoring of the haematocrit levels or tests such as lateral decubitus chest X-rays to detect small pleural effusions are not performed. The frequency of chest Xrays and serial blood tests in this cohort of patients varied with the hospitals that were visited. For example, chest Xrays were performed in fewer than 10% of the patients admitted to private hospitals but in over 60% of the patients in one public hospital. Serial blood tests were performed in approximately 20% of dengue cases in private hospitals but in 40-80% of patients admitted to three public institutions\[22\].

Furthermore, there are no locally developed reference ranges for haematocrit by age and sex in use in many laboratories in Trinidad where the reference ranges developed in primarily the Caucasian populations have been adopted for use. Moreover, haemoglobinopathies such as thalassaemia and sickle cell traits are not uncommon among the Trinidian population and these persons tend to have normal haematocrit levels below the reference ranges in use. Consequently, such patients presenting with 20% or more increase in haemoconcentration may fall within the adopted reference range, and if there is no repeat of haematocrit concentration in the convalescent period, evidence of haemoconcentration would have been completely missed and the patient wrongly diagnosed as DF instead of a mild form of DHF\[22\].

In summary, the DEN-1 epidemic in Trinidad in 1996 was characterized by a large number of clinically suspected but unconfirmed cases of dengue infection. Laboratory analysis of a third of all reported cases revealed that most of these cases were not of dengue. Furthermore, the variability in the data available from clinical records, wherever these could be found, resulted in less than optimal information retrieval for further analysis. From the available data set, the Trinidian dengue-infected patients were mainly older children and adults from
rural and urban communities. South Asians were predominant. A wide range of clinical manifestations was recorded, but the most common were gastrointestinal. Bleeding manifestations occurred in over 30% of DF cases but features of DHF were noted in only 4%. Improvement in clinical diagnosis and record-keeping is urgently required to underpin future clinical research in Trinidad.

References


