CLINICAL PROFILE OF DENGUE FEVER AND DENGUE HAEMORRHAGIC FEVER IN CHILDREN DURING AN OUTBREAK IN TIMOR LESTE, 2005

Hem Rimal, Daisy Joy Espejo, Jocelyn Reyes, Domingas Angela Da Silva Sarmento, Ana Magno and Milena Maria LayDos Santos.

Abstract

Introduction: Dengue fever (DF) is a disease first termed "water poison" in a Chinese encyclopedia of disease symptoms and remedies published during the Chin Dynasty (265 to 420 A.D.)

Objectives: This study aimed to find out the main clinical presentations and laboratory changes of Dengue fever (DF) and Dengue hemorrhagic fever (DHF) and also to review the various treatment modalities.

Method: Retrospective study of DF and DHF cases admitted to Hospital Nacional Guido Valederes (HNGV) in Dili, from January to March 2005. WHO protocol and management guidelines were used for diagnosis and management.

Results: A total of 105 IgM positive cases were studied with 79% DHF and 21% DF. The median age of the patient was 42 months. The most frequent age group affected was 1 - 5 years. The Severity of the outbreak was evidenced by the most common presentations apart from fever being melena (36%) and epistaxis (32%).

Discussion: This outbreak of DF/DHF was of high severity causing significant mortality and morbidity in East Timor. The commonest age group affected was 1-5 years, which is the most vulnerable age group in developing countries. Hemorrhagic manifestations were main presentations to come to hospital rather than headache, arthralgia and rashes. We had higher than expected requirements of blood transfusion .The description of the nature and severity of presentations may be useful for clinicians working in similarly sub-optimal conditions.

Key words: *DF, DHF,DSS, Tourniquet test.*

Introduction

Dengue fever (DF) is a disease first termed "water poison" in a Chinese encyclopedia of disease symptoms and remedies published during the Chin Dynasty (265 to 420 A.D.) (1). It has reemerged in the past 20 years with an expanded geographic distribution of both the virus and the mosquito vector. It has been estimated that 50 million cases of dengue fever occur annually (2).

Dengue Fever is characterized by sudden onset of fever, which usually lasts for 2 to 7 days, accompanied by nonspecific flu-like symptoms. During the acute phase of illness it is difficult to distinguish DF from other illnesses found in tropical areas. (3). Dengue Haemorrhagic Fever (DHF) is primarily a disease of children under the age of 15 years, although it may also occur in adults (4,1). The WHO case definition of DHF is presence of DF with high-grade continuous fever of 2-7 days, and a hemorrhagic diathesis, thrombocytopenia (platelet count < 100,000/dl), or with evidence of plasma

leakage. Haemorrhagic manifestations commonly include skin (petechiae, purpura, ecchymoses or a positive "Tourniquet Test") and less frequently epistaxis and bleeding gums, gastrointestinal haemorrhage, and haematuria.(5,6,7) Plasma leakage is defined as a rise in hematocrit > 20% from baseline, or drop > 20% after sufficient fluid therapy, hypoproteinemia, pleural effusion or ascites.

The WHO grades the severity of DHF I-IV. Grades II and I are non-shock DHF. In grade I DHF the only hemorrhagic manifestation is a positive tourniquet test or tendency to bruise, while in grade II there is spontaneous bleeding, usually in the form of petechiae, purpura and echymoses of skin, bleeding from the nose or gums, hematemesis or melena. Grades III and IV DHF are cases with impending shock or shock..

A definitive diagnosis of dengue infection can be made only in the laboratory and depends on isolating the virus, detecting viral antigen or RNA in serum or tissues, or detecting specific antibodies in the patient's serum (8, 9,10,11).

In 2005 Timor Leste was recovering from political crisis. This was a time when Timor Leste's medical system was being rebuilt with developing health strategies and planning, and only very limited resources. Timor Leste's GDP of US$400 per capita in 2004 rated the nation 212th in the world. Hospital Nacional Guido Valederes (HNGV) in East Timor's capital is the only tertiary level hospital in Timor Leste. The hospital has 264 beds of which 35 are for pediatric patients. At the time of this outbreak of dengue fever the hospital had three paediatricians. This article aims to describe the manifestations of DF and DHF in children who presented to HNGV during the dengue fever outbreak in 2005.

Methods

The data for this study were retrieved from the medical records of patients who were admitted to the pediatric ward with dengue fever and dengue hemorrhagic fever between January and March 2005. Ethical approval was obtained from the hospital director to do this study. Cases were identified from the hand- written discharge register on the ward with a diagnosis of DF or DHF. Those patients with serologically confirmed Dengue infection were analyzed further.

Testing for Dengue infection was performed at the Hospital Nacional Guido Valederes (HNGV) Laboratory using PanBio dengue duo IgM and IgG rapid strip tests. The presence of IgM was interpreted to mean current infection. Dengue Fever and Dengue Hemorrhagic Fever were diagnosed based on standard WHO definitions. Data recorded were age and sex, clinical features, severity of disease, length of stay and treatment. National data was obtained from the Timor Leste Ministry of Health, on August 1st, 2005. Data was analysed using SPSS software.

Results

By 1st August 2005, Timor Leste Ministry of Health had noted 1070 cases of DF and DHF throughout the country so far that year. 453 were DF, 598 DHF and 19 DSS with a reported case fatality rate of 3.6%.

596 patients were admitted during the study period to HNGV with a diagnosis of dengue fever or dengue hemorrhagic fever. Because of resource limitations only 161 cases underwent serology testing, of which 105 (65.2%) cases were IgM positive. Only those IgM positive cases are included for this analysis.

The median age of patients was 42 months and age range was 6 months to 14 years with a slight female preponderance (Table 1).

Table 1: Distribution of Dengue Fever and Dengue Haemorrhagic Fever cases by Age

Age range	Number (%)
< 1year	8 (7.6)
1-5 years	62 (59)
5-9 years	32 (30.5)
10-14years	3 (2.9)
Total	105 (100)

Table 2: Clinical manifestations of Dengue Fever and Dengue Haemorrhagic Fever

Clinical feature	N (%) n = 105
Fever n (%)	105 (100%)
Melena	36 (34.3%)
Epistaxis	32 (30.5%)
Vomiting with or without blood	32 (30.5%)
Rashes	26 (24.8%)
Arthralgia	12 (11.4%)
Convulsion	14 (13.3%),
Diarrhoea	14 (13.3%),
Headache	10 (9.5%)
Altered sensorium	1 (0.95%).

The commonest presenting features of children with confirmed Dengue infection were fever (100%), melena (34.3%), epistaxis (30.5%) and vomiting (30.5%) (Table 2).

Of these, 83 (79%) had Dengue Haemorrhagic Fever, of which 36 (44%) were Grade III or IV (Table 3).

Table 3: Distribution of Dengue Haemorrhagic Fever by Grade

DHF Grades	Number (%) n=83
Grade I	22 (26%)
Grade II	25 (30)
Grade III	32 (39)
Grade IV	4 (5)
Total	83 (100)

Those with Grade III or IV DHF had significantly increased mortality (Table 4).

Table 4: Length of stay, haematological findings and mortality in Dengue Fever and Dengue Haemorrhagic Fever (DHF).

Grade	Number (%)	Mean Length of stay	Leucopaenia (WBC count < 5,000/dl).	Thrombocytopaenia (platelet count <100,000/dl).	HCT >20% N (%)	Deaths (%)
DHF, Non-Shocked group (Grades I & II)	47(45)	4.46	14 (29.7)	45(95.7)	25(53)	2 (4.2)
DHF, Shocked group (Grades III&IV)	36(34)	5	13 (36.11)	30(83.3)	16(44)	13 (36)
Dengue Fever	22 (21)	3.95	5	1	3(14)	0
TOTAL	105	xx	xx	xx	xx	15 (14)

The Tourniquet test was routinely done in almost all dengue suspects. In DF alone (n=22), only 13(59%) patients were positive. In DHF non-shock group (n=47) 31(65%) were positive while in DHF shocked group (n=36), 19 (52.7%) had a positive TT test.

Convulsions appeared to us to carry a poor prognosis, with four of the fifteen deaths occurring in this group. However, X^2 test demonstrates no statistical difference from the overall mortality rate (p= 0.10).

Co-infections included pneumonia in 8 children, malaria in 7 and 1 with septicemia. Therapy was based on the WHO guidelines for smaller hospitals and consisted mainly of IV fluid therapy and blood transfusions.

Discussion

The dengue outbreak of 2005 in Timor Leste caused significant paediatric morbidity and mortality. In this study, the number of cases of DHF (n=83) was nearly 4 times the cases of DF (n=22), which is similar to the outbreak in Neivea, Columbia in 2004 (12). The median age of affected children, 42 months, is slightly younger than outbreaks among children in Bangkok, where a trend of increasing age was proposed. In their study they found the median age of children increased from 5.6 years in 1970 to7.4 years in 1980 (13).

The reasons for an increased number of cases and severity of disease found in children compared with adults is not well understood but it is proposed that previous infection, or strain of virus are implicated (14).

In this study, the highest percentage of cases of DHF were grade III (39%), a group with a high potential for complications and a worse prognosis (15).

A positive tourniquet test is one of the several clinical parameters considered by the world health organization to be important in the diagnosis of dengue hemorrhagic fever (16). We found a higher rate of positive tourniquet tests (60%) than in a Columbian study (34%) and the study by Malavige (17,18). The TT positivity was high in non-shock group of DHF patients (65%) than shock group (52.7*%)*

We were surprised by the relatively low co-infection rate of malaria in a region where it is endemic, but a higher than expected rate of co infection with pneumonia.

Significant interventions were needed for management of the shocked group of DHF patients. Among DHF patients, 38% being treated with a blood transfusion is higher than reported elsewhere (19). This may relate to severity of presentation, but also to availability of resources. As we had no blood bank facility, family members were asked to donate blood for transfusion, if required.

The small proportion of children who underwent confirmation of the diagnosis by serology testing limits this study. Our study has a bias towards greater severity because we were more likely to admit and test cases who were sicker. Hence the case fatality rate (CFR) of 14% among tested cases was far higher than the rate reported by the Ministry for Health for this outbreak, and the CFR of 7.5% noted during the 1996 outbreak in Delhi in a hospital based study (20) Nevertheless, the description of the nature and severity of presentations may be useful for clinicians working in similarly sub-optimal conditions.

Conclusion

This study looked at the various clinical and laboratory features DF and Dengue Hemorrhagic fever in Children. The

description of the nature and severity of presentations may be useful for clinicians working in similarly sub-optimal conditions. This study also adds the fact that Due to Dengue virus infection childrens are affected very severly and can cause severe morbidity and mortality.

Limitation

Since this study was retrospective in nature and documentation of information was missing a lot of cases were excluded from the study. This study was completed in a very resource poor setting our sample size was much smaller than the actual cases admitted in the hospital. Our study was biased towards severity of cases as we were more likely to admit them and test as well. This study has added important important information about the varied presentation of Dengue infection in children and dofferent modality of treatment.

Acknowledgements

We are grateful to Senor Antonio Caleres, Director of Hospital Nacional Guido Valederes (HNGV), and the medical records staff for their support. We would like to thank all the doctors, nurses and other team members who worked additional long hours during the dengue fever outbreak, working day and night to save the lives of Timorese children. We would like to extend our sincere gratitude to Dr Rob Roseby for his thoughtful comments and great support in writing the manuscript.

References

1. **Gubler, D.J.** Dengue and Dengue Hemorrhagic Fever. *Clinical Microbiology Reviews* 1998; 11(3): 480-496.

2. World Health Organisaion. Dengue hemorrhagic fever case management guidelines, WHO collaborating center for case management of Dengue/DHF/DSS.Queen Sirikit National Institute of child health, Bangkok.

3. **Guha-Saphir D, SchimmerB**.Dengue fever: new paradigms for a changing epidemiology.Emerging Themes In Epidemiology 2005, 2:1

4. **Dietz V, Gubler DJ, Ortiz S, Kuno G, Casta-Velez A, Sather GE, Gomez I, Vergne E**. The 1986 dengue and dengue hemorrhagic fever epidemic in Puerto Rico: epidemiologic and clinical observations. P R Health Sci J 1996; 15:201–210.

5. **Eram S, Setyabudi Y, Sadono TI, Sutrisno DS, Gubler DJ, Sulianti-Saroso J.** Epidemic dengue hemorrhagic fever in rural Indonesia: clinical studies. Am J Trop Med Hyg 1979; 28:711–716.

6. **Sumarmo SPS, Wulur H, Jahja E, Gubler DJ.** Clinical observations on virologically confirmed fatal dengue infections in Jakarta, Indonesia. Bull W H O 1983;61:693–701.

7. **Halstead S.B.** Pathogenesis of dengue: Challenges to molecular biology. Science 1998; 239(4839): 476-81

8. **Feres , V.C, C.M Martelli, et al**. Laboratory surveillance of dengue virus in Central Brazil, 1984-2003. J Clin Virol 2006;37(3):179-83.

9. **Guzman MG, Kouri G**. Advances in dengue diagnosis. Clin Diagn Lab Immunol 1996; 3:621–627.

10. **Vorndam, V. Kuno, G**. Laboratory diagnosis of dengue virus infections. In: Gubler DJ, Kuno G. . Dengue and dengue hemorrhagic fever—1997. London, United Kingdom: CAB International; 1997; 313–334.

11. **Pei-Yun Shu and Jyh-Hsiung Huang**,Current advances in Dengue Diagnosis. Clinical and diagnostic lab immunology, 2004; 4: 642-650.

12. **Salgado, D.M , J.A, Rodriguez, et al** . Clinical and epidemiological characterisation of dengue haemorrhagic fever in Neiva , Columbia 2004. Rev Salud Publica (Bogota),2007 ; 9 (1) : 53-63.

13. **Nimamannitya ,S**. Dengue hemorrhagic fever in Thailand. Southeast Asian Journal of Tropical medicine and public health,1987; 18:291-294.

14. **Barns&Rosen**. Fatal hemorrhagic disease and shock associated with primary dengue infection on pacific island. American Journal of Tropical medicine and hygie*n*e,1974: 23,595-606.

15. **Quereshi Ja et al.** An epidemicof Dengue fever in Karachi-associated clinical manifestations. Journal of Pak Med Assoc.1997; 47(7):178-81.

16. **Cao , X.T, T.N Ngo, et al** . " Evaluation of the world health organization standard tourniquet test and a modified tourniquet test in the diagnosis of dengue infection in Vietnam Trop Med Int Health ,2002:7 (2): 125-32.

17. **Mendez A et al**.Dengue hemorrhagic fever in children: Biomedica,2003 ;23(2):180-93

18. **G.N.Malavige,PK Ranatunga,vgns Velathanthiri et al**.Patterns of disease in Sri Lankan dengue patients.Arch Dis Child 2006;91:396-400.

19.**Chuansumrit,A.V.Philmolthares et al**.Transfusion requirements in patients with dengue hemorrhagic fever. South East Asian journal tropical medicine Public Health,2000;31(1):10-4.

20**. Kabra, S.K, Y.Jain,et al**. Dengue haemorrhagic fever in children in children in the 1996 Delhi epidemic. Trans R Soc Trop Med Hyg. 1999; 93 (3): 294-8.

Address of Correspondence: *Dr Hem Sagar Rimal,* Pediatrician ,Department of pediatrics Nobel Medical college teaching hospital, Kanchanbari—5 , Biratnagar , Nepal.