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Clinico-Haemato-Serological Study of Dengue Cases

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ABSTRACT

Objectives: To study and establish clinical, haematological and serological correlation in dengue cases and to evaluate the incidence of common clinical presentation.

Material and methods: Dengue IgM antibody testing by ELISA was performed during August 2011 to July 2012 and the data were analyzed retrospectively. A total 3989 serum samples were received from V.S.G.H. (O.P.D. & Indoor), malaria department (AMC) & others for the detection of Dengue IgM were tested & clinic haematological case study was done.

Results: Total serum samples tested were 3989 out of which, 576(14.43%) were positive for IgM antibodies. Out of the total serum samples, Male: Female ratio and Urban: Rural ratio was 1.6:1 and 2.8:1 respectively. Peak incidence of the disease is seen in October- November .Age group 0-15 years comprises 1596 (40%), 16-30 years were 1476 (37%) and above 30 years were 917(23%).Clinically fever was the commonest presentation in 491(85%) followed by headache and muscle pain ie 365(63%) and 152(26%) respectively least common was epistaxis in 20 (3.4%) patients. Retrobulbar pain was in 36(6.25%) rash was in 104 (18%) and hemorrhagic manifestations in 110 (19%). Patients with platelet count less than 50,000 were 185(32%), 50,000 to 1, 00000 were 174(30.2%) and greater than 1,00,000 were 189(33%).

Conclusion: New dengue virus strains and serotypes will likely continue to be introduced into urban areas where the densities of Aedes aegypti are at high levels. Control strategy basically depends upon efficient and sustainable surveillance system and prevention and control measures.

KEYWORDS : Dengue Fever , IgM antibody ELISA

Introduction:

Dengue fever is a febrile illness caused by an RNA flavivirus . *It is transmitted* by the female Aedes aegypti *mosquito that primarily lives in the tropical and subtropical regions of the world. The virus is found within the salivary glands of the female mosquito and can be passed from adult to egg, which allows it to survive from season to season*[1]

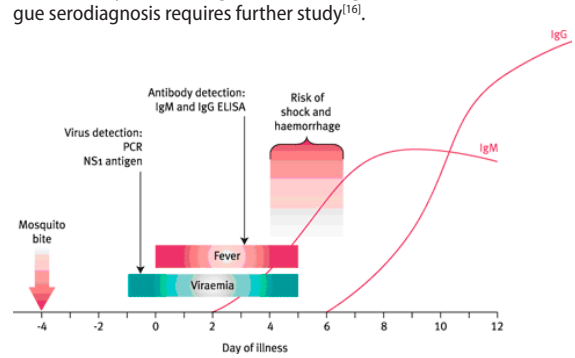
There are 4 serotypes namely, DENV-1, DENV-2, DENV-3 and DENV-4. One of the characteristics of this virus is that it is a positive-sense, single stranded RNA virus. Each serotype provides specific lifetime immunity by homotypic neutralising antibody and short-term cross immunity by heterotypic non neutralising antibody. All serotypes can cause severe and fatal disease .

Symptoms such as headache, fever, exhaustion, severe joint and muscle pain, swollen glands (lymphadenopathy), and rash. The presence (the "dengue triad") of fever, rash, and headache is particularly characteristic of dengue fever. The acute phase of the illness with fever and myalgias lasts about one to two weeks.[2]

Dengue hemorrhagic fever *is a more severe form of the viral illness. Symptoms include headache, fever, rash, and evidence of hemorrhage in the body.* Petechiae *(small red or purple splotches or blisters under the skin),* bleeding in the nose *or* gums, black stools, or easy bruising *are all possible signs of hemorrhage. This form of dengue fever can be life-threatening and can progress to the most severe form of the illness,* dengue shock syndrome.[3]

DENVs produce several syndromes that are conditioned by age and immunological status. During initial dengue infections, most children experience subclinical infection or mild undifferentiated febrile syndromes. During secondary dengue infections the pathophysiology of the disease changes dramatically, particularly sequential infections in which infection with DENV-1 is followed by infection with DENV-2 or DENV-3, or infection with DENV-3 is followed by infection with DENV-2[4,5,6]. Such infections can result in an increase acute vascular permeability syndrome known as dengue shock syndrome (DSS). The severity of DSS is age-dependent, with vascular leakage being most severe in young children, a phenomenon that is thought to be related to the intrinsic integrity of the capillaries.[7,8] In adults, primary infections with each of the four DENV serotypes, particularly with DENV-1 and -3, often results in DF. Some outbreaks of primary DENV-2 infections have been predominantly subclinical.[5]

The acquired immune response to dengue infection consists of the production of antibodies that are primarily directed against the virus envelope proteins. The response varies depending on whether it is a primary or secondary infection[9,10]. A primary antibody response is seen in individuals who are not immune to dengue and a secondary immune response is observed in patients who have had a previous dengue infection . A primary infection is characterized by a slow and low-titre antibody response. Immunoglobulin IgM antibodies are the first isotype to appear, by day 3–5 of illness in 50% of hospitalized patients and by day 6–10 of illness in 93–99% of cases. The IgM levels peak ~2 weeks after the onset of fever and then generally decline to undetectable levels over the next 2–3 month[11,12,13]. Dengue-specific IgG is detectable at low titre at the end of the first week of illness and slowly increases. By contrast, during a secondary infection, high levels of IgG antibodies that crossreact with many flaviviruses are detectable even in the acute phase and rise dramatically over the following 2 weeks.[13] The kinetics of the IgM response are more variable; as IgM levels are significantly lower in secondary dengue infections, false-negative test results for dengue-specific IgM have been reported during secondary infections[12,14,15]. Following a dengue infection, IgG can be lifelong, which complicates the serodiagnosis of past, recent and current infections[13,15]. IgA and IgE responses have also been documented but the utility of detecting these immunoglobulins as markers for dengue serodiagnosis requires further study[16].



Material and methods:
Dengue IgM antibody detection by capture ELISA (Panbio & NIV pune) was performed between August 2011 to July 2012 and the data were analyzed retrospectively.

From 1st week to 3 months of starting of illness in clinically suspected cases of Dengue fever were selected for testing. Single blood sample was obtained from each patient on treatment with antimicrobials and stored at 2- 8^0 c until used. A structured format containing information of the patient and family members, clinical features , details of treatment and recurrence was used for data collection .Total 3989 human blood samples of all age group & gender from clinically suspected cases of Dengue fever attending different OPDs & IPDs from August 2011 to July 2012 in V.S. General Hospital, Ahmadabad were collected with standard laboratory precautions. Each sample was conformed in sufficient quantity & quality. Serum was separated by centrifugation. All the samples were tested within three days of collection by Qualitative Capture ELISA IgM antibodies detection against Dengue virus.

Results:
Total samples tested were 3989 out of which, IgM antibodies positive were 576 (14.43%).

Male: Female ratio and Urban: Rural ratio was 1.6:1 and 2.8:1 respectively.

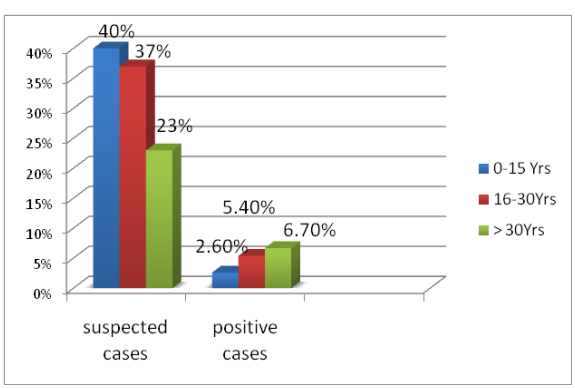
Peak incidence of disease is seen in October – November .

Age group 0-15 years comprises 1596 (40%), 16-30 years were 1476 (37%) and above 30 years were 917(23%).

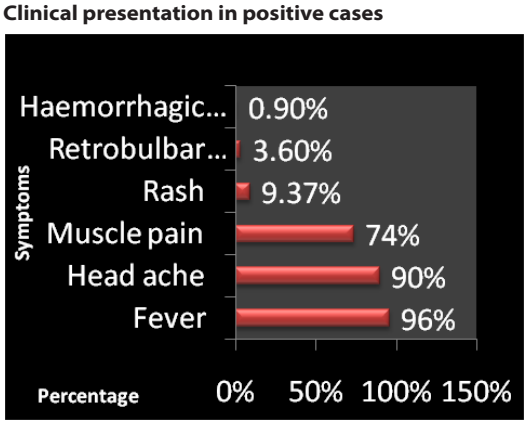
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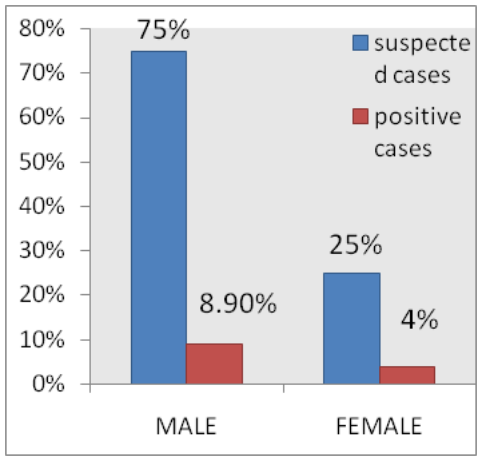
Age wise distribution



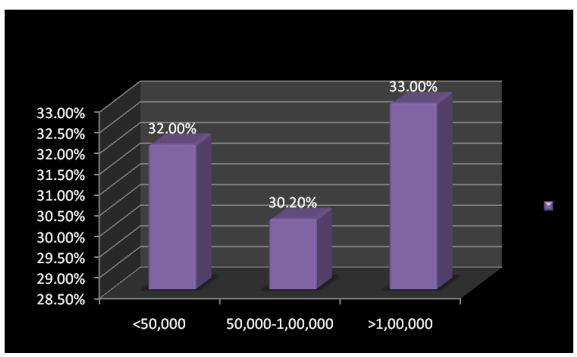
Clinical presentation in positive cases



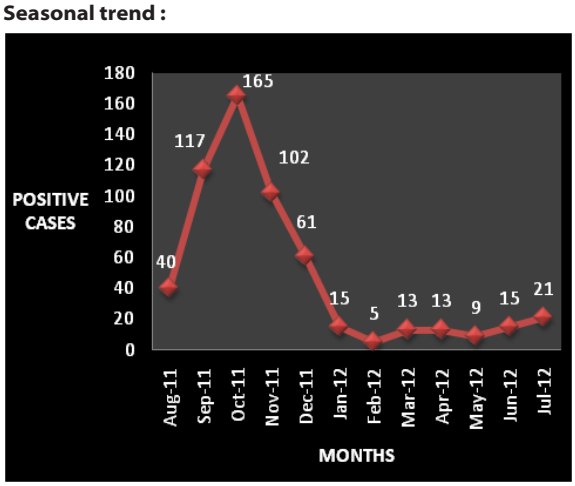
Sex Distribution



Distribution of Platelet count in positive cases



Seasonal trend :



Discussion:
Total cases studied are 3989, out of which IgM positive are 576(14.43%)

Clinically, fever is the most common presenting symptom i.e, 96%, followed by headache i.e, 90%.

Fever typically begins on the third day of illness and persists 5-7 days, abating with the cessation of viremia. Leukopenia, lymphopenia near the end of the febrile phase, and thrombocytopenia are common findings in dengue fever and are believed to be caused by direct destructive actions of the virus on bone marrow precursor cells. The resulting active viral replication and cellular destruction in the bone marrow are believed to cause the bone pain.

In the study, positive cases with platelet count >1lakh are 33%. Bleeding is caused by capillary fragility and thrombocytopenia and may manifest in various forms, ranging from petechial skin hemorrhages to

life-threatening gastrointestinal bleeding.

Urban males are affected more due to several factors like , changing lifestyle, traditional water storage practices, water receptacles.

Laboratory plays an important role in detection of IgM antibody in primary infection. In secondary infections, the virus may be complexed with antibody, making it undetectable by most current virus isolation techniques.

Glance at similar study :

	PRESENT STUDY	STUDY AT TERTIARY CARE HOSPITAL MUMBAI
Study duration	AUG 2011-JUL 2012	JAN-2011-FEB-2012
No. of samples tested/positive samples	3989/576 (14.43%)	4677/503(13.67%)
Most common clinical symptom	Fever (96%), Headache (90%)	Fever (95%), Icterus (25.8%)
Platelet count <50,000	32%	64%
1lakh-50,000	30.20%	17.6%
>1lakh	33%	19.9%
Seasonal variation (peak incidence)	October and November	July and November

Conclusion:

Presenting illness of fever and headache should not be neglected . Platelet count plays a valuable role in confirmation of dengue infection. As early detection is not possible by IgM antibody before one week, other methods like detection of NS1 antigen should be established. In the absence of any specific treatment and vaccine, the global dengue prevention and control strategy basically depends upon prevention and control measures to eliminate or drastically reduce the population of mosquito vector, Aedes aegypti, in a sustainable manner.

It is also very important to have an efficient and sustainable surveillance system for the vectors and their resistance to various insecticides.

REFERENCES

1. Roach, John P. Dengue Fever and Dengue Hemmorrhagic Fever. Insect Science at Boston College. Mar. 1, 2002. | | 2. Mortimer, Roland. "Aedes aegypti and Dengue Fever". Micscape Editor. (1995). May 3, 2007. | | 3. . Dengue Fever: essential data. (1999). May 4, 2007 | | 4. Guzman, M. G. et al. Dengue hemorrhagic fever in Cuba, 1981: a retrospective seroepidemiologic study. Am. J. Trop. Med. Hyg. 42, 179–184 (1990). | | 5. Guzman, M. G. et al. Epidemiologic studies on Dengue in Santiago de Cuba, 1997.Am. J. Epidemiol. 152, 793–799; discussion 804 (2000). | | 6. Alvarez, M. et al. Dengue hemorrhagic fever caused by sequential dengue 1–3 virus infections over a long time interval: Havana epidemic, 2001–2002. Am. J. Trop. Med. Hyg. 75, 1113–1117 (2006). | | 7. Guzman, M. G. et al. Effect of age on outcome of secondary dengue 2 infections.Int. J. Infect. Dis. 6, 118–124 (2002). | | 8. Gamble, J. et al. Age-related changes in microvascular permeability: a significant factor in the susceptibility of children to shock? Clin. Sci. 98, 211–216 (2000). | | 9. Vorndam, V. & Kuno, G. In Dengue and Dengue Hemorrhagic Fever (eds Gubler, D. J. & Kuno, G.) 313–333 (CAB International, New York, USA, 1997). | | 10. Guzman, M. G. & Kouri, G. Dengue diagnosis, advances and challenges. Int. J. Infect. Dis. 8, 69–80 (2004). | | 11. TDR/WHO. In Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control. 23–55 (TDR/WHO, Geneva, Switzerland, 2009). | | 12. PAHO. Dengue and Dengue Hemorrhagic Fever in the Americas: Guidelines for Prevention and Control. (Pan American Health Organization, Washington, DC, USA1994). | | 13. Innis, B. L. et al. An enzyme-linked immunosorbent assay to characterize dengue infections where dengue and Japanese encephalitis co-circulate. Am. J. Trop. Med. Hyg. 40, 418–427 (1989). | | 14. Chanama, S. et al. Analysis of specific IgM responses in secondary dengue virus infections: levels and positive rates in comparison with primary infections. J. Clin. Virol. 31, 185–189 (2004). | | 15. Gubler, D. J. Serologic diagnosis of dengue/dengue haemorrhagic fever. Dengue Bull. 20, 20–23 (1996). | | 16. Vazquez, S. et al. Kinetics of antibodies in sera, saliva, and urine samples from adult patients with primary or secondary dengue 3 virus infections. Int. J. Infect. Dis. 11, 256–262 (2007). | |