

Prevalence of undifferentiated fever in adults of Rawalpindi having primary dengue fever

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Abstract

The objectives of the study were to highlight early subclinical presentation of dengue viral infection (DVI) as an undifferentiated febrile illness. The descriptive cross-sectional study was carried out at Microbiology Department, Rawalpindi Medical College from March to September 2009. Stratified random sampling was used to select subjects from various urban and rural areas of Rawalpindi, and Serum IgG anti-dengue antibodies were detected by using 3rd generation enzyme-linked immunosorbent assay (ELISA). Out of the total 240 subjects, 69 (28.75%) were found to be positive for anti-dengue IgG antibodies. Of the positive cases, 41 (59.4%) - comprising 31 (44.9%) urban residents - and 10 (14.4%) rural residents presented with a previous history of undifferentiated fever ($p < 0.05$). It was concluded that primary DVI can present as subclinical form in healthy population residing in rural and urban areas of Rawalpindi, which is an alarming situation indicating the spread of disease in the study area.

Keywords: Dengue viral infection, Undifferentiated fever, Healthy adults.

Introduction

Dengue viral infection (DVI) is an endemic viral disease in many tropical and subtropical regions of the world. It usually affects the residents of urban and semi-urban areas. It is now endemic in >100 countries of Africa, America, Eastern Mediterranean, South East Asian and Western Pacific regions.¹ It infects about 50-100 million people annually. More than 2.5 million cases have dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS), resulting in 24,000 deaths annually.^{2,3} The clinical manifestations of dengue fever (DF) range from mild undifferentiated fever to fatal outcomes i.e. DHF and DSS. The mortality rate with these complications might reach up to 5%.⁴ The term 'undifferentiated fever' usually refers to a febrile illness with no organ-specific disease.⁵ DVI, leptospirosis, enteric fever and Japanese encephalitis are among the few common

examples which can present as undifferentiated fever.⁶ The absence of specific vaccine and anti-viral drugs for DF are mainly responsible for making this infection a global health problem.⁷ Moreover, the geographical expansion of DF vector, the *Aedes aegypti* and co-circulation of multiple serotypes increases the severity of the disease 30-fold.⁸

Diagnosis on clinical grounds is not reliable and it must be confirmed by serological tests as more than half of the infected individuals are either asymptomatic or have a mild fever. Keeping this in view, the detection of anti-dengue IgG antibodies by enzyme-linked immunosorbent assay (ELISA) was used as the main procedure as it is a highly sensitive (97.5%) and specific method, therefore minimising the chances of erroneous results.⁹

In Pakistan, like many other regions of the world, DF is becoming an endemic viral disease. This alarming situation is troublesome because the main focus for disease control remains on reducing the spread of vector population until the discovery of specific vaccine or anti-viral therapy is made.¹⁰ This can otherwise cause DVI and its complications to grow phenomenally. The current study was carried out to highlight the hidden cases of primary DF among healthy adult population of Rawalpindi, Pakistan.

Methods and Results

Using stratified random sampling in 14 different areas of the city (urban) and five nearby villages (rural), the study was conducted from March to September 2009. A total of 240 adults, >18 years of age were included in the study. The sample size was established based upon the prevalence of DVI in Rawalpindi and also depending on the urban and rural population distribution. The subjects were selected systematically from the relevant area voter lists after obtaining approval from the Ethical Review Committee of Rawalpindi Medical College, Rawalpindi. Individuals with previous history of dengue fever, immunisation for yellow fever, Japanese encephalitis and tick borne fever were excluded from the study to reduce the chances of cross-reacting antibody formation during ELISA test procedure, which was for the detection of IgG anti-dengue antibodies. The participation in the study was on a voluntary basis.

The subjects were asked various questions according to the

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Table: Undifferentiated fever in anti-dengue IgG positive individuals.

Undifferentiated Fever	Urban (n=50) n (%)	Rural (n=19) n (%)	Total no. of positive cases n=69 (%)	Mean duration of complaints (Days)	Standard Deviation (SD)	Chi Square (χ^2)	P-value
Present	31 (62)	10 (53)	41 (59.4)	141.3	9.19	0.479	0.030
Absent	19 (38)	9 (47)	28 (40.5)				

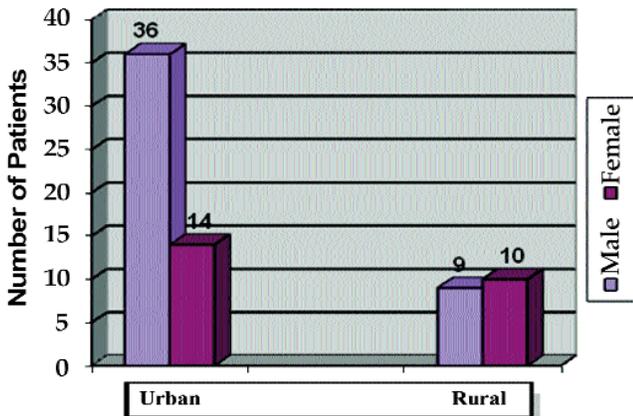


Figure: Male and female distribution of the exposed subjects.

inclusion and exclusion criteria. The answers were recorded on the biodata proformas. 3 ml of venous blood was drawn aseptically from the subjects, and the samples were transported to the Microbiology Department, Benazir Bhutto Hospital, Rawalpindi, for further processing.

The samples were centrifuged at 3000 revolutions per minute (rpm) for 5 minutes to separate sera which were stored at -20°C. The sera were used to detect the anti-dengue IgG antibodies by 3rd generation ELISA kits (Omega, Scotland) in serial batches using Microplate reader, Dia 710, Diamate (Germany). The positive and negative control samples were run along with each batch to maintain the quality of results.

The data was analysed using SPSS version 16. Frequencies and percentages were calculated and chi square test was applied to compare the observed data with the expected data according to the hypothesis of the study. A p value of <0.05 was considered significant for statistical inference.

Out of the total 240 subjects, 69 (28.75%) were positive for anti-dengue IgG antibodies. There were 144 (60%) subjects from urban areas, and 96 (40%) from rural areas. Of the rural population, 50 (34.7%), including 36 (72%) males and 14 (28%) females, were positive for anti-dengue IgG antibodies. Out of the rural population, 19 (19.8%), including 9 (47%) males and 10 (53%) females, were positive for anti-dengue IgG antibodies.

Overall, there was a very high prevalence of DF (n=50; 21%) in urban areas and in rural areas (n=19; 8%) of Rawalpindi (Figure).

Out of the 69 cases positive for anti-dengue IgG antibodies, 41 (59.4%), including 31 (44.9%) from urban areas and 10 (14.4%) from rural areas, presented with a history of undifferentiated fever (Table).

Housewives were mostly affected (n=18; 26%). The history of mosquito bite (n=61; 88.4%) and history of interaction with DF patients (n=11; 15.9%) were the most important predisposing factors.

Conclusion

Primary DF can present as undifferentiated fever and is prevalent both in rural and urban areas of Pakistan. The situation highlights the need for measures to prevent life-threatening complications.

References

- Shu PY, Hang JH. Current advances in dengue diagnosis. *Clin Diag Lab Immunol* 2004; 11: 642-50.
- Gubler DJ. Dengue and dengue hemorrhagic fever: its history and resurgence as a global health problem. Fort Collins, Colorado. *CAB Intern* 1997; 1: 22.
- Rigau Perez JG, Clark GG, Gubler DS, Reiter, Sanders EJ, Vorndam AV. Dengue and dengue hemorrhagic fever, New York. *Lancet* 1998; 352: 971-7.
- Noisakran S, Perng GC. Alternate hypothesis on the pathogenesis of dengue hemorrhagic fever (DHF) / dengue shock syndrome (DSS) / and Dengue virus infection. *Exp Biol Med* 2008; 233: 40-8.
- Joshi R, Colford JM, Reingold AL, Kalantri S. Non-malarial acute undifferentiated fever in a rural hospital in central India: Diagnostic uncertainty and over treatment with anti-malarial agents. *Am J Trop Med Hyg* 2008; 78: 393-9.
- Phoung HL, Vries PJ, Nga TT, Giao PT, Hung LQ, Binh TQ et al. Dengue as a case of undifferentiated fever in Vietnam. *BMC Infect Dis* 2006; 6: 123.
- Hapugoda MD, Barta G, Abeewickreme W, Swaminathan S, Khanna N. Single antigen detects both immunoglobulin M (IgM) and IgG antibodies elicited by all four dengue virus serotypes. *Clin Vaccin Immunol* 2007; 14: 1505-14.
- Deen JL, Harris E, Willi B, Bemaseda A, Hammoud SN, Rocha C et al. The WHO dengue classification and case definition: time for a re assessment. *Lancet* 2006; 368: 170-3.
- Khanna S, Vij JC, Kumar A, Siragel D, Tandon R. *Annals of Trop Med Parasitol* 2004; 98: 757-60.
- Guzman MG, Kouri G. Dengue and Dengue hemorrhagic fever in America. Lesson and challenges. *J Clin Virol* 2003; 27: 1-13.