JE VIRUS ENCEPHALITIS: 1988 EPIDEMIC AT GORAKHPUR

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ABSTRACT

Gorakhpur region experienced the most serious outbreak of Japanese encephalitis (JE) in 1988 in which 875 children were admitted in the Department of Pediatrics, BRD Medical College, Gorakhpur. Children between 7-10 years age group constituted half (49.3%) of these cases, convulsions (83.8%), altered sensorium (78.2%), headache (68.8%) and hypertonia (77.0%) were the main presenting features. IgM against JE virus was demonstrated in 18/25 CSF and 27/53 sera collected from these children. Significant titres of HI antibodies against JE were present in 498/670 patients.

Patients were managed symptomatically. Dexamethasone and dopamine were given to only 137 (15.7%) children admitted with shock and peripheral circulatory failure.

Almost a third (31.8%) of the patients expired, 51.4% recovered completely and 10.7% recovered partially. Corticosteroids did not improve the outcome.

Twenty four patients had recurrence of symptoms after excellent recovery from acute attack of whom two died and 5 developed neurological deficits.

Key words: *Japanese virus encephalitis, Epidemic, Neurological dificits, Recurrence.*

Japanese encephalitis (JE) has become an important health problem in India, more so in children, who bear the major brunt of the disease. The disease was first reported in India in 1954 by Khan(1) from Jamshedpur. This was followed by several reports of occurrence of JE epidemics from other parts of the country(2). Gorakhpur and surrounding districts of eastern Uttar Pradesh first experienced an epidemic of JE in 1978 and then in 1980, 1985 and 1986(3). A severe epidemic of JE seen in Gorakhpur area in the late rainy season of 1988 is reported in the present communication.

Material and Methods

Patients clinically diagnosed as encephalitis and admitted to the pediatric wards of Nehru Hospital, BRD Medical College, Gorakhpur from September to November, 1988 constituted the case material for the present study. Laboratory investigations done included hemoglobin, total and differential leucocyte counts and complete cytochemical examination of cerebrospinal fluid (CSF). On admission blood samples were taken for demonstrating anti-JE virus antibodies (IgM and IgG) with repeat sampling after 15 days to see the rise in IgG antibody titre. Sera separated were stored in sterile containers at –20°C till tested. CSF samples obtained at the time of admission were examined for IgM antibodies to JE virus. Needle biopsy of brain was also done in 4 children immediately after death for isolation of virus.

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Patients were largely managed symptomatically and supportively. Airway was kept clean, fever brought down with antipyretics and cold sponging. Phenobarbitone, phenytoin and diazepam were used for seizures. Brain edema was reduced by mannitol, glycerine and in selected cases by dexamethasone. Most patients were on intravenous fluids for 4-5 days keeping in mind the syndrome of inappropriate release of anti-diuretic hormone. Dopamine was used to maintain blood pressure in patients with peripheral circulatory failure (PCF). Dexamethasone was used only in children with PCF and those with central cardiorespiratory involvement and other features of brain edema, not responding adequately to mannitol and glycerine. Oral prednisolone (1 mg/kg/day) was administered to selected patients not showing recovery in 3 weeks, to see its possible effect on the outcome.

After the initial discharge from the hospital, patients were followed up every fortnight. Cases with neurological deficits, sensory/motor and behavioral problems were managed symptomatically with judicious use of physiotherapy.

The isolation of the virus was done employing infant mice model and was carried out at the Department of Microbiology, KG Medical College, Lucknow. The estimation of IgM against JE by MAC ELISA method(4) using 1:5 dilution of serum or CSF was carried out at the National Institute of Virology, Pune. Hemagglutination inhibition (HI) test for IgG antibodies(5,6) was carried out in Department of Microbiology, BRD Medical College, Gorakhpur. HI antibody titre >80 in single sample and minimum of four fold rise in titre in second sample taken after 10-15 days was considered positive. A titre <80 without subsequent rise was taken as negative.

Results

A total of 875 children (3 months to 15 years) with clinical features of encephalitis were admitted to the Pediatric wards of Nehru Hospital during a period of 3 months (375, 456 and 44 children in September, October and November 1988, respectively). Of them, 431 (42.3%) were between 7-10 years of age and boys outnumbered girls (*Table I*). Fever, headache, convulsions and altered sensorium were the main presenting features (*Table II*).

TABLE I–*Age and Sex Distribution of JE Cases*

Age group	Male	Female	Total
3 mo-3 yrs	18 (72.0)	7 (28.0)	25 (2.9)
3–6 yrs	174 (68.8)	79 (31.2)	253 (28.9)
7–10 yrs	305 (70.8)	126 (29.2)	431 (49.3)
11–15 yrs	119 (71.7)	47 (28.3)	166 (19.0)
Total	616 (70.4)	259 (29.6)	875 (100)

Figures in parentheses indicate percentages.

The total duration of signs and symptoms and the outcome of these cases is shown in *Table II & III.* About one third children (31.8%) died. Most of the patients who expired did so within first 3 days of admission. The causes of death included cardiac failure, respiratory failure, PCF associated with toxemia and gastro-intestinal bleeding. Neurological deficits

TABLE II–*Presenting Features and Outcome in JE*

Features	(n=875)	Outcome of illness			
		Recovery	Partial recovery	Death	LAMA*
Fever	865(98.9)	467(54.0)	94(10.0)	269(31.1)	35(4.1)
Convulsions	733(83.8)	356(48.6)	87(11.9)	259(35.5)	31(4.2)
Altered sensorium	684(78.2)	322(47.1)	99(14.5)	231(33.8)	32(4.7)
Headache	558(63.8)	330(59.1)	65(11.7)	138(24.7)	25(4.5)
Vomiting	476(54.4)	201(42.3)	54(11.3)	178(37.4)	43(9.0)
Constipation	346(39.5)	169(48.8)	25(7.2)	145(41.9)	7(2.0)
Neck rigidity	223(25.5)	107(48.0)	33(10.3)	91(40.8)	2(0.9)
Gastric bleeding	115(13.1)	21(18.3)	14(12.2)	80(69.5)	--
Central respiration irregularities	113(12.9)	15(13.3)	27(23.9)	70(61.9)	1(0.9)
Positive Kernig's	69(7.7)	30(43.5)	11(15.9)	26(37.7)	2(2.9)
Diarrhea	32(3.4)	21(65.6)	1(3.1)	10(31.3)	--
Other					
–PCF	59(6.7)	8(13.5)	5(11.8)	45(77.6)	1(1.6)
–Pneumonia	26(3.0)	13(50.0)	9(34.7)	2(7.6)	2(7.6)

Figures in parentheses denote percentages.

* Left agaisnt medical advice; outcome not known.

and behavioral problems were seen in 94 (10.9%) children comprising mainly of mental retardation, aphasia, paresis, dystonia and seizures (*Table IV*).

Dopamine and corticosteroids were administered to 137 (15.7%) cases admitted in the acute stage with PCF and shock. Of the 35 children who were administered prednisolone at 3 weeks of illness, 20 (57.1%) recovered completely, 10 (28.6%) partially and 3 expired (*Table V*). When compared with non-steroid group (56 children) findings were not statistically significant.

TABLE III–*Duration of Signs and Symptoms in Patients who Survived*

Presenting features	(n=597)	Duration in days			
		3	3–7	7–10	10
Fever	531	185 (34.8)	239 (45.0)	76 (14.3)	31 (5.8)
Convulsions	542	178 (32.8)	291 (53.6)	47 (8.6)	26 (4.7)
Altered sensorium	378	172 (45.5)	153 (40.4)	29 (7.6)	24 (6.3)
Headache	317	317 (100)	--	--	--
Vomiting	223	223 (100)	--	--	--
Constipation	162	126 (77.7)	36 (22.2)	--	--
Neck rigidity	177	21 (11.8)	119 (67.2)	37 (20.9)	--
Gastric bleeding	34	23 (67.6)	11 (32.3)	--	--
Central respiratory irregularities	59	34 (57.6)	16 (27.1)	9 (15.2)	--
Positive Kernig's	54	9 (16.6)	33 (61.1)	12 (22.2)	--
Diarrhea	32	14 (43.7)	8 (25.0)	--	--

Figures in parentheses indicate percentages.

Out of the 278 children who were discharged after complete recovery in one week, 24 had recurrence of symptoms and were readmitted. Two of these children expired and rest showed variable recovery (*Fig. 1, Table VI*).

The laboratory investigations showed moderate leucocytosis in 661 (80.3%) cases (*Table VII*) with neutrophil predominance in 60%. Rise in CSF protein level was seen in 70.8% cases of whom 20% showed levels above 100 mg/dl or more whereas CSF

TABLE IV– *Neurological and Behavioral Problems in Patients Showing Partial Recovery*

Sequelae	Number	Percentage
Mental retardation	38	40.3
Hemiparesis	34	36.2
Aphasia	34	36.2
Dystonia	33	35.1
Seizures	26	27.7
Incontinence of bladder anal canal	19	20.2
Involuntary movement	19	20.2
Cranial nerve palsy	6	6.4
Monoparesis	5	5.3
Irrelevant behaviour	11	11.7
Irrelevant talk	10	10.6
Insomnia	10	10.6
Tongue protrusion	10	10.6
Weeping	8	8.5
Excitement	7	7.5
Irritability	6	6.4
Inappropriate laughing	2	2.1
Assaultive behavior	2	2.1

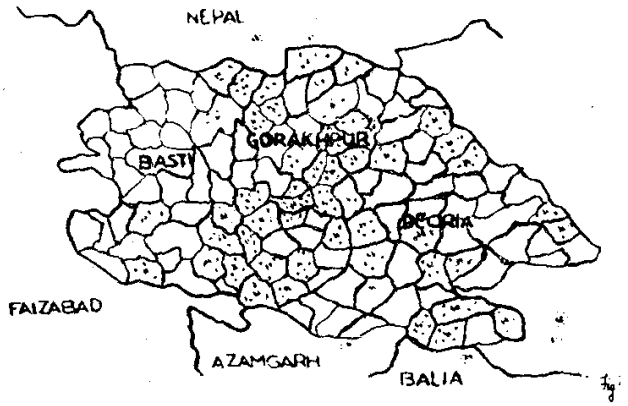

Fig. 1. Geographical distribution of cases of JE (1988-89).

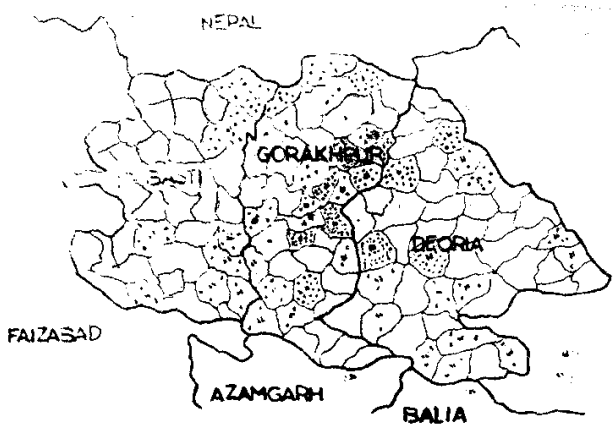

Fig. 2. Geographical distribution of cases of JE (1987-88).

sugar levels were not much altered. Majority of CSF samples had cell count upto 50 $\times$ 10^6/L, in 17% samples count was still higher. The virological investigations showed evidence of IgM antibodies in 18/25 CSF and 27/53 sera. HI antibodies (IgG) to JEV in significant titres were seen in 498/670 sera tested (*Table VII*). A four fold or more rise in HI antibodies was seen in sera of 13/14 patients tested out of 24 children readmitted with recurrence of symptoms.

Discussion

The 1988 epidemic of encephalitis in Gorakhpur region was one of the most serious epidemics in India so far with 875 children admitted to Nehru Hospital alone in a period of 3 months. Most of the cases from Gorakhpur and Deoria districts and some were from Basti and Azamgarh districts and bordering towns of Nepal (*Fig. 2*). As in past epidemics (1978, 1980, 1985, 1986)(3,7) the present epidemic too occurred at the end of rainy season. Occurrence of these epidemics at the end of rainy season has also been reported from West Bengal(8).

Encephalitis affected all age groups but the brunt of the disease fell on children

TABLE V–*Effect of Steroids in Chronic Phase*

Groups	Cases	Complete recovery	Partial recovery	Expired	LAMA*
Steroid	35 (4.0)	20 (57.1)	10 (28.6)	3 (8.6)	3 (5.7)
Non-steroid	56 (6.4)	38 (67.9)	14 (25.0)	-	4 (7.1)

χ^2 2df = 1.448; $p > 0.05$.

Figures in parentheses indicate percentages.

* Left against medical advice.

TABLE VI–*Profile of Patients Admitted with Recurrence*

Presenting features	(n=24)	Complete recovery	Partial recovery	Expired	LAMA
Fever	13 (54.2)	10 (76.9)	2 (15.4)	-	1 (7.7)
Altered sensorium	3 (12.5)	1 (33.3)	1 (33.3)	1 (33.3)	-
Involuntary movements	6 (25.0)	4 (66.7)	2 (33.3)	-	-
Convulsions	14 (58.3)	11 (78.6)	2 (14.3)	1 (7.1)	-
Total	24 (100.0)	16 (66.7)	5 (20.8)	2 (8.3)	1 (4.2)

Figures in parentheses indicate percentages.

between 7-10 years of age. Males were often affected in all age groups and is in line with the earlier reports(9, 10).

Clinical features of JE epidemic were similar to these reported earlier(11,12), as were the findings in CSF(10,11,13) and blood showing marked polymorphonuclear leucocytosis(11,13). The early and high mortality and the causes of death are also similar to previous reports(14,15). Most patients came in the acute stage and more than half of them showed complete recovery in 7-10 days. Significant number of children died in acute phase, mainly within first three days of admission. a third group of children went into a chronic phase, 41% of them developing neurological deficits and behavioral problems. A fourth course

TABLE VII–*Laboratory Findings in JE*

	Feature	Investigation	Result
Blood (n=823)	Hemoglobin (g/dl)	>12	101 (12.3)
		10–12	268 (32.6)
		<10	454 (55.1)
	Leucocyte counts ($\times 10^9$/L)	TLC	
		18	243 (29.5)
		12–18	418 (50.8)
		4–11	162 (19.7)
		Neutrophils (10^9/L)	
		>10	486 (59.1)
		5–10	309 (33.5)
		<5	28 (7.4)
CSF (n=768)	Proteins (mg/dl)	≤40	242 (70.6)
		>40	226 (29.4)
	Pleocytosis ($\times 10^6$/L)	50	131 (17.1)
		5–50	434 (56.5)
Virology (n=745)	Virus isolation from brain		2/4 (50.0)
	IgM – CSF		18/25 (72.0)
	Serum		27/53 (51.0)
	IgG Serum		498/670 (74.3)

Figures in parentheses indicate percentages.

also came to light in the present epidemic. Twenty four children who had shown complete recovery in early phase of epidemic and were sent home in 7 days came back after variable period with recurrence of symptoms (*Table VI*). On readmission, 16/24 recovered completely, 5/24 partially and 2 died. Such a course of JE has not been reported so far. It has been suggested that host defence mechanisms play an important role in viral encephalitis, dominance of which by the virus in early post recovery phase from first attack led to the recrudiscence of illness which again was controlled due to further stimulation of the immunological apparatus chiefly cell mediated immune response. It is as best a speculation as investigations were not carried out to see the behavior of immune mechanisms in these children. Role of auto-antibodies in recurrence too can be possible(16). It has been shown that JE virus persists in body in lymphocytes particularly in thymus and spleen for many months and can be reactivated at a later date (Mathur A, personal communication). In our cases this may be the source of relapse.

Mental retardation, hemiparesis, aphasia and seizures were the chief

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NOTES AND NEWS

THIRD COMMONWEALTH CONFERENCE ON DIARRHEA AND MALNUTRITION

The Third Commonwealth Conference on Diarrhea and Malnutrition is to be held in Shatin, New Territories, Hong Kong from *November 11th–14th, 1994*. This conference is organized jointly by the Department of Pediatrics, The Chinese University of Hong Kong and the Hong Kong Pediatric Society. Participation by over 300 delegates from throughout the Commonwealth is anticipated and, in this special meeting, we will be joined by colleagues from China.

Further details are available from:

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