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RESEARCH ARTICLE

SEROLOGICAL PROFILE OF DENGUE FEVER IN A TERTIARY CARE HOSPITAL

Dr. B. Naga Srilatha, *Dr. M. Bharathi, Dr. M. Sasidhar and Dr. A. Sasikala

Department of Microbiology, RIMS Medical College, Kadapa

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ABSTRACT

Introduction: Dengue fever is one of the emerging infectious diseases which cause significant morbidity and mortality in children and adults especially in developing countries. According to World Health Organization two fifths of the world population is at risk from dengue disease and every year 50 million dengue virus infections are suspected world over.
Aim: To know the serological profile of dengue infection in our area in different age groups.
Material and Methods: It is a retrospective study. Serum samples from 563 acute febrile illness cases were subjected for detection of dengue sero markers: NS1, Ig M & Ig G by immuno-chromatographic method (J. Mitra diagnostics Ltd).
Results: More than 55% of cases were from the age group of 01 – 20 years. 2.8% of samples from OP cases (285) and 11.5% of samples from IP cases (278) were sero positive. As a total sero positivity of dengue was almost equal in both genders. But NS1 antigen seropositivity was high among females. Out of 39 sero positives, 22 were positive for NS1 antigen (9 in males & 13 in females) followed by 12 for IgM (6 in males & 6 in females), three for both antibodies (3 in males) and two IgG (one in each gender).
Conclusions: Seropositivity was more in IP cases. Laboratory diagnosis is important in differentiating primary and secondary infection which helps clinicians to anticipate complications of dengue.

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INTRODUCTION

Dengue fever is one of the emerging infectious diseases which cause significant morbidity and mortality in children and adults especially in developing countries (Kushal D. Shah *et al*., 2015). According to World Health Organization two fifths of the world population is at risk from dengue disease and every year 50 million dengue virus infections are suspected world over (WHO fact sheets, 2010**)** Since 2000, epidemic dengue has spread to new areas and has increased in the already affected areas of the South-East Asia region. Cyclic epidemics are increasing in frequency and in-country geographic expansion is occurring in Bangladesh, India and Maldives -- countries in the deciduous dry and wet climatic zone with multiple virus serotypes circulating. In India, Indonesia and Myanmar the reported case fatality rate is about 3-5% where as it is around 1% in other Asian countries (WHO guide lines for Dengue 2009). Dengue virus (DEN) is a small, single-stranded RNA virus comprising four distinct serotypes (DEN-1 to -4). These closely related serotypes of the dengue virus belong to the genus Flavi virus, family Flavi viridae.

Corresponding author: Dr. M. Bharathi
Department of Microbiology, RIMS Medical College, Kadapa

Dengue illness, an acute mosquito- borne infection with dengue virus, is due to four antigenically distinct serotypes, which don't offer cross protection (Balvinder Singh Arora *et al*., 2011). In India, the disease is prevalent and all four serotypes are known to be circulating either singly or in combination (Barde *et al*., 2012) and cause epidemics (Sharmila Raut *et al*., 2012). Recovery from infection by one serotype provides lifelong immunity against that serotype but confers only partial and transient protection against subsequent infection by the other three. There is good evidence that sequential infection increases the risk of more serious disease resulting in dengue hemorrhagic fever (DHF) (WHO).

Clinical manifestations of dengue viral infection range from -'asymptomatic cases to nonspecific febrile illnesses or classical Dengue Fever (DF) or Dengue Hemorrhagic Fever (DHF), or else as Dengue Shock Syndrome (DSS) (Balvinder Singh Arora *et al*., 2011). For practical reasons it was desirable to split the large group of patients with non-severe dengue into two subgroups -- patients with warning signs and those without them (WHO guide lines for Dengue 2009). Warning Signs of Dengue that requires strict observation and medical intervention are abdominal pain or tenderness, persistent

vomiting, clinical fluid accumulation (ascites, pleural effusion), mucosal bleeding, lethargy, restlessness, liver enlargement >2 cm, increase in HCT concurrent with rapid decrease in platelet count (CDC case definitions for Dengue; 2009).

Dengue secondary infection can lead to complications like DHF & DSS and subsequent mortality. As there is no prevention in the form of any vaccine for dengue, early diagnosis and treatment is recommended for preventing such complications (Gargi Ghosh *et al*., 2013). For confirmed diagnosis, following methods can be used – (1) Serology, (2) Viral isolation, & (3) Reverse Transcriptase- Polymerase Chain Reaction (Pramiladevi *et al*., 2013). Immuno chromatographic tests for dengue NS1 antigen and IgM antibody are good for screening purpose, while confirmation with ELISA and RT-PCR is required as they have better sensitivity and specificity (Gargi Ghosh *et al*., 2013). As our area is endemic and it is the season for dengue fever, there is increasing number of febrile illness cases in our hospital, we want to know the serological profile of Dengue infection.

Aim

To know the serological profile of dengue infection in our area in different age groups.

Study Design: Retrospective study.

MATERIAL AND METHODS

Serum samples from 563 acute febrile illness cases were received by the department of microbiology. All received samples were subjected for detection of dengue sero markers: NS1, Ig M & Ig G by immuno-chromatographic method. (J. Mitra diagnostics Ltd).

RESULTS

Out of 563 samples 288 were from males (51.15%) and 275 from females(48.84%). More than 55% of cases were from the age group of 01 – 20 years. Out of total out patient cases (285) only 8 were positive (2.8%).

Table 1. Age and gender vise distribution of samples

Age	Male	Female	Total (%)
1-10	78	87	165 (29.3)
11-20	90	63	153 (27.17)
21-30	48	58	106 (18.82)
31-40	27	24	51 (9.05)
41-50	23	24	47 (8.34)
51-60	08	11	19 (3.37)
>60	14	08	22 (3.9)
Total	288 (51.15%)	275 (48.84%)	563

Table 2. OP and IP vise distribution of samples

Age group	Male			Female			Grand total		
	OP	IP	Total	OP	IP	Total	OP	IP	Total
1-10	38	40	78	51	36	87	89	76	165
11-20	32	58	90	29	34	63	61	92	153
21-30	23	25	48	33	25	58	56	50	106
31-40	22	05	27	16	08	24	38	13	51
41-50	07	16	23	13	11	24	20	27	47
51- 60	05	03	08	05	06	11	10	09	19
>60	07	07	14	04	04	08	11	11	22
TOTAL	134	154	288	151	124	275	285	278	563

Table 3. Age, OP, IP wise distribution of Positive results

Age	OP	Positive cases	IP	Positive cases	Total No.	Positive cases
1-10	89	3	76	14	165 (29.3)	17
11-20	61	4	92	10	153 (27.17)	14
21-30	56	1	50	3	106 (18.82)	4
31-40	38	-	13	2	51 (9.05)	2
41-50	20	-	27	2	47 (8.34)	2
51-60	10	-	9	-	19 (3.37)	-
>60	11	-	11	-	22 (3.9)	-
Total	285	8 (2.8%)	278	31 (11.15%)	563	39 (6.92%)

Table 4. Age & Gender wise distribution of Positive results

Age group	Male					Female					Grand Total
	Ns1	IgM	IgG	Both IgM & IgG	Total	NS1	IgM	IgG	Both IgM & IgG	Total	
1-10	03	02	01	02	08	06	02	01	-	09	17
11-20	04	04	-	01	09	03	02	-	-	05	14
21-30	01	-	-	-	01	01	02	-	-	03	04
31-40	-	-	-	-	-	02	-	-	-	02	02
41-50	01	-	-	-	01	01	-	-	-	01	02
51- 60	-	-	-	-	-	-	-	-	-	-	-
>60	-	-	-	-	-	-	-	-	-	-	-
Total	09	06	01	03	19	13	06	01	-	20	39

Whereas among total In-patients samples (278) 31 were positive i.e 11.15% as shown in Table 3. As a total sero positivity of dengue was almost equal in both genders. But NS1 antigen seropositivity was high among females. Out of 39 sero positives, 22 were positive for NS1 antigen (9 in males & 13 in females) followed by 12 for IgM (6 in males & 6 in females), three for both antibodies (3 in males) and two IgG (one in each gender)as shown in Table 4.

DISCUSSION

First evidence of occurrence of dengue fever in the country was reported during 1956 from Vellore district in Tamilnadu. The 1st DHF outbreak occurred in 1963 with 30% of showing hemorrhagic manifestations (DNVBDCP 2008). Infections by dengue virus continue to increase, threatening the health of people in over a hundred countries worldwide (Laura L Hermann *et al*., 2014). The high mortality associated with DF mandates early diagnosis and therapeutic interventions (Sreejith, 2014). There is a need for specific, inexpensive dengue diagnostic tests that can be used for clinical management, surveillance and outbreak investigations and would permit early intervention to treat patients and prevent or control epidemics. Serological tests are more commonly used to diagnose dengue infections because of their ease of use compared to techniques such as cell culture or RNA detection (Rosanna W Peeling *et al*., 2010). Among available sero diagnostic methods immuno chromatographic method is more commonly used as these are rapid, easy to perform, all sero markers can be detected by single kit and test can be done even for one sample. Where as to perform ELISA it takes several hours, requires trained personnel and it will be done for pool of samples. All the sero markers cannot be detected by a single ELISA kit. Hence immuno chromatographic methods were used for the diagnosis of dengue in our laboratory. (J. Mitra diagnostics)

NS1 antigen of dengue virus is detected from day 1 of infection. But Ig M antibody will be detected from 5-7 days of infection in higher titres and its presence represents primary infection. In secondary infections, IgM appears earlier or in the same time frame but are usually at lower titres than in primary infection. IgG is present from the previous infection and the titre increases rapidly (Rosanna W Peeling *et al*., 2010). Detection of Ig G indicates past infection. Presence of Ig M & Ig G represents secondary infection which alerts clinicians to monitor the case for the possibility of DHF & DSS. About 10% of secondary dengue is estimated to have developed DHF (Hati, 2006). As the complications of DF especially in secondary infection are severe, fear of missing detection of dengue infection is high among clinicians. This led to sending of every sample of acute febrile illness for laboratory diagnosis of dengue infection without screening the cases clinically for dengue according to WHO guide lines. Moreover our area is endemic and it is the season for dengue fever, pressures from patient attendants also led the clinicians to send the samples for screening of dengue infection from all acute febrile illness cases. These were the reasons for getting less percentage of sero positivity. Clothing that minimizes skin exposure during daylight hours when mosquitoes are most active affords some protection from the bites of dengue vectors (WHO Guide lines for Dengue 2009). The presence of more seropositivity among 1-10 age group was explained by the fact that children were more exposed than adults because of minimum clothing. That led to their vulnerability for getting mosquito bites and then dengue infection.

The immature stages of Aedes aegypti are found in water-filled habitats, mostly in artificial containers closely associated with human dwellings and often indoors. Studies suggest that most female Ae. aegypti may spend their lifetime in or around the houses where they emerge as adults. Typically, these mosquitoes do not fly far, the majority remaining within 100 metres of where they emerged (WHO Guide lines for Dengue 2009). As females spend most of the time in and around household they are prone for mosquito bites and getting viral infections. It might be reason for high incidence of primary infection in females.

The lack of effective mosquito control, licensed dengue vaccines or specific therapeutics to treat dengue infections presents challenges to reduce the burden of this disease. Rapid and accurate diagnosis of dengue infections is critical for the reduction of patients' morbidity and mortality (Laura L Hermann *et al*., 2014). Transovarian transmission in Ae.aegypti has been reported and another vector Aedes albopictus was also become known to be more active than Ae.aegypti in rural surroundings. Recently Aedes albopictus was reported to be the vector of dengue from south India (AK Hati, 2006). The above factors stressed the importance of creating awareness in public regarding mosquito control measures in addition to implementing the vector control measures by the government. There is a need for encouraging research on anti-dengue drugs and vaccines.

Conclusion

Seropositivity was more in IP cases. Laboratory diagnosis is important in differentiating primary and secondary infection which helps clinicians to anticipate complications of dengue.

Recommendation

Dengue transmission can be prevented by taking simple measures like complete covering of body with clothes and by fixing fine mesh to windows & doors. Mosquito propagation can be controlled by taking measures such as changing of water regularly in house hold containers, cover the containers with lids, regular changing of water in vases, watering of plants with sufficient quantities, avoidance of saucers for potted plants, filling of the pits to land level to prevent collection of water etc. All the above simple measures play an important role in the control of vector borne diseases including dengue.

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