

Research Article**Mortality and Severity Predictors of Dengue Fever****Jagjit Singh^{1*}, M T Zeya², Geetika Dhir³, Simarpreet Mann⁴, Umrao Singh Bawa⁵, Paramdeep Singh⁶, Hardeep Sidhu⁷, Tanish Dhir⁸, Parneet Kaur Grewal⁹**¹Associate Professor, ⁵⁻⁸Intern., ⁹Junior Resident, Department of Medicine, Adesh Institute of Medical Sciences and Research (AIMSR), Bathinda (Punjab), India²Assistant Professor, Department of Anaesthesia, Adesh Institute of Medical Sciences and Research (AIMSR), Bathinda (Punjab), India³Junior Resident, Department of Pathology, Adesh Institute of Medical Sciences and Research (AIMSR), Bathinda (Punjab), India⁴M.D Medicine, Physician, Bathinda (Punjab), India***Corresponding author**

Dr. Jagjit Singh

Email: jagjeetsinghbahia@yahoo.co.in

Abstract: Dengue fever epidemic had emerged in Bathinda, Punjab, India. During the summer of 2012 and the epidemic period a wide spectrum of atypical presentations of dengue fever had been observed. Our objective of this study was to retrospectively see the dengue outbreak which occurred in the years between 2012- 2013 and its causes of mortality and severity. In this study of dengue was analyzed in 100 patients of dengue like fever and investigated thoroughly for cause of fever. IgM and IgG were done by ELISA method. Out of the total patients 100 patients we found that 60 patients were IgG positive and 40 patients were IgM positive. Patients developed complication in the form of thrombocytopenia (platelets less than 150,000) and other hemorrhagic features. It was concluded from this study that a total of 100 patients who were serological positive with either IgG and IgM antibodies with the help of ELISA. Subsequent infection with a different type increases the risk of severe complications.**Keywords:** Dengue, Elisa, IgG/IgM

INTRODUCTION

Dengue is the most common arthropod-borne viral (Arboviral) illness in humans. Globally 2.5-3 billion individuals live in 112 countries that have experienced dengue transmission. Annually, approximately 50-100 million individuals are infected. It is caused by infection with 1 of the 4 serotypes of dengue virus, which is a *Flavivirus* (a genus of single-stranded non-segmented RNA viruses). Infection with one dengue serotype confers life long homo-typic immunity to other serotype and a very brief period of partial heterotypic immunity to other serotypes, but a person can eventually be infected by all 4 serotypes [1]. Several serotypes can be in circulation during an epidemic. Dengue is transmitted by mosquitoes of the genus *Aedes*, which are widely distributed in subtropical and tropical areas of the world. *Aedes aegypti* is predominant mosquito vector for dengue infection [2]. Other *Aedes* species (Asian tiger mosquito, *Aedes albopictus* etc..) can also transmit dengue with varying degrees of infection. Humans serve as the primary reservoir for dengue. Persons with dengue viruses in their blood can transmit the viruses to the mosquito 1 day before the onset of the febrile period. The patient

can remain infectious for the next 6-7 days [3]. The mosquito can transmit dengue if it immediately bites another host. In addition, transmission occurs 8-12 days of viral replication in the mosquito's salivary gland (extrinsic incubation period) [4]. The virus dose not adversely affects the mosquito. The span of *Aedes aegypti* is usually 21 days but ranges from 15 to 65 days [5]. Vertical transmission of dengue virus in mosquitoes has been documented. It causes a wide spectrum of illness from mild asymptomatic illness to severe fatal dengue hemorrhagic fever/ dengue shock-syndrome (DHF/DSS). Approximately 2.5 billion people live in dengue-risk regions with about 100 million new cases each year worldwide [6]. Dengue fever (DF) is a mosquito borne viral illness caused by types 1 to 4 closely related, but anti-genetically distinct serotypes of dengue virus (DENV 1-4). Infection with one serotype confers lifelong homo-typic immunity and a brief period of heterotypic immunity, but each individual can eventually be infected by all 4 serotypes. The epidemic in 2010 while was mainly due to DENV2, few by DENV3 and very few by DENV1 while dengue hemorrhagic fever was infected by multiple serotypes. Multiple endemic has occurred during last decade in

Delhi [7]. Serotypes detected are the same as all serotypes were indentified in 2003 while data from 2004, 2005 and 2006 showed predominance of DENV3, DENV2 in 2007 and DENV1 in 2008 [8-11].

The first epidemic of DF was reported in 1635 in West-Indies. Thereafter in 1779-1780 confirmed epidemics simultaneously in Asia, North America and Africa were reported. The first epidemic of DHF/DSS was described in 1953 in Manila, thereafter frequent epidemics spread all over the world including in India. In India DENV was first isolated in 1946 and many outbreaks have been reported [12]. In Kolkata it was first documented in 1824 and several epidemics took place in years 1836, 1906, 1911, 1972, 2005 and 2010. The frequency of DF outbreak is increasing worldwide [13-19]. DF, DHF and DSS (Current WHO classification) During the last few decades, frequent DF outbreaks has occurred with increasing number of severe and atypical illness requiring hospitalization, pancreatitis, cranial nervous system involvement, myocarditis, hepatitis, calculus cholecystitis and even death.

With this background the present study was undertaken among 100 (dengue serology positive) patients in the department of medicine at Adesh Institute of Medical Sciences and Research, Bathinda. To assess the mortality and morbidity predictors of dengue fever. The mosquito virus has four types; infection with one type usually gives lifelong immunity to that type, but only short-term immunity to the others. Subsequent infection with a different type increases the risk of severe complications. As there is no commercially available vaccine, prevention is sought by reducing the habitat and limiting exposure. A retrospective type of study was conducted of dengue outbreak which occurred in the years between 2012-2013 to see the mortality and severity rate with respect to IgG/IgM antibodies.

MATERIAL & METHODS

All patients with high grade fever with low platelet counts, with antibodies positive (IgG, IgM,) and bleeding disorders were analyzed in a retrospective manner. During the process of study, 100 patients having dengue like fever were seen. These patients were investigated thoroughly of there cause of fever and saw that all 100 patients were serology positive (IgM and IgG) and these antibody positive patients were confirmed by using Enzyme Linked immuno Sorbent Assay method (ELISA). The 100 patients taken were looked for complications as thrombocytopenia, hemorrhage, shock and saw that the complication rate was increased in serology positive patients. The study was done in the department of medicine, Adesh Institute of Medical Sciences and Research, Bathinda. The patients were classified according to age, gender, duration of symptoms on admission, associated co-morbidities and co-infections, complication that

developed after admission, the final outcome and duration till recovery after symptoms developed.

The patients having other causes of fever were excluded from the study.

RESULTS

In this study we analyzed 100 dengue fever patients and the following results were obtained. Out of the 100 patients we took; 60 were IgG Positive and 40 were IgM positive. Low platelet count was recorded in all 100 patients, and 10 patients had a co-infection with malaria (P.Vivax), the remaining patients had died (5 out of 100 patients). All 5 deaths were either IgG or IgM positive.

Theses test were confirmed by routine laboratory using sero-diagnosis of dengue virus. IgG/IgM- done by ELISA methods.

- IgG positive- 60 Patients.
- IgM Positive - 40 Patients.

Low platelets count thrombocytopenia- (< 150,000) 100 Patient.

Death: Deaths of 5 patients out of 100 patients.

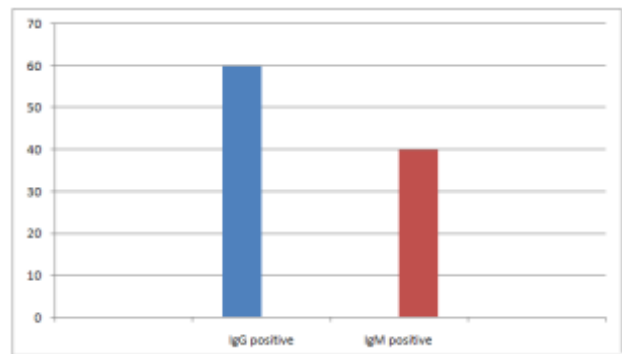


Fig. 1: Comparison between patients with IgG and IgM antibody infection out of 100 patients

The mortality and morbidity rate is higher in patients with a second infection (IgG and IgM positive), such as in patients of co infection and co-morbid conditions.

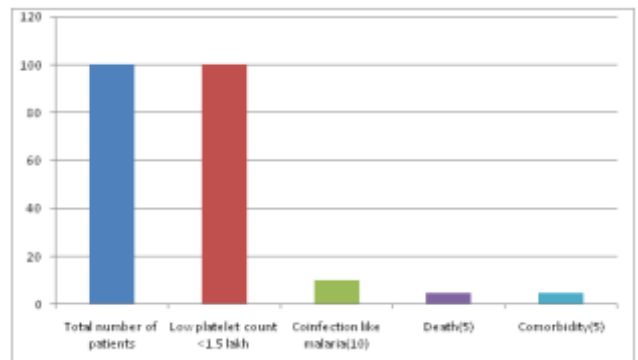


Fig. 2: Total no. of patients versus coinfections, death, comorbidity

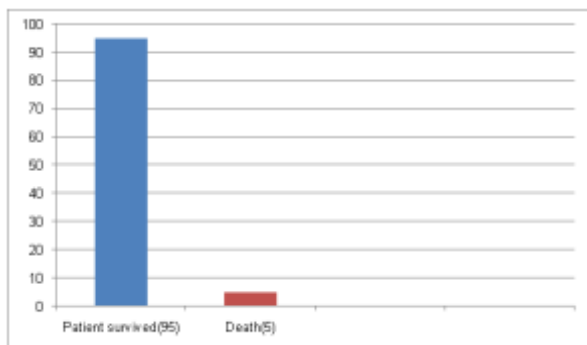


Fig. 3: Patients with Dengue who survived versus who had died

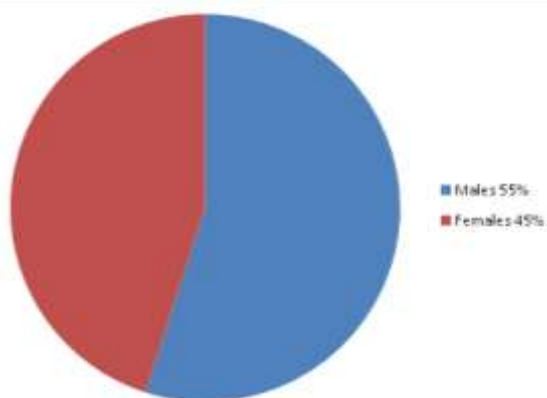


Fig. 4: Male and Female infection percentage

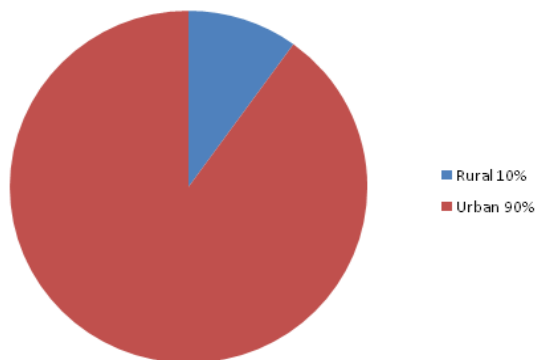


Fig. 5: Percentage of Rural versus Urban cases of infections

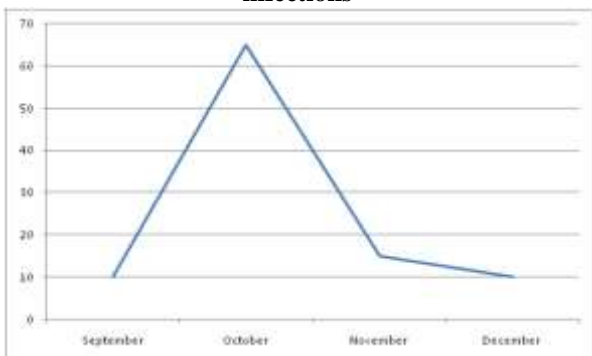


Fig. 6: Seasonal variation of Infections

DISCUSSION

The detection of immunoglobulin (IgG and IgM antibodies) to dengue During the summer of 2012 and 2013 Dengue fever epidemic emerged in Bathinda, Punjab, India. During the epidemic period, wide spectrum of presentations of dengue fever had been observed. Here in this study, the spectrum of dengue was analyzed in 100 patients of dengue fever. All patients were investigated thoroughly for cause of fever. Where we found that out of 100 patients, 60 patients, 40 patients were serology positive of IgG & IgM, which was recorded adequately by card method and confirmed by ELISA, as shown in Fig. 1. The study was done in, Bathinda, Punjab, India. The patients that we took were classified according to age, gender, duration of symptoms on admission, associated co-morbidities, co-infections and complication that developed after admission to the hospital, as shown in Fig. 2. The final outcome and duration of signs and symptoms developed before death had occurred, as shown in Fig. 3. The dengue fever cases started to appear from the month of September, but attained its peak during October as shown in Fig. 6. All ages were affected, males were affected more as shown in Graph 4 and urban patients were more affected compared to their rural counterparts as shown in Fig. 5. It was observed from the study that mortality and morbidity rate was higher in patients who had high IgG and IgM antibody. In other words, repeated infection of dengue fever was causing higher mortality and morbidity rates than a single episode of dengue. The patients who died were having higher complications in the form of dengue shock syndrome with bleeding. Patients required platelet transfusions, fluid therapy and pressure agents. The mosquito virus has four types; infection with one type usually gives lifelong immunity to that type, but only short-term immunity to the others. Subsequent infection with a different type increases the risk of severe complications. The mortality and morbidity rate is higher in second infections (IgG and IgM positive), and in patients with co-infection and co-morbidity conditions. Virus was studied by a simple enzyme immunoassay (ELISA), in which infected cultured cells infected with dengue virus were used as antigen. Detection of anti-dengue 1 IgG by EIA-ICC was correlated with haemagglutination assays. EIA-ICC anti-dengue 1, IgM detection was less sensitive than IgM capture enzyme-linked immunosorbent assay. IgG and IgM responses in dengue 1 infection were studied by EIA-ICC, using sera collected at different intervals after onset of illness. IgM and IgG appeared on the 4th day of disease, the highest IgM mean titres were detected on the 7th day and IgM was not detected in sera obtained after the 60th day. The highest mean titers of anti-dengue 1 IgG were seen in sera obtained between 22 and 30 days after onset of illness. EIA-ICCs for 6 flaviviruses and 1 alpha virus were conducted with sera from patients infected with dengue 1, and primary and secondary infections of other flaviviruses. The results showed that anti-dengue 1 IgG detection was

sensitive, and the antibodies were cross-reactive among the flaviviruses. Anti-dengue 1 IgM detected in dengue 1 patients was mostly type specific. The pattern of secondary dengue infection, i.e. the presence of IgG and a low titre or absence of IgM antibodies, was observed in the sera of 6 patients obtained in the first week after onset of illness. EIA-ICC is useful for dengue diagnosis, surveillance and sero-epidemiological studies.

CONCLUSION

It was concluded from the study that 30% had no complications and 70% developed complications and 4% causes had underlying co-morbidities and co-infections. The mosquito virus has four types; infection with one type usually gives lifelong immunity to that type, but only short-term immunity to the others. Subsequent infection with a different type increases the risk of severe complications. The mortality and morbidity rate is higher in second infections (IgG and IgM positive), and in patients with co-infection and co-morbidity conditions.

REFERENCES

1. Chakravarti A, Maltani M, Kashyap B, Kumar A; Awareness of changing trends in epidemiology of dengue fever is essential for epidemiological surveillance. *Indian J Med Microbiol.*, 2012;30: 222-226.
2. Dussart P, Baril L, Petit L, Beniquet L, Quang LC, Azevedo S *et al.*; Clinical and virology study of dengue cases and the members of their household ; the multifunctional Denerame project. *PlosNeg Trop Dis.*, 2012; 6: e1482.
3. Endy TP, Anderson KB, Nisalak A, Yoon IK, Green S, Rothman AL *et al.*; Determinants of in apparent and symptomatic dengue infection in a perspective study of primary school children in Kamphaeng Phet, Thailand. *PlosNeg Trop Dis.*, 2011; 5:
4. Yousaf KR, Atik S, Khalid S, Sheik QS, Mansoor Z, Nisar MS; Sonographic features of poly-serositis as an adjunct to clinico-pathological parameter in diagnosing and predicting the severity of dengue fever. *Pak J Med Health Sci.*, 2011; 5: 184-189
5. Almas A, Parkash O, Akhter J; Clinical factor associated with mortality in dengue infection at a tertiary care center Islamabad, Pakistan. *Southeast Asian J Trop Med.*, 2010; 41: 333-340.
6. Prakash O, Almas A, Hamid S, Aktar J, Safni SMW, Alishah H *et al.*; Severity of acute hepatitis and its outcome with dengue fever in a tertiary care hospital Karachi Pakistan (South Asia). *BMC Gastroenterol.*, 2010; 10: 43.
7. Bhatti S, Shaikh NA, Fatima M, Sumbhuani AK; Acute acalculous cholecystitis in dengue fever. *J Pak Med Assoc.*, 2009; 59: 519-521.
8. Rigau-Perez JG, Clark GG, Gubler DJ, Reiter P, Sanders EJ, Vorndam AV. Dengue and dengue hemorrhagic fever. *Lancet*, 1998; 352: 971-977.
9. Shah I, Deshpande GC, Tardeja PN; Outbreak of dengue in Mumbai and predictive markers for dengue shock syndrome. *J Trop Pediatr.*, 2004; 50: 301-305.
10. Parida MM, Dash PK, Upadhyay C, Saxena P, Jana AM; Serological & virological investigation of an outbreak of dengue fever in Gwalior, India. *Indian J Med Res.*, 2002; 116: 248-254.
11. Kurukumbi M, Wali JP, Broor S, Aggarwal P, Seth P, Handa R *et al.*; Seroepidemiology and active surveillance of dengue fever/dengue haemorrhagic fever in Delhi. *Indian J Med Sci.*, 2001; 55: 149-156.
12. UB, Maitra A, Broor S, Rai A, Pasha ST, Seth P; Partial nucleotide sequencing and molecular evolution of epidemic causing dengue 2 strains. *J Infect Dis.*, 1999; 180: 959-965.
13. M, Issac A, Mathew T, Philip S, Kareem NA, Unnikrishnan R *et al.*; Genetic characterization of dengue virus serotypes causing concurrent infection in an outbreak in Ernakulam, Kerala, South India. *Indian J Exp Biol.*, 2010; 48: 849-857
14. Mukhrjee K, Chakravarti SK, Dey PN, Dey S, Chakraborty MS; Outbreak of febrile illness due to dengue virus type 3 in Calcutta during 1983. *Trans R Soc Trop Med Hyg.*, 1987; 81: 1008-1011.
15. PK, Saxena P, Abhyankar A, Bhargava R, Jana AM; Emergence of dengue virus type-3 in northern India. *Southeast Asian J Trop Med Public Health*, 2005; 36: 370-377.
16. PK, Saxena P, Abhyankar A, Bhargava R, Jana AM; Reemergence of dengue virus type-3 (subtype-III) in India: implications for increased incidence of DHF & DSS. *Viol J.*, 2006; 3: 55-65.
17. Dayaraj C, Kakade MB, Bhagat AB, Vallentyne J, Singh A, Patil JA *et al.*; Detection of dengue-4 virus in Pune, western India after an absence of 30 years - its association with two severe cases. *Viol J.*, 2011; 8: 46-49.
18. Dar L, Gupta E, Narang P, Broor S; Cocirculation of dengue serotypes, Delhi, India, 2003. *Emerg Infect Dis.*, 2006; 12: 352-353.
19. Bharaj P, Chahar HS, Pandey A, Diddi K, Dar L, Guleria R *et al.*; Concurrent infections by all four dengue virus serotypes during an outbreak of dengue in 2006 in Delhi, India. *Viol J.*, 2008; 5: 1.