

Sero-epidemiological Study of Dengue/Dengue Haemorrhagic Fever in a Metropolitan Hospital in Bangladesh

by

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Abstract

A collaborative study initiated by the Chittagong Medical College Hospital (CMCH) and the Integrated Control of Vector-Borne Diseases (ICOVED) Project, during September 1996 to June 1997, was a hospital-based descriptive cross-sectional survey in the paediatric age group which identified DF/DHF serologically. The total number of patients were 155 males (60.7%) and 100 females (39.3%), the ratio being 1.5:1 and the mean age 7.1 years. Thirty-five (13.7%) cases were found to be positive for dengue, of which 71.4% were males and 28.5% females; 14.3% were primary, 37.1% secondary and 48.6% mixed primary/secondary. The dengue virus subtypes alone or in combination were: DEN-2: 2.9%, DEN-3: 47.7%, DEN-4: 28.6%, DEN-2+DEN-3: 2.9%, DEN-2+DEN-4: 11.4% and DEN-3+DEN-4: 8.6%. There was no DEN-1 case. Seasonal occurrence of positive cases was: pre-monsoon 28.5%, monsoon 25.7% and post-monsoon 45.7%. Most cases were from thickly populated old quarters of Chittagong city, but 2 cases also were found from far off rural areas of Chittagong. Test results from both labs were in full agreement and no clinical correlation was possible. Contrary to our common notion, dengue is present in Bangladesh with high male preponderance, higher frequency related to monsoon, predominant secondary and mixed types and all serotypes of virus except DEN-1. The present situation is possibly an alarming harbinger of a catastrophe warranting appropriate measures in all relevant spheres.

Keywords: Dengue sero-survey, Bangladesh, ICOVED Project.

Introduction

Dengue fever (DF) is a lesser known infectious disease among the public and

the medical profession in Bangladesh. The classical form of dengue has been known for more than a century in tropical south-East Asia and the Western Pacific region.

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However, dengue haemorrhagic fever (DHF) was reported for the first time in Thailand in 1958⁽¹⁾, in Myanmar in 1970⁽²⁾, and in India in 1963⁽³⁾, with regular epidemics and endemicity. These countries geographically surround Bangladesh. On the other hand, Bangladesh is a country where most infectious diseases are prevailing. Of these, vector-borne diseases such as malaria, filariasis and kala-azar are endemic. Dengue is a similar vector-borne disease transmitted by *Aedes aegypti*. All favourable environmental conditions conducive for maintaining such mosquitoes are present here. In clinical practice many febrile infectious cases with features similar to dengue are found without any evidence of bacterial/ etiological agent by available tests. In 1964, there was an outbreak of dengue called 'Dhaka fever', which was the first documented outbreak of dengue infection in Bangladesh⁽⁴⁾ and only one serotype DEN-3 was incriminated. This followed an outbreak in Kolkata (India) in 1963. A few cases of dengue fever were found in 1977-78 in selected areas of Bangladesh by a serological survey done by the Institute of Epidemiological Diseases Research (IEDCR). Some other sporadic studies undertaken with the help of WHO detected evidence of dengue in Dhaka city in the Seventies and Eighties. But no formal documentation was done and, up to 1986, it was thought that four major cities of Bangladesh were free of dengue haemorrhagic fever⁽⁵⁾. But over the last decade the scenario has changed. Dengue and DHF have evolved as serious emerging infectious diseases causing high morbidity and significant mortality in almost all countries in south-east Asia.

Bangladesh has an active relationship with all these countries in all sectors, necessitating cross-border communication and travel by people. Thus, there is reason to believe that dengue has a significant presence in the country, which is escaping clinical attention because of the non-availability of appropriate lab facilities and the clinical features of dengue being non-specific.

In view of the above, the Directorate-General of Health Services, in collaboration with WHO, included a formal sero-epidemiological survey of DF and DHF as one of the components of the Integrated Vector-Borne Diseases Control Project (ICOVED). The aims of this survey were: (i) to identify the proportion of dengue/DHF amongst patients aged 1–15 years attending the Chittagong Medical College Hospital; and (ii) to attempt clinical correlation, if possible.

Materials and Methods

This hospital-based descriptive cross-sectional survey (September 1996–June 1997) was based on random accidental sampling to define and identify eligible patients suspected of DF/DHF. Paired serum samples from each index case were taken. The *first* sample on attendance at the outpatient department was accepted only after confirmation as per inclusion/exclusion criteria after 48 hours. The *second* sample was taken after seven days of the first sample. The Chittagong Metropolis was chosen for the study and the centre was the Chittagong Medical College Hospital, the only tertiary health care delivery centre covering the

population of the city, the suburbs and the adjoining hill districts.

Case inclusion criteria: 1-15 years of age, febrile illness for 72 hours, no focal clinical signs within next 48 hours, chest X-ray (CXRPA), complete blood count (CBC), urine routine examination (URE) negative for any other infectious diseases, and negative blood slide examination for malaria parasite.

Case exclusion criteria: Clinical review and routine tests revealing any confirmatory evidence of other infectious diseases, refusal to give consent and or samples plus lost from follow-up.

Serological diagnosis and tests: The diagnosis was done with serological test, the haemagglutination inhibition test (HIT) as per 'Clarke & Casals Technique 1958'⁽⁶⁾, which was done at the Virology Laboratory of IEDCR. A total of 152 samples were cross-checked at the Armed Forces Research Institute of Medical Science (AFRIMS) in Bangkok, Thailand.

Sample collection and transportation: Samples were collected and stored at -20°C and were bulk transported to IEDCR for testing.

Data collection and analysis: A specified data collection form was used for each case. The data was analysed with EPI6 software following the standard format.

Results

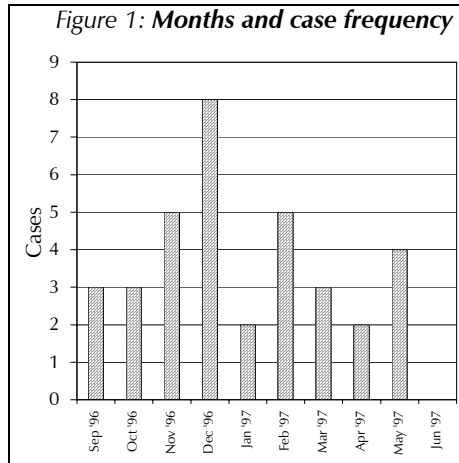
A total of 283 cases were screened, out of which 255 cases with a mean age of 7.1 years were included for the study,

generating the same numbers of paired sera. Out of these, 35 (13.7%) cases were found to be positive by HI test, of which 25 were males and 10 females (Table 1).

Table 1: Patients and HI test profile

Parameters	Results
Cases included for the study	Total 255, male 155 (60.7%), female 100 (39.3%). Age: mean 7.1±2.8 years, maximum 15.0, minimum 2.0, mode & median 7.0, 95%CI 6.76-7.44
HI positive cases	Total 35, male 25 (71.4%), female 10 (28.5%). Age: mean 7.1±2.8 years, maximum 15, minimum 2.0, median and mode 7.0, 95%CI 6.17-8.03
Viral sero-types	D ₁ : 00(0.0%), D ₂ :01(2.9%), D ₃ :16(47.7%), D ₄ :10(28.6%), D ₂ +D ₃ : 01(02.9%), D ₂ +D ₄ :04(11.4%), D ₃ +D ₄ :03(08.6%)
Infection types	Primary:05(14.3%), secondary: 13(37.1%), primary/secondary: 17(48.6%)

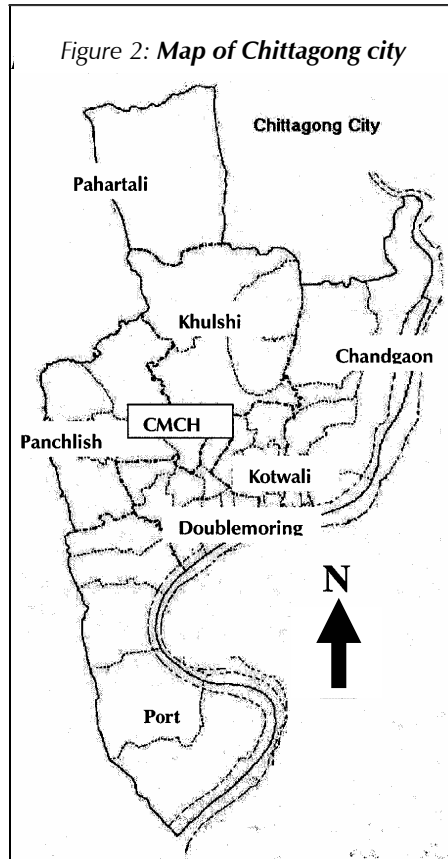
The sample collection did not spread over the whole year and all the seasons as it was done only from September 1996 to June 1997. Roughly, the collection covered a part of the monsoon, post-monsoon and pre-monsoon periods. The positive cases showed higher frequencies during the pre- and post-monsoon periods. But the highest yield was found during the autumn and winter periods (Figure 1).



The area-wise distribution of cases showed that 33 cases came from different zones of Chittagong city and one each from a contiguous and a non-contiguous rural area. But most cases were from the thickly populated old quarters of the city (Table 2 and Figure 2)

Table 2: Area-wise frequency distribution of positive cases

Zone	Cases	Comments
Kotwali	17 (48.5%)	Old quarter, thick population
Pahartali	05 (14.2%)	Old quarter, thick population
Doublemoring	04 (11.5%)	New quarter, less thick population
Panchlish	04 (11.5%)	New quarter, less thick population
Chandgaon	03 (08.5%)	New quarter, less thick population
Anowara	01 (02.8%)	Contiguous rural area
Chandanish	01 (02.8%)	Non-contiguous rural area



The clinical and lab features, including patterns of haemorrhagic features and their frequencies, were compared between the positive and negative groups, which was found to be non-significant (Table 3).

Of the lot, 152 paired samples were cross-checked at AFRIMS, Bangkok, Thailand. The results were in complete agreement with those of IEDCR, Dhaka ($\chi = 1.0$).

Table 3: Haemorrhagic features comparison

Haemorrhagic features	Positive group (N=35)	Negative group (N=230)
Ecchymosis	00 (00.0%)	00 (00.0%)
Epistaxis	01 (02.9%)	00 (00.0%)
Gum bleeding	00 (00.0%)	00 (00.0%)
Hematokezia*	00 (00.0%)	00 (00.0%)
Hematuria	00 (00.0%)	00 (00.0%)
Hemoptysis	01 (02.9%)	00 (00.0%)
Melena	00 (00.0%)	01 (00.5%)
Rash	03 (08.6%)	20 (09.1%)
Red eyes	02 (05.7%)	13 (05.9%)
Tourniquet test	00 (00.0%)	00 (00.0%)

Discussion

This study revealed that dengue infection was present in the country among a significant proportion of febrile patients. The presence of more secondary responses pointed to the fact that the transmission was continuing. Moreover, the evidence of more than one viral serotypes should be taken as a warning that outbreaks of DHF might occur in the future⁽⁷⁾. The interpretation of the study was based on the WHO criteria for HI test, so there might be some lacunae of cross-reaction by other *falvivirus* infection as evident through some equivocal test results. However, the overall interpretation was that a low-grade infection and transmission was present.

* Hematokezia is unaltered per anal bleeding in contrast to melena.

This should warn the health authorities and policy-makers that dengue outbreaks might occur in the future. From the experiences of other dengue-endemic countries an inference can be drawn that a similar situation might occur in Bangladesh as well⁽⁸⁾.

The clinical correlation was not possible as clinicians were not acquainted with the presentation and management of dengue cases. Thus in this study, some subtle changes were perhaps ignored which one would take into account after becoming conversant with the condition. During this period a serious dengue outbreak was occurring in neighbouring India (1996)⁽⁹⁾ and in Thailand (1997). There might have been a linkage with the outbreak in India as there is intense population exchange between that country and Bangladesh, not to speak of only the city of the study. The outbreak in Chittagong possibly was of low grade and therefore without any severe syndrome to draw attention by visible characteristic features. But covert changes may, in future, lead to cases with severe characteristic features.

Most cases were from the old quarters of the city which have a high population density. This reaffirms the role of the predisposing factors for the breeding and sustenance of the vector. These factors are not only present but are constantly increasing. The real concern, however, is the reporting of cases from rural areas; though it is not unusual for dengue to spread to rural areas.

The full matching of test results made by IEDCR and AFRIMS suggests that if appropriate measures are taken, efficient capacity for lab diagnosis can be built within Bangladesh. In fact, confirmatory specific lab test is neither essential nor is needed for guiding the clinical management of dengue. But these tests are important for the epidemiological and control programmes. Ideally, sentinel surveillance should be continued where these tests become necessary.

From this study it can be concluded that dengue infection is present in Bangladesh, and that its outbreaks may occur any time, and DHF may also take the usual toll of life. Therefore, national programmes should address the issue appropriately in all its aspects such as diagnosis and clinical management, continued surveillance, capacity-building

for lab confirmation and viral isolation. Moreover, linkages and collaboration should be developed with countries and centres conversant with this public health problem by appropriate utilization of WHO portals and channels.

Acknowledgement

The authors are grateful to the AFRIMS, IEDCR and M&PDC units for their continued support in making this study a success. Special thanks to Dr Ananda Nisalok of AFRIMS for her painstaking endeavours in training our lab technicians in dengue serology and to Dr Timothy P Endy also of AFRIMS for his generous help in providing the dengue antigen.

References

1. Jatnasan S, Skuntanaga P and Dhanasiri C. Some aspects of epidemiology of Thai haemorrhagic fever 1958-1961. In Symposium on haemorrhagic fever, SEATO Medical Research Monograph No 2, Bangkok, Post Publ Co Ltd, 1962, pp 6-21.
2. Thuang U. Dengue Haemorrhagic fever in Burma. *Asian J Inf Dis*, 1978, 2: 23.
3. Pavri KM. Does dengue haemorrhagic fever occur in India as a clinical entity? *Asian J Inf Dis*, 1978, 2: 31-33.
4. Aziz MA, Gorham R and Gregg MB. 'Dhaka Fever'. *Pakistan Journal of Medical Research*, 1967, 6: 83-92.
5. Khan M and Ahmed T. Dengue status in Bangladesh. *Dengue News Letter*, 1986, 12: 11.
6. Clarke DM and Casals J. Technique for hemagglutination and hemagglutination inhibition with arthropod-borne-viruses. *Am J Trop Med*, 1958, 7: 561.
7. Nimmannitya S. Assignment Report: 20-28 August - Clinical management of Dengue/Dengue Haemorrhagic Fever in Bangladesh. WHO/STC, SEA/VBC/58, 1997.
8. Richards AL, Bagus R, Baso SM, Follows GA, Tan R, Graham RR, Sandjaja B, Corwin AL and Punjabi N. The first reported outbreaks of dengue haemorrhagic fever in Irian Jaya, Indonesia. *Am J Trop Med Hyg*, 1997, 57(1): 49-55.
9. Kabra SK, Jain Y, Pandey RM, Madhulika T, Singhal T, Tripathi P, Broor S, Seth P and Seth V: Dengue haemorrhagic fever in the 1996 Delhi epidemic. *Trans Royal Soc Trop Med Hyg*, 1999, 93: 294-298.