A Comparison of Clinical and Radiological Findings in Adults and Children With Japanese Encephalitis

J. Kalita, DM; U. K. Misra, DM; S. Pandey, MD; T. N. Dhole, MD

**Background:** Japanese encephalitis (JE) is the most common human endemic encephalitis, prevalent mainly in Southeast Asia. It affects both adults and children in different areas, but there is no comparative study of their clinical features and outcomes.

**Objective:** To evaluate clinical and radiological features in adults and children with JE.

**Methods:** Patients with serologically or virologically confirmed JE who were treated during the past 10 years were included in this study. All patients underwent a detailed neurological examination, computed tomography, or magnetic resonance imaging. The presence of movement disorders, anterior horn cell involvement, and electroencephalographic changes was noted. After 6 months, each patient's outcome was defined as poor, partial, or complete recovery. The clinical and radiological findings for both adults and children were compared using χ² tests.

**Results:** The results are based on 30 children and 37 adults. Seizure was present in 23 adults (62.2%) and in 17 children (56.7%). Three children had associated neurocysticercosis, and all of them had partial seizures. The occurrence of focal neurological deficit, anterior horn cell involvement, and parkinsonian features was not significantly different between adults and children. Dystonia was more common in children, occurring in 20 (66.7%) compared with 7 adults (18.9%). Six adults died, but none of the children did; however, the 6-month outcome was better for surviving adults compared with the children. Computed tomography and magnetic resonance imaging findings were not significantly different between the 2 groups.

**Conclusions:** Children with JE are more likely to have dystonia and a poor outcome at 6 months compared with adults. The difference in clinical findings and outcome in children and adults with JE may be owing to immunological factors, maturation of the central nervous system, and neuronal plasticity.

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This study was based on a retrospective analysis of patients with JE diagnosed and treated during the past 10 years. Diagnosis of JE was determined by virus-specific antibody titers, polymerase chain reaction, or virus isolation. The antibody titers were assessed using the following methods: hemagglutination inhibition (HI) titer for the JE virus infection in acute and convalescent serum samples of patients with JE or a 2-mercaptoethanol test in the serum.1 IgM capture through an enzyme-linked immunosorbent assay,1 isolation of the JE virus,1 and polymerase chain reaction.1 Patients with acute encephalitis syndrome and positive results for 1 or more of the previous tests were included in this study. The choice of method was based on the availability of the test at that particular time. The HI titer was used until 1998 (9 children and 23 adults); the remaining 25 patients were tested using 1 of the remaining 3 methods alone or in combination with the HI titer. The tests were performed in cerebrospinal fluid except for the HI titer and 2-mercaptoethanol tests, which were assessed in serum samples. Acute encephalitis syndrome refers to fever with altered sen-
sorium without a diagnosis of malaria or bacterial meningitis.

Patients underwent a detailed clinical evaluation. Con-
sciousness was assessed by the Glasgow Coma Scale and muscle power by the 0-V Medical Research Council scale.10 Muscle tone was categorized as reduced, normal, or increased and was fur-
ther classified by spasticity or rigidity. Deep tendon reflexes were classified as normal, reduced, or exaggerated. Presence of lo-
focal reflex loss with exaggerated or normal response in another area was categorized according to mixed pattern. Depending on the patient’s consciousness level, the sensations were tested for pinprick, joint position, vibration, and cortical sensations. Extrapyramidal signs such as rigidity, dystonia, dyskinesia, tremor, and other movement disorders were noted.

A cranial computed tomographic scan was performed using a high-resolution computed tomographic scanner, and 10-mm axial sections were obtained parallel to the orbitome-
aminal plane. Cranial magnetic resonance imaging was performed using a 2-T scanner operating at 1.5 T (Magnetom SP; Siemens, Munich, Germany). T1-weighted (repetition time [TR]/ echo time [TE]/excitation=500 ms/50 ms/3 ms), proton density (TR/TE/excitation=2000-2500 ms/15-20 ms/1 ms), and T2-weighted (TR/TE/excitation=200-2500 ms/80-90 ms/1 ms) spin-echo sequences were obtained. Electroencephalography (EEG) was performed using a 10- to 18-channel EEG with a 10-20 system of electrode placement. Sagittal, temporal, and transverse montages were recorded using bipolar and referen-
tial derivations. Response to intermittent photic stimulation vary-
ing from 3 to 30 Hz, hyperventilation, and eye opening were evaluated in the patients who could cooperate. A 30-minute EEG record was obtained for all patients. The EEG was ana-
yzed for background activity, any right-to-left asymmetry, rhyth-
mic activity, and epileptiform discharges.11

Cerebrospinal fluid was examined in all patients for pro-
tein, glucose, cells, bacteria, and fungi. Outcome was defined at the end of 6 months as poor (bedridden), partial (needing help with daily activities), or complete recovery (able to perform daily activities independently).12 Patients who were younger than 13 years were included in the pediatric group; those older than 13 years were included in the adult group. Various clini-
cal, radiological, and laboratory parameters in children and adults were compared using the $\chi^2$ test.

### RESULTS

During the last 10 years, we treated 67 patients with vi-
rolologically diagnosed JE of whom 30 were children and
37 were adults. These patients came from the nearby In-
dian districts of Uttar Pradesh (87%), Bihar (5.2%), and Madhya Pradesh (2.6%) and Nepal (5.2%).

In the pediatric group, a positive result was ob-
tained for the HI titer in 18 patients, the IgM enzyme-
linked immunosorbent assay in 17, the polymerase chain reaction in 6, and virus isolation in 1. In the adult group, positive findings occurred for the HI titer in 21 patients, the IgM enzyme-linked immunosorbent assay in 5, and the polymerase chain reaction in 8. The positivity of these tests was not statistically different between the 2 groups ($\chi^2=7.30; P=0.05$). The mean age of the children was 9.5 years; the mean age of the adults was 35.5 years.

Seizures were present in 23 adults (62.2%) and in 17 children (56.7%), and the difference was not statistically significant. Most seizures were generalized tonic-clonic, although focal seizures with secondary generalization were present in 6 children and 7 adults. The seizures were generally infrequent and easily controlled with phenytoin sodium or carbamazepine monotherapy except in a 2-year-
old patient with status epilepticus. At the 6-month follow-up visit, none of the patients had had recurrence of seizures.

The depth of coma was comparable in adults and chil-
dren. Focal neurological deficit was present in 19 chil-
dren (63.3%) and 20 adults (54.1%). Quadriplegia was the most common characteristic, present in 28 patients (71.8%), followed by hemiplegia, which was present in 11 patients (28.2%). Features of anterior horn cell involve-
mation as evidenced by focal reflex loss, localized wasting, and fibrillations on the electromyogram were present in 25 adults (67.6%) and 17 children (56.7%).

Movement disorders were common in both adults and chil-
dren; however, the pattern and frequency of the movement disorders differed between the 2 groups. Dys-
tonia was more common in children (20 [66.7%] of the children vs 7 [18.9%] of the adults), whereas parkinso-
ian features were frequent in both groups (22 [59.5%] of the adults and 21 [70%] of children).

The EEG results were abnormal in all of the chil-
dren; they revealed a slowing of background activity in all patients and spike-wave discharges in 4 patients. In adults, the EEG results were abnormal in 34 patients, which included 4 patients with alpha coma; 29 patients had a slowing of background activity. Of these patients, 1 patient each had associated right-to-left asymmetry and spike-wave discharges. Cranial magnetic resonance imaging results were more frequently abnormal than computed tomographic results, and the abnormalities were similar in both adults and children (Figure 1 and Figure 2). The only difference was the presence of cysticercosis in 3 children; none of the adults had this infec-
tion. The patients with cysticercosis did not have a history of seizure before developing JE, and all had partial sei-
zures during the acute encephalitic phase.

At 6 months, 6 adults died, whereas none of the chil-
dren did. Surviving adults, however, had better outcomes compared with the children. Details of the clinical parameters in adults and children are presented in Table 1, and the radiological changes are listed in Table 2.

Comparison of the clinical parameters in adults and children revealed that dystonia ($\chi^2=13.78; P<0.001$) was
more frequent in children and the 6-month outcome ($\chi^2=9.70; P=.02$) was worse in children compared with adults. The pattern of abnormalities in EEG results (K$^2=8.71; P=.03$) was also significantly different between the 2 groups.

**COMMENT**

Our study reveals some important differences between adults and children with JE. Although the adult patients with JE had a higher mortality rate in the acute stage, their 6-month outcome was better compared with the children's. The children, on the other hand, had a higher frequency of dystonia. The pattern of abnormalities in EEG results was also different between the 2 groups.

Our results differ from those in the published literature in several ways. Children with JE reportedly have more severe encephalitis as evidenced by deep coma, high frequency of seizures, and higher mortality and morbidty rates. In the literature, seizures have been reported to be more common in children compared with adults; only 10% of adult patients have seizures compared with 64% to 80% of children. A recent study from Vietnam, which included mainly children, also reported a high frequency of seizures. The higher frequency of seizures in the children from the Vietnamese study could be owing to a difference in the herd immunity as well as referral bias. In the Vietnamese study, 24 (62%) of 40 patients with seizures died or had severe sequelae. In a study of 65 patients with JE, which included 19 children, 11 had seizures, but seizure was not associated with poor prognosis. Diagnosis of JE in this study was, however, based on epidemiological, clinical, radiological, or virological criteria. In the present study, none of the children died. Seizures were not a serious problem and did not correlate with sequelae. Coinfection of cysticercosis and JE in the same patient was reported and was attributed to the role of pigs in the life cycle of both JE and cysticercosis; pigs are the amplifying host in JE and the intermediate host in cysticercosis. Three children with JE in our study also had neurocysticercosis, and all these children had partial seizures during the acute stage of encephalitis. A high frequency of association between JE and neurocysticercosis was reported in an autopsy study from southern India, which exceeded the chance association. Coinfection of JE and cysticercosis was also reported in 8 of 26 brain autopsy results from China. The pathological changes in patients with JE were more prominent in the patients who had neurocysticercosis. Cysticercosis may alter the blood-brain barrier and may account for central nervous system invasion by the JE virus. The high frequency of seizures and poor prognosis in patients with JE found by Solomon et al raises questions about other underlying causes. In the absence of computed tomographic scans and magnetic resonance imaging, the association of cysticercosis or other infection with JE needs further evaluation before attributing it to the higher frequency of seizures in patients with JE.

A wide variety of movement disorders have been reported in patients with JE, including parkinsonian features, myoclonic jerk, ocular deviations, opulogyric crisis, orofacial dyskinesia, mouth-open dystonia, tongue dystonia, torticollis, and teeth-clenching dystonia. In another study, movement disorders were found in 10.5% of patients with JE. During the acute phase of the illness, the movement dis-
orders included head nodding, coarse tremor, choreoathetosis, dystonia, and parkinsonian features. Movement disorders were also reported as late sequelae of JE; of 68 patients with JE examined 5 years after the acute phase of the illness, the movement disorders included monotonous speech in 7 patients; masked facies in 11 patients; tremor in 7 patients; chorea, tics, and athetosis in 7 patients; and parkinsonian syndrome in 8 patients. In our study, parkinsonian features were prominent in adults, whereas both dystonia and parkinsonian features were prominent in children. The difference was statistically significant ($P < .001$). Dystonia is more common in children following hypoxic-toxic-metabolic insult and is attributed to the vulnerability of the developing central nervous system. Dystonia is more refractory and has been associated with a worse prognosis. A higher mortality rate in adults with JE may be owing to the inability to bear the acute stress, associated comorbidity, and immunological status. The surviving adults, however, had better outcomes compared with the children. The present study was conducted in a tertiary care teaching hospital where patients pay for their treatment, so there was a bias for patients with a high socioeconomic status or those with more serious illness. However, these variables are likely to be equally applicable to both adults and children and are unlikely to influence the conclusions of this study. The observed differences between adults and children need further evaluation.

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Table 1. Comparison of Clinical Parameters in Children and Adults With Japanese Encephalitis

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Children (n = 30)</th>
<th>Adults (n = 37)</th>
<th>$\chi^2$ Value</th>
<th>df</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizures</td>
<td>17 (56.7)</td>
<td>23 (62.2)</td>
<td>0.42</td>
<td>1</td>
<td>.84</td>
</tr>
<tr>
<td>Behavioral abnormalities</td>
<td>5 (16.7)</td>
<td>7 (18.9)</td>
<td>0.01</td>
<td>1</td>
<td>.94</td>
</tr>
<tr>
<td>Focal deficit</td>
<td>19 (63.3)</td>
<td>20 (54.1)</td>
<td>0.27</td>
<td>1</td>
<td>.61</td>
</tr>
<tr>
<td>AHC involvement</td>
<td>17 (56.7)</td>
<td>25 (67.6)</td>
<td>0.44</td>
<td>1</td>
<td>.51</td>
</tr>
<tr>
<td>Movement disorder</td>
<td>25 (83.3)</td>
<td>26 (70.3)</td>
<td>0.92</td>
<td>1</td>
<td>.34</td>
</tr>
<tr>
<td>Parkinsonian</td>
<td>21 (70)</td>
<td>22 (59.5)</td>
<td>0.41</td>
<td>1</td>
<td>.52</td>
</tr>
<tr>
<td>Dystonia</td>
<td>20 (66.7)</td>
<td>7 (19.9)</td>
<td>13.78</td>
<td>1</td>
<td>&lt;.001</td>
</tr>
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</table>

Table 2. Comparison of Computed Tomographic and Magnetic Resonance Imaging Findings in Adults and Children With Japanese Encephalitis

<table>
<thead>
<tr>
<th>Features</th>
<th>Children (n = 27)</th>
<th>Adults (n = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal</td>
<td>10 (37.0)</td>
<td>12 (38.7)</td>
</tr>
<tr>
<td>Thalamic</td>
<td>10 (37.0)</td>
<td>11 (35.0)</td>
</tr>
<tr>
<td>Basal ganglia</td>
<td>2 (7.5)</td>
<td>3 (9.7)</td>
</tr>
<tr>
<td>Midbrain</td>
<td>1 (3.7)</td>
<td>1 (3.2)</td>
</tr>
<tr>
<td>Pons</td>
<td>0 (0)</td>
<td>1 (3.2)</td>
</tr>
<tr>
<td>Cortex</td>
<td>2 (7.5)</td>
<td>3 (9.7)</td>
</tr>
</tbody>
</table>

Abbreviations: AHC, anterior horn cell; EEG, electroencephalography.
*Values are expressed as number (percentage) of patients unless otherwise indicated.
REFERENCES


