



DENGUE-JE CO-INFECTION OR CROSS- REACTIVITY AND NEEDED CONSIDERATIONS

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ABSTRACT The dengue virus and Japanese encephalitis virus are members of the same family Flaviviridae. Both are genetically and anti-genetically closely related. There are increasing reports regarding neurological complications of dengue virus infection. Antibodies produced against various flavivirus infections often complicates the issue of correct diagnosis and can mislead in the treatment. So, there is dire need to consider these co-infection or cross-reactivity to prevent mortality as well as the incidence of post-encephalitis neurosequale. Key Words :- Dengue, JE, Co-infection, Cross-reactivity.

KEYWORDS :

INTRODUCTION:-

The dengue virus and Japanese encephalitis virus are members of the Flaviviridae virus family that causes very high global disease burdens. JE is the predominant cause of Acute Encephalitis Syndrome (AES) in India.[1]. JE virus and dengue virus is genetically and anti-genetically closely related. Japanese encephalitis virus and dengue virus share 54.3% amino acid sequence homology in the envelope protein.[2]. There are increasing reports regarding neurological complications of dengue virus infection. Dengue associated acute brain involvement is frequently classified into either dengue encephalopathy or dengue encephalitis. Antibodies produced against various flavivirus infections are known to cross-react with each other. [1]. Although cross-reactivity and cross protection within flavivirus have been demonstrated, the effect of JE vaccination on susceptibility to dengue virus infection has not been well elucidated. [2]. WHO in their 2009 guidelines have proposed to include all the cases of dengue fever with neurological features under the classification of 'severe dengue' without differentiating dengue encephalopathy and dengue encephalitis.[3]. To prevent mortality as well as high incidence of post-encephalitis neurological problem, several countries (like India) have started dedicated programmes for routine immunizations against JE in affected regions.[4].

MATERIALAND METHODS:-

Patient's sample in the duration of January 1st 2017 to 31st December 2017 were taken as subject of study. Blood and/or CSF samples of patients complaining any of the symptoms of Acute Encephalitis Syndrome (AES) were collected at the Paediatric Department, Medicine Department or any other places and referred to the Virology lab of Department of Microbiology, Patna Medical College, Patna. Our study comprised of total 360 samples which were suspected for AES cases. Patients having any or few symptoms like fever, headache, seizures, irritability, confusion, body rigidity, altered sensorium etc. were included in the study. A Case Report Form (CRF) was properly filled with the help of patient's attendant. The form included basic details of the patient and the clinical symptoms which patients were suffering from. The collection, transport and storage of specimens were done very properly and according to the standard procedures followed at National Institute of Virology (NIV), Pune. Samples were analysed for the IgM antibody against Japanese encephalitis virus and dengue virus through IgM Antibody Captured Enzyme Linked Immunosorbent Assay (MAC ELISA). Serum samples were tested for both JE as well as dengue virus where CSF samples were tested for JE only. Data so obtained were arranged and analysed very carefully.

RESULT:-

Since Dengue and JE belongs to the same family, Flaviviridae and their mode of transmission is also same, cross reactivity and co- infection has also been found in many of the patients. IgM antibody detection were done for the dengue virus as well as JE virus. A total of 360

samples were observed during the period of January 2017 to December 2017. Out of 360 patients 42 (11.6%) patients were positive for JE virus, 58 (16.1%) patients were positive for Dengue virus, 13 (3.6%) patients were positive for dengue virus as well as JE virus. Whereas 260 (72.2%) patients were neither positive for dengue virus nor for JE virus. Though these samples were sent by the clinicians for testing of IgM antibody against JE virus only but interestingly we found more positivity in dengue than JE. Table 1 shows the total patients coming for testing, the total number of dengue positive patients, total number of JE positive patients, the total number of patients positive for dengue virus as well as JE virus and the total number of patients which were neither positive for dengue virus nor positive for JE virus. Table 2 shows the month wise positivity of dengue as well as JE virus out of 360 patients. This is expressed in graph in figure 1. We can see a peak in the month of September and October that is in the monsoon or post monsoon season in Bihar in both the diseases. Almost same trend has been found in disease susceptibility as both diseases spread by mosquito bites and monsoon and post monsoon seasons are the high time for breeding in mosquitoes.

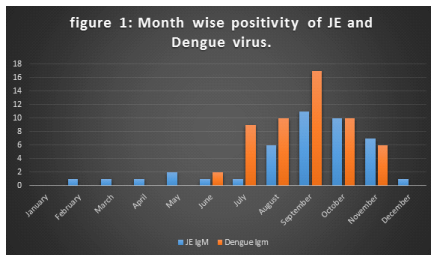
Table 1:- Total no. of patients and their positivity by respective virus.

Parameters	Numbers	Percentage
Total no. of patients	360	100
No. of patients positive for JE	42	11.6%
No. of patients positive for Dengue	58	16.1%
No. of patients positive for both, Dengue & JE	13	3.6%
No. of patients neither positive for Dengue nor for JE	260	72.2%

Table 2:- Month wise positivity of dengue as well as JE virus.

Months name	Total no. of patients	Patients positive for JE	Patients positive for Dengue
January	13	00	00
February	12	01	00
March	15	01	00
April	15	01	00
May	10	02	00
June	18	01	02

July	29	01	09
August	38	06	10
September	67	11	17
October	71	10	10
November	54	07	06
December	18	01	04



DISCUSSION:-

There are increasing reports regarding neurological complications of dengue virus infection. Cross-reactivity among various flavivirus infections often complicates the issue of correct diagnosis by serological methods in endemic areas where dengue and Japanese encephalitis viruses co-circulate and frequent sequential infections are likely to occur. Cross-reactivity complicates the assessment of the relative burdens of each virus in co-epidemic areas and their possible interactions.. There is dire need of establishing the clear cut discrimination between dengue encephalopathy and dengue encephalitis and also between dengue encephalitis and JE. Clinicians of the tropical regions should treat the case cautiously keeping both the aetiologies in mind and not relying solely on one finding. That is indeed a tough clinical dilemma as one disease has higher chances of mortality with no long term sequel and the other, a high chance of lifelong morbidity. [4]. Diagnosis is usually based on detection of antibodies in serum or Cerebrospinal Fluid (CSF). Cross-reactivity of antibody with dengue can be miss- diagnosed as JE unless antibodies for both are tested in parallel.[5]. Since both the dengue and JE viruses are flavivirus and share a number of common features such as transmission via mosquitoes, and they cross react with each other in serological tests because of which cross -reactivity can occur with either infection. [6]. In our study, we also found that out of 360 patients 42 (11.6%) patients were positive for JE infection, 58 (16.1%) were positive for dengue infection, whereas 13 (3.6%) patients were positive for both, Dengue as well as JE virus and 18 samples were not processed for Dengue virus.. Though these samples were diagnosed for AES and sent by the clinicians for testing of IgM antibody against JE virus only. But interestingly the number of samples positive for dengue virus was more than that of positive for JE virus. The samples positive for dengue virus as well as JE virus was because of dual infection or it might be because of cross reactivity. The samples neither positive for JE virus nor positive for dengue virus should be tested for another causative agents which comes under AES, such as Chikungunya virus, Scrub Typhus, West Nile, Yellow fever, etc. In rare instances, dengue virus may cause encephalitis, and JE virus, an undifferentiated fever. Laboratory evaluation therefore essential for confirmation and discrimination between the two viral infections.[7]. In table 1, we can see that there is peak in the suspected AES as well as the positivity in JE cases in the month of September and October that is the monsoon and the post monsoon season in Bihar. Though the suspected AES cases can be seen throughout the year, so there is dire need to do the testing for another AES diseases in parallel for better diagnosis. Realizing the gravity of this problem, preventive measures should be taken to minimize its consequences. This can be done by awareness programme for disease, proper immunization and proper maintenance of cold chain of vaccines, early case detection and referral to competent hospitals if needed. Sanitization, regular fogging in the season that is in the monsoon and post monsoon period, can minimize these problems to a much extent. Taking the fever in lighter way in first few days of illness until it goes worst also leads to more mortality rate and can result in neurological sequel after recovery. Since people in rural areas are much dependent on quack for their treatment and they don't go to a competent doctor until case worsens and it is quite late when they reach to right place. So, it is dire need to do awareness programme at district level, block level, even at village level.

CONCLUSION:-

There might be possibility of dual infection or cross- reactivity between JE and dengue which is a matter of strict consideration, if clinical and serological evidences are seen in the same patient. The clinicians should be concerned about the patients showing the symptoms of dengue with change in mental status as preventing steps for wrong diagnosis. In dengue epidemics, patients with altered mental status needs to be considered for JE infection also because it may be common for both diseases to be present in the community at the same time. There is chances of serological cross- reactivity, since both are flavivirus. We can go for PCR for these viruses to determine the simultaneous occurring of these disease in single individual. Apart from all these, basic measures such as regular fogging, awareness regarding sanitation, vaccination, early visit to meet doctor when symptoms are seen are some of the measures that should be taken to minimize its consequences.

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