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ORIGINAL ARTICLE

Incidence Of Japanese Encephalitis In A Tertiary Care Centre

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ABSTRACT

Background: Arbovirus are responsible for a significant number of viral encephalitis cases worldwide. Japanese Encephalitis virus is a mosquito-borne flavivirus that causes a major epidemic of acute encephalitis in humans throughout Asia [5]. Scientific literature unequivocally shows the prevalence of Japanese encephalitis in various parts of India [4]. In India, cases have been reported from Tamil nadu , Andra Pradesh , Uttar Pradesh , Bihar , Assam , West Bengal , Karnataka , Goa and Maharashtra [6]. In recent years, South India has become endemic for the Japanese Encephalitis Virus. While there are reports from other parts of Karnataka which are on the border of Tamil Nadu and Andhra Pradesh, till date, no data is available from South Karnataka.

Aim : The present study was conceived to estimate the incidence and clinical profile of Japanese Encephalitis among the patients which were clinically diagnosed with Viral Encephalitis at a tertiary care centre in South India.

Material and Methods: One hundred randomly selected cases of clinically diagnosed Encephalitis who were admitted in K.M.C. , Manipal, were included in the study . In - house MAC ELISA was used to detect specific IgM antibodies in the Cerebrospinal fluid [25,26].

Results : Anti- JEVirus IgM antibodies were detected in 8 % cases of clinicallydiagnosed encephalitis who were admitted to the K.M.C. Hospital. The mortality rate of the Japanese Encephalitis cases was 12.5 % . No sequalae was recorded in the Japanese Encephalitis cases who survived in our study.

Key Words : Japanese encephalitis virus , Viral encephalitis , IgM antibody capture ELISA

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Introduction

A number of neurotropic viruses like Herpes Simplex Virus , St. Louis Encephalitis Virus , Japanese Encephalitis Virus , West Nile Virus and Arbovirus are attributed to be the causative agents of Viral encephalitis worldwide [3]. Japanese Encephalitis which is caused by a mosquito borne neurotropic RNA virus, has emerged as a disease with major epidemics, with a very high mortality and morbidity [7],[8].

All flaviviruses are antigenically related , cross reactions being most evident and hence, the need for tests showing the greatest specificity [9]. Culex tritaeniorhychus and Culex vishnuii species are the main vectors which transmit the disease from the reservoir hosts to man . They generally breed in paddy fields and are

invariably found outdoors [10]. The virus is transmitted in the zoonotic cycle among mosquitoes and vertebrate amplifying hosts , chiefly pigs and wading birds [30].
Viral encephalitis is an acute inflammation of brain parenchyma which is characterized by fever , headache , confusion , seizures , altered levels of consciousness and focal neurological disturbances in various combinations. Patients who seek medical attention may have aseptic meningitis or encephalitis, of whom 5 % to 25 % die [14],[20].

The rate of asymptomatic and symptomatic infection varies between 25 : 1 to 1000: 1 . The incubation period varies from 1 – 6 days, or as long as 14 days . The onset of illness can be abrupt, acute (< 1 day), subacute (1-3 days) or gradual (> 3 days). Children under 15 years of age were principally affected in endemic areas [19]. Waning immunity or other biological factors associated with aging, have been speculated to be risk factors [12],[13] . This is followed by the encephalitis stage which manifests with altered sensorium, convulsions, neck stiffness , muscular rigidity , mask like facies and abnormal movements [17,18,19] . The principal complications are secondary bacterial infectionsand gastro-intestinal haemorrhage in the acute and subacute phase of the illness [20],[21]. Japanese encephalitis which is acquired during the first two trimesters of pregnancy may lead to foetal infection and miscarriage [15],[22]. The causes of relapse, seizures and sequale were convulsions , frank mental retardation , frank motor defecits, scholastic backwardness , behavioural problems and subtle neurological signs [20],[21],[27].

Method

One hundred clinically diagnosed cases of Encephalitis who were admitted in the K.M.C. Hospital, Manipal, were included in the retrospective study . The cerebrospinal fluids were randomly selected after excluding bacterial and other viral etiology for meningitis and encephalitis The diagnostic criteria for Japanese encephalitis which was adopted in this study was the demonstration of IgM antibodies in cerebrospinal fluid samples . The Avidin – Biotin system which was used in this test was used to increase the sensitivity and specificity to 100 % . CSF for serology which was received from all cases were collected and stored at – 70 degrees centigrade until they were tested by MAC ELISA [28],[29].
Control group : To check the specificity of the ELISA technique which was employed for the detection of the Japanese Encephalitis Virus infection , Fifteen Cerebrospinal fluid samples which were diagnosed as caused by the Herpes Simplex Virus (5 cases) , Subacute Sclerosing Panencephalitis (5 cases) and Mumps (5 cases) were included in the study . A detailed history and clinical examination was carried out in all cases . Other investigations like Blood count and Haematological and Biochemical Analysis were also compared.

IgM Antibody Capture ELISA (MAC ELISA) is the method of choice to demonstrate virus specific antibodies in both in Blood and Cerebrospinal fluid samples [23],[25].

Principle : Solid phase support (microtitre plate wells) were coated with Anti – Human IgM antibodies which were capable of binding all IgM isotype antibodies which were present in the specimen. Specific Antigen was then added , followed by enzyme labeled antigen – specific antibodies. If IgM antibodies which were specific for the antigen in question were present , the sandwich complex would result in an enzymatic colour change which was proportional to the concentration of the IgM specific antibody which was present. This method is highly specific and more sensitive.[29,30]

In the present assay, known positive and negative controls were provided by the Department of Neurovirology, NIMHANS, Bangalore. The assay was considered to be valid only when the controls gave expected results (Quality control) by in house MAC ELISA for the detection of IgM antibodies to the Japanese Encephalitis Virus by an IgM antibody capture ELISA. [22,23,24,25,29]

Results

The study was performed over a period of two years among patients with clinically diagnosed Viral Encephalitis at a tertiary care centre in South India. **IgM Antibody Capture ELISA (MAC ELISA) is the gold standard to demonstrate the presence of virus specific antibodies in cerebrospinal fluid [23],[25],[29].**

The number of CSF samples tested = 100
Japanese Encephalitis Positive by MAC ELISA = 8 cases (8 %).

Any test sample with more than **100 units** is considered to be **Positive for IgM antibodies to the Japanese Encephalitis Virus**

Samples with ELISA units between 30 –99 were considered to be probably positive for the IgM antibodies to the Japanese Encephalitis Virus, but they required further testing with the DengueWest Nile Virus Antigen, as well as with the Normal mouse brain Antigen in order to exclude false positive reactions.

A sample with ELISA units less than **30 units** was considered to be **Negative for the IgM antibodies to the Japanese Encephalitis Virus**

In our study, it was noticed that children younger than 15 years of age were affected with the Japanese encephalitis virus infection, which was also well documented by several earlier reports [11],[28]. The age distribution of the Japanese Encephalitis cases is as mentioned in [Table/Fig 1]. Various clinical features which were reported in these cases have been compiled in [Table/Fig 2]. The mortality rate of the Japanese Encephalitis was 12.5 %. No sequalae were recorded in the Japanese Encephalitis cases who survived in our study.

(Table/Fig 1) Age distribution of Japanese Encephalitis cases

Age group	Number of cases
2 months – 3 years	4 (50 %)
5 – 10 years	1 (12.5%)
> 25 years	3 (37.5%)

Predominance of infection was observed in males .Male to female ratio was 3 : 1
Out of 8 positive cases , 75 % were males and 25 % were females.

(Table/Fig 2)Clinical profile of Japanese Encephalitis cases

Signs and Symptoms	Duration	No.of Positives
Fever	2 – 5 days 10 – 15 days	7 (100%) 1
Convulsions		2 (25 %)
Headache		2 (25 %)
Altered sensorium		4 (50%)
Vomiting		1 (12 . 5 %)
Respiratory Irregularitie		1 (12.5%)
Neck rigidity Kernig's sign		2 (25 %) 1
Exaggerated deep tendon reflexes		3 (37.5%)
Abnormal movements		3 (37.5%)

(Table/Fig 3) Cerebrospinal Fluid Profile in Japanese Encephalitis cases

Parameter	Values	Number of cases
Pleocytosis	< 5 cells / ml	0
	5 – 10	1
	> 10	4
CSF Glucose	Normal	1
	Increased	-
	Decreased	7
CSF Protein	Increased	1
	Normal	7
	Decreased	-

Disscussion

Japanese Encephalitis is one of the leading causes of Acute Encephalopathy, affecting children and adolescents in Tropical and Sub – tropical Asia. Epidemic outbreaks of Japanese Encephalitis continue to pose a significant public health problem in most parts of India, especially in the Southern states.[16]. Manipal being only 70 kilometres away from the Kerala border, which is endemic for Japanese Encephalitis along the west coast did not have any recorded outbreaks of Japanese Encephalitis till date. The present study was carried out to diagnose Japanese Encephalitis cases among patients who were clinically diagnosed as Encephalitis in the K.M.C Hospital , Manipal .

The diagnostic criteria for Japanese Encephalitis which was adopted in this study was the demonstration of the IgM antibodies

by MAC ELISA in CSF samples, as reported by others, which is the Gold standard for the diagnosis of Japanese Encephalitis .[94,95]. Among the clinical manifestations, reported fever was present in 100 % of the cases and altered sensorium and headache accounted for 85 % - 100 % and 50 % of the cases respectively , Male preponderance , Pleocytosis and incidence in children younger than 15 years of age which were noticed in our study is also well documented by several earlier reports [11],[19],[28].

The diagnostic criteria for Japanese Encephalitis which were adopted in this study was the demonstration of the IgM antibodies by MAC ELISA in CSF samples, as reported by others, which is the Gold standard for the diagnosis of Japanese Encephalitis [28],[29].

To ensure the specificity of the assay, known positive and negative controls were included . There was no geographical or temporal clustering of cases.

Conclusion

The disease was of a sporadic nature affecting all age groups , but predominantly, children formed 8 % of the cases which were admitted to the K.M.C .Hospital during ourstudy. The mortality rate of Japanese Encephalitis was 12.5 %. No sequalae was recorded in the Japanese Encephalitis cases who survived.

No specific antiviral therapy is available for Japanese encephalitis . The specific aetiological diagnosis of Japanese Encephalitis cases helps the patient management protocols and avoids unnecessary use of antiviral therapy . Acyclovir therapy which is of no proven advantage in the cases of Encephalitis which were caused due to the Japanese Encephalitis Virus needs supportive and symptomatic treatment Thus, the management protocol was restricted to temperature control, seizure control, sedation and the control of aggravating intracranial pressure and fluid and electrolyte management [.26,27).

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