JAPANESE ENCEPHALITIS IN CHILDREN IN BELLARY KARNATAKA: CLINICAL PROFILE AND SEQUELAE

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ABSTRACT

Objectives: To study the clinical profile and outcome of Japanese Encephalitis (JE)
Methods: Prospective study was done in Vijayanagara Institute Medical Sciences hospital, Bellary, Karnataka. 233 patients below 12 years of age presented with acute encephalitic picture during the epidemic period formed the subjects and were worked up according to a predesigned protocol. CSF and serum samples were tested for JE specific IgM antibodies. Patients were followed up for 4 months to over one year.

Results: The predominant age group was 5 to 12 years. Fever (94.84%), seizures (73.39%) and altered sensorium (91.84%) were the important presenting symptoms. Onset of illness was acute in 28.32% and subacute in 38.62%. CSF showed lymphocytosis and 45.06% had cell count of 6-50/cmm and in majority it was <200/cmm. 55.36% patients were positive for JE. Mortality was 22.74%. Deeper level of coma, respiratory irregularities and meningeal signs were associated with mortality. 147 patients survived the acute attack. Of that 40.85% completely recovered. Speech disturbance (47.61%), motor deficits (36.73%), behavioural disturbance (14.96%), involuntary movements (12.24%) and seizures (1.36%) were the morbidities. The deficits found to be gradually improving. Motor deficits and speech disturbances were found in 25.68% and 22.01% respectively at one year follow up.

Conclusions: The characteristic clinical features of JE include fever, seizure, altered sensorium, aphasia, relative absence of cranial nerve involvement and irregular and rapidly changing motor and tone abnormality. Deeper level of coma, respiratory abnormalities and meningeal signs were associated with mortality. Speech disturbance and motor deficits were frequently encountered sequelae.

Keywords: Japanese encephalitis; Clinical profile; Sequelae

1. INTRODUCTION:

Encephalitis means inflammation of the brain, which can have different causes: most are the result of bacterial, viral or fungal infections. Among the infectious agents viruses top the list. [1,2] Japanese Encephalitis (JE) is the most prevalent and important mosquito borne viral encephalitis of man in the world in terms of morbidity and mortality with an estimated 50,000 cases and 10,000-15,000 deaths annually[3,4,5]. The disease commonly affects children[3]. At present it is a major public health problem in India, China, Thailand, Nepal, Sri Lanka and Vietnam and to a lesser extent in Indonesia, Malaysia, Republic of Korea and Japan.

JE is basically a zoonotic disease - infects animals and accidentally man. Domestic pigs have been incriminated as the major vertebrate host for the JE virus. The principal vectors of JE virus are mosquitoes of Culex complex (C. tritaeniorhynchus - most important). JE in the epidemic setting doesn’t cause much diagnostic confusion. The diagnosis is based on the clinical features suggestive of acute encephalitis. IgM capture ELISA technique
utilising monoclonal antibodies is the most sensitive test for detecting IgM antibodies against JE \[^{6}\].

At present, there is no specific agent available against JE. Treatment of JE is therefore essentially symptomatic and intensive supportive care \[^{7}\]. A significant number of patients who survive the acute phase of JE are left with neurological deficits. Safe and effective JE vaccines are now available to the entire at-risk population and should greatly diminish the burden of disease \[^{8}\].

The earliest evidence of JE virus infection in Bellary District of Karnataka came in 1979 \[^{9}\]. Since then Bellary and neighbouring districts have been experiencing many major and minor outbreaks of JE. This study was undertaken to study the epidemiological features, clinical profile and outcome of Japanese Encephalitis. Though the study was done some time back, the results are very much relevant.

2. MATERIALS AND METHODS:

All cases of encephalitis under 12 years of age admitted in Paediatric wards of Vijayanagara Institute of Medical Sciences, Bellary, Karnataka during two epidemics (years 1995-96 and 1996-97) were included in this study, after ruling out important differential diagnosis. All the patients were worked up according to a predesigned protocol. This included detailed history, physical examination and relevant investigations. The staging of altered sensorium was modified from the classification of progressive cerebral dysfunction of Plum and Posner \[^{13}\].

**Grade I:** Drowsy but responsive to voice commands.

**Grade II:** Unresponsive to voice but responsive to pain (light coma)

**Grade III:** Unresponsive to pain (deep coma).

Routine investigations of blood and urine were done. Peripheral smears to rule out malarial parasite, liver enzymes, renal function tests, serum electrolytes, Mantoux test and X-ray of the chest were done. After ruling out papilloedema lumbar puncture was done and CSF samples were obtained. CSF sample was analysed for sugar, protein, cell count and cell type and culture, while part of the CSF sample was kept for viral antibody study.

CSF and serum samples at admission and one more set of samples at about 7 to 10 days later were collected, in sterile containers and transported under cold chain to the virological laboratory (National Institute of Virology Field Station, Bangalore). These samples were subjected to Mac Elisa test to demonstrate JE specific Ig M antibodies. Second samples could not be collected in a few patients who had an early death or those who were taken from the hospital against medical advice. In such patients results were based on higher titres.

All the patients were treated with anti oedema measures, anticonvulsants, intravenous fluids in addition to general nursing and supportive care. Ampicillin was given to prevent secondary infections. There were no on-site facilities for acute CT or MRI scanning and for electively ventilating patients.

Patients were discharged when they were able to take feeds orally and when we did not expect any more complications and also when patient’s condition was reasonably accepted by the parents. The condition of the patients during discharge was noted. Parents of those with morbidity were taught how to look after their child at home including physiotherapy.

Patients were followed up for a variable period ranging from 4 months to over one year. At each visit a detailed physical and neurological examination was done. Intellectual deficits were based on parent’s assessment that the child was not as bright as prior to the illness or deteriorated school performance.

Results were analysed statistically by frequency, percentage and chi square test.

3. RESULTS:

A total of 233 patients diagnosed as JE during two epidemics were included in the study. Their demographic characteristics are given in Table 1. The predominant age group affected was 5.1 to 12 years and the youngest affected was of 8 months old. None of these children were vaccinated against JE. The patients belonged to Bellary district (57.51%) and neighbouring Raichur (10.30%), Chitradurga (3.86%), Kurnool (2.14%) and Anantapur (26.18%) districts. The patients were admitted during September to January.

Clinical features were that of viral encephalitis (Table 2). Generalised seizures (92.98%) were the predominant type of seizures. In the prodromal stage of the disease the main symptoms were fever, vomiting and head ache. The onset of neurological symptoms were divided into abrupt (1-6hours of prodromal symptoms); acute (6-24hours); subacute(2-
3 days) and gradual (>4 days). 20.6% were abrupt, 28.32% were acute, 38.62% subacute and 12.44% were gradual in onset. One peculiar feature that was noticed was rapidly changing CNS signs. CSF analysis showed lymphocytosis with cell counts 6 - 50/cmm in 45.06% patients and by and large majority had cell counts < 200/cmm. CSF Proteins were between 21-50mg/dl in 74.67% of the patients. CSF sugar remained normal in 89.6%. CSF and Serum samples were tested for Ig M antibodies against JE virus. 129 (55.36%) patients were positive for JE. Out of 233 cases, 60 (25.75%) had complete recovery, 87(37.33%) patients had some morbidity, 53 (22.74%) died and remaining 33(14.15%) left against medical advice. Average duration from onset of symptoms to death was 8.19 days. 56.60% of the deaths occurred within a week from the onset of symptoms. Deeper level of coma, respiratory irregularities and meningeal signs were found to be significantly associated with mortality (Table 3).

Speech disturbance 70 (47.61%), motor deficit 54 (36.73%), behavioural disturbance 22 (14.96%), cranial nerve deficit 21 (14.28%), involuntary movements15 (12.24%) and seizures 2 (1.36%) were the morbidities noted at discharge. 70 (47.61%) patients had speech disturbance (20- global aphasia; 33 - expressive aphasia; 17 - slow speech).

Patients were followed up for a variable period. Neurological features at 4-6 months and 9-12 months are summed up in table 4.

4. **Discussion:**

JE is a major encephalitic illness affecting children in this part of the country with significant mortality and morbidity. The predominant age group affected was 5.1-12 years. Even in Nepal significant numbers of patients were between 5 to 15 years and males were found to be at more risk for JE [1]. Sex ratio in our study was 1.3: 1 (M: F). Even in other studies male predominance was observed [10, 11]. It is likely that males get more medical attention and it is also possible that boys play outdoors making them more prone for mosquito bites. Majority of the patients were from rural areas. Previous studies have also made similar observations [10, 11]. The epidemics occurred in the post monsoon season, thereby increased mosquito density. Even during epidemics, it is rare for more than three cases to occur in a village and most records are only of a single case [12]. This is because of the high ratio of subclinical to overt infection in JE ranging from 1000: 1 in Japan to 200: 1 to 300:1 in other parts of Asia [3].

Clinical features were well correlated with viral encephalitis. Patients typically presented with fever, headache, vomiting, and altered sensorium often heralded by a seizure. The variable mental status abnormalities included abulia or aphasia with masked facies ranging from lethargy to coma. Similar observations were reported in other studies [13, 14, 15].

The clinical features of encephalitis seen during an epidemic strongly suggest the diagnosis of JE. In our series 55.36% patients were tested positive for JE. Even with the best of facilities it is difficult to prove the etiological agents in each case under epidemic circumstances. However if a few cases are proved to be JE, a fairly accurate clinical diagnosis can be made in other cases [15]. IgM capture ELISA is the most sensitive test for JE [6]. This may be negative very early in the illness, when viral antigen detection assay are more useful. Though less sensitive than IgM ELISA, it complements the result. Using a combination of IgM antibody detection and antigen detection assays diagnosis of JE could be confirmed in 80% of clinically suspected cases [3]. In a South Indian study JE infection was confirmed in 70.7 %(212/300) of the patients [5]. In India it is observed that a third of the patients die in JE [3]. Considering the discharge against medical advice cases who left the hospital with poor general condition case fatality would have gone up in our series also which may be similar to that of other studies. 36.3%, 50%, and 31.8% in Kumar et al, Vajpayee et al and Rathi et al studies respectively [10,11,16]. Severely disturbed sensorium, disturbed tone, decerebrate posturing and breathing abnormalities were found to be associated with a higher mortality in Lucknow [10]. In our study mortality was associated with deeper level of coma and respiratory irregularities and meningeal signs. In a study of certain prognostic features in 49 patients of JE in Thailand only deep coma found to correlate with mortality [17]. Combination of coma, multiple seizures, brainstem signs and illness for 7 days or more predicted a poor outcome in Vietnamese patients [14]. The morbidity pattern at discharge was well correlated with other studies. In our series
patients were followed up for variable periods. Large number of patients (41.98%) had intellectual deficits. It was observed in 39.90% at 12-18 months follow up by Kumar et al [10]. Seizures were less in our series probably because those with neurological sequelae were given long term anticonvulsants. Speech disturbances had improved during follow up. Speech disturbances were observed in 18/75 patients at 5 year follow up by Gourie Devi. In a Nepali study neurological sequelae were observed in 50% at discharge, which resolved in two-thirds of cases at follow-up [18].

In conclusion JE is an important cause of mortality and morbidity and should be suspected in a patient with characteristic features in the setting of endemic areas and treated with intensive supportive care and proper follow up.

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### Table 1: Demographic characteristics

| Characters          | No. of patients | Percentage (%) |
|---------------------|-----------------|----------------|
| **Age in years**    |                 |                |
| < 1                 | 4               | 1.7            |
| 1.1 - 3             | 28              | 12.0           |
| 3.1 - 5             | 48              | 20.6           |
| 5.1 - 12            | 158             | 65.6           |
| **Sex**             |                 |                |
| Male                | 133             | 57.09          |
| Females             | 100             | 42.91          |
| **Epidemiological Features** |             |                |
| Urban               | 36              | 15.45          |
| Rural               | 197             | 84.54          |
| History of JE in the Village | 9         | 3.86           |
| Pigs in surroundings| 196             | 84.12          |
| Use of mosquito nets| 4               | 1.71           |
| Presence of mosquito breeding places | 159 | 68.24 |
| Low socio economic group | 220 | 94.42 |

### Table 2: Symptoms and signs

| Symptoms                               | No. of patients (233) | %     | Signs                        | No. of patients (233) | %     |
|----------------------------------------|-----------------------|-------|------------------------------|-----------------------|-------|
| Fever                                  | 221                   | 94.84 | Abnormal respiration         | 35                    | 15.02 |
| Vomiting                               | 85                    | 36.48 | Tachycardia                  | 11                    | 4.72  |
| Headache                               | 61                    | 26.18 | Hepatomegaly                 | 7                     | 3.00  |
| Convulsions                            | 171                   | 73.39 | Coma Grade I                 | 57                    | 24.46 |
| Altered sensorium                      | 214                   | 91.84 | Coma Grade II                | 98                    | 42.06 |
| Behavioural disturbance                | 19                    | 8.15  | Coma Grade III               | 59                    | 25.32 |
| Motor deficits                         | 16                    | 6.86  | Cranial Involvement          | 75                    | 32.18 |
| Involuntary movements                  | 7                     | 3     | Papilloedema                 | 10                    | 4.29  |
| Diarrhoea                              | 4                     | 1.71  | Motor Deficits               | 72                    | 30.90 |
|                                        |                       |       | Generalised hypertonia       | 66                    | 28.32 |
|                                        |                       |       | Generalised hypotonia        | 21                    | 9.01  |
|                                        |                       |       | Decerebrate rigidity         | 7                     | 3.00  |
|                                        |                       |       | Decorticate rigidity         | 5                     | 2.14  |
|                                        |                       |       | Involuntary movements        | 18                    | 7.72  |
|                                        |                       |       | Meningal signs               | 71                    | 30.47 |
Table 3: Association of mortality with clinical features

| Features                             | Cases * | Deaths | %    | Significance |
|--------------------------------------|---------|--------|------|--------------|
| 1. Age                               |         |        |      |              |
| < 1 year                             | 4       | 0      | 0    | P=0.294, NS  |
| 1.1 - 3 Years                        | 18      | 7      | 38.88|              |
| 3.1 - 5 years                        | 38      | 12     | 31.57|              |
| 5.1 - 12 years                       | 140     | 34     | 24.28|              |
| 2. Sex                               |         |        |      |              |
| Male                                 | 115     | 35     | 30.43| P=0.142, NS  |
| Female                               | 85      | 18     | 21.17|              |
| 3. Onset                             |         |        |      |              |
| Abrupt                               | 39      | 11     | 28.20| P=0.952, NS  |
| Acute                                | 62      | 15     | 24.19|              |
| Subacute                             | 75      | 21     | 28.00|              |
| Gradual                              | 24      | 6      | 25.00|              |
| 4. Days of illness before admission  |         |        |      |              |
| < 1 day                              | 26      | 6      | 23.07| P=0.674, NS  |
| 1.1 - 2 days                         | 19      | 6      | 31.57|              |
| 2.1 - 5 days                         | 125     | 31     | 24.80|              |
| > 5 days                             | 29      | 10     | 34.48|              |
| 5. Coma Grade                        |         |        |      |              |
| I                                    | 53      | 2      | 3.77 | P<0.001, Highly Significant |
| II                                   | 79      | 16     | 20.25|              |
| III                                  | 49      | 35     | 71.42|              |
| 6. Papilloedema                      | 8       | 3      | 37.50| P=0.727, NS  |
| 7. Decerebrate posture               | 6       | 2      | 33.33| P=0.688, NS  |
| 8. Tone                              |         |        |      |              |
| Hypertonia                           | 58      | 13     | 22.41| P=0.552      |
| Hypotonia                            | 17      | 5      | 29.41| NS           |
| 9. Respiratory abnormalities         | 28      | 19     | 67.85| P<0.001, Highly Significant |
| 10. Meningeal signs                  | 68      | 9      | 13.23| P<0.05, Significant |

* Cases who left against medical advice were excluded as outcome is not known. NS: Not Significant.

Table 4: Follow up at different periods

| Features                             | @ 4-6 months n=131 | @ 9-12 months n=109 |
|--------------------------------------|---------------------|---------------------|
| Complete recovery                    | 65 (49.61%)         | 62 (56.88%)         |
| Intellectual deficits                | 55 (41.98%)         | 33 (30.27%)         |
| Seizures                             | 1 (0.76%)           | -                   |
| Speech disturbance                   | 48 (36.64%)         | 24 (22.01%)         |
| Cranial nerve deficit                | 5 (3.81%)           | 1 (0.91%)           |
| Behavioural disturbance              | 15 (11.45%)         | 10 (9.17%)          |
| Involuntary movements                | 11 (8.39%)          | 4 (3.66%)           |
| Motor deficits                       | 44 (33.58%)         | 28 (25.68%)         |
| Contractures/deformities             | 19 (14.50%)         | 16 (14.67%)         |