International Journal of Research in Medical Sciences
Shrivastava P et al. Int J Res Med Sci. 2016 Apr;4(4):1062-1067
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20160784

Research Article

A study of sequelae of acute encephalitis syndrome in district Gorakhpur, Uttar Pradesh, India

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Received: 15 February 2016
Revised: 24 February 2016
Accepted: 08 March 2016

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ABSTRACT

Background: Each year more than 2000 AES cases are admitted in BRD Medical College, Gorakhpur, Uttar Pradesh, India with about 20-25 per cent mortality. Out of the survivors many develop neurological sequel after discharge. There is little information on the extent of disabilities, and no published literature on the subsequent follow-up of the survivors especially children after discharge. Objectives were to study the status of neurological sequelae and other complications, if any, in patients with JE and non-JE AES in the past three years.
Methods: All the cases of acute encephalitis syndrome belonging to Gorakhpur District who were discharged after treatment at BRD Medical College, Gorakhpur from Jan 2008 to Dec 2010 was taken. Sample size – Study was conducted in 171 subjects. Out of 19 blocks in Gorakhpur district, three blocks were randomly chosen by simple random sampling method and it was decided to study all available cases in these blocks. Liverpool outcome score, was used as an assessment tool to determine practical level of disability and the likelihood that a child will be able to live independently after illness.
Results: Out of 171 cases studied, 21 (12.3%), 48 (28.1%), 56 (32.7%) and 22 (12.9%) had full recovery, mild sequelae, moderate sequelae and severe sequelae respectively. The sequelae were more in forms of behavioural problems (77.6%), low intellect in school or routine task (57.2%), poor speech (20.4%), hearing (14.3%), motor and locomotion (8.9%).
Conclusions: Mental & behavioural problems were more frequently encountered sequel in patients with JE and non-JE AES.

Keywords: AES, Japanese encephalitis, Liverpool outcome score, Sequelae, Liverpool outcome score

INTRODUCTION

Acute encephalitis syndrome (AES) including Japanese encephalitis (JE) is a group of clinically similar neurological manifestation caused by several different viruses, bacteria, fungus, parasites, spirochetes, chemical/toxins etc. Clinically, a case of AES is defined as a person of any age, at any time of year with the acute onset of fever and a change in mental status (including symptoms such as confusion, disorientation, coma or inability to talk) and/or new onset of seizures (excluding simple febrile seizures).[1] The disease affects the central

nervous system and can cause severe complications, seizures and even death. The World Health Organization (WHO) estimates that JE causes at least 45,000 cases of clinical disease each year, mostly among children under 15 years of age, resulting in about 10,000 deaths and 15,000 cases of long-term, neuropsychiatric sequelae.[2] In India JE was first reported in Vellore in 1955, since then it continues to expand its geographical area. An estimated 378 million population is living at the risk of JE in 12 states/ Union Territories that are frequently affected. Uttar Pradesh (UP) experienced its first epidemic in 1978 when 1002 cases and 297 deaths occurred.[3] Since 1978, eastern UP is facing the problem of encephalitis epidemics. The underdeveloped nature of the region with one of the lowest per capita income also contributes to the overall health status of people in that region. Each year more than 2000 cases are admitted in BRD Medical College Hospital, Gorakhpur with about 20-25 per cent mortality. Out of the survivors many developed neurological sequelae after discharge. There is little information on the extent of disabilities, and no published literature on the subsequent follow-up of children after discharge, so no information on persistence of sequelae or death post-discharge is available.

Objectives of Study

1. To study the status of neurological sequelae and other complications, if any, in patients with JE and non-JE AES in the past three years.

2. To compare neurological sequelae and other complications in patients with JE and non-JE AES patients.

METHODS

Study type Cross sectional study

Study Setting: Present study has been carried out in Gorakhpur district; it is divided into seven Tehsils which are further subdivided into nineteen Development Blocks. The cases were selected among the patients who were diagnosed as acute encephalitis syndrome and were discharged alive after treatment from Nehru Hospital, BRD Medical College Gorakhpur, Uttar Pradesh, India from Jan 2008 to Dec 2010.

Sample size : Minimum sample size was calculated with the help of following formula:-

$$n = \frac{NZ^2P(1-P)}{d^2(N-1) + Z^2P(1-P)}$$

Thus taking 1752 as population size (N), considering about 40% of AES cases (P=0.4) might have developed sequelae after discharge, taking z=1.96 at 95% confidence level and allowing 7% permissible error.[4-7] It was found that a minimum of 170 cases were to be sampled. Adding 20% owing to no consent and 30% to incorrect address/incomplete address/loss due to change of address, it was decided to sample 255 cases.

Sampling technique

From the line list of AES/JE cases of 2008, 2009 and 2010, cases belonging to Gorakhpur district were selected and were arranged block wise. There were a total of 1752 cases in 19 blocks, averaging to 92 cases per block. Owing to limited resources, it was decided to randomly select three blocks and study all available cases within those blocks. The selected blocks were Bhathat, Chargawa and Pipraich.

Inclusion criteria for study subjects:

1. The patient enrolled as AES/JE, who after treatment was discharged alive from Nehru Hospital, BRD Medical College, Gorakhpur during the above mentioned period.

2. AES/JE cases <15 year age at the time of admission.

Exclusion criteria for study subjects:

1. AES/JE cases whose addresses were found incorrect /incomplete /loss due to change of address.

2. AES cases whose parents or caregivers had not given their consent to participate in the study.

3. AES cases who were not found at home on two revisits.

Data Collection

An assessment tool that can be used to rapidly determine practical level of disability and the likelihood that a child will be able to live independently after illness, the Liverpool Outcome Score (LOS),[8]was used.

Statistical analysis

Differences between proportions were tested using chi-square and a two-sided Fisher's exact test. A p value of <0.05 was considered significant.

Ethics

Ethics approval for the assessments was obtained from Institutional Ethic Committee for Human Research (IECHR), BRD Medical College, Gorakhpur. On an informed consent form, signatory consent was obtained from the parent or legal guardian of each child.

RESULTS

Table 1: Outcome and extent of sequelae among AES cases, Gorakhpur, Uttar Pradesh, India.

Characteristic	Outcome	No.	%
Speech or Communication	Same	117	79.6
	Changed or Reduced	27	18.4
	Not Speaking or Communicating	3	2
Feeding	Same	138	93.9
	Occasionally Need Help	7	4.8
	Always Need more Help	2	1.4
Leaving Alone	Too Young	46	31.3
	Yes	74	50.3
	Briefly In familiar environment	19	12.9
	No	8	5.4
Behaviour	Completely Normal	33	22.4
	Gets angry easily	46	31.3
	Other Behaviour change	51	34.7
	Severely abnormal	17	11.6
Recognition	Too Young	52	35.4
	Yes	86	58.5
	Some	8	5.4
	None	1	0.7
School or Routine Work at home	Now back to normal at school or work	63	42.9
	Not doing as well	38	25.9
	Dropped a school grade or no longer attending school or work	46	31.3
	No seizure & not on anti-epileptic drugs	114	77.6
Epilepsy/ Seizures (in the last 2 month)	No seizure & on anti-epileptic drugs	30	20.4
	Yes, has had seizures	3	2
Dressing themselves	Too Young	46	31.3
	Yes	81	55.1
	Occasionally Need Help	5	3.4
	Always Need more Help	3	2
Bladder & Bowel Control	Same as other children of same age	116	78.9
	Occasionally Need More Help or occasionally is incontinent	24	16.3
	Needs more help or is incontinent of bowel or bladder	7	4.8
Hearing	Normal	123	83.7
	Reduced in one or both ears	21	14.3
	Can't hear at all	2	1.4
Sitting	Independently	142	96.6
	Needs Help	3	2
	Not at all	1	0.7
Standing Up	Independently	141	95.9
	Needs help	5	3.4
	Not at all	1	0.7
Walking	Normally	134	91.2
	Abnormally, but independently +/ crutches/stick	11	7.5
	Not able to walk	2	1.4
Hands on head	Normal both hands	143	97.3
	Abnormal 1 or more both hands	2	1.4
	Unable 1 or both hands	2	1.4
Picking Up	Normal pincer grasp both hands	143	97.3
	Abnormal 1 or more both hands	2	1.4
	Unable 1 hand	1	0.7
	Unable both hands	1	0.7

Figure 1 shows outcome of AES on the basis of Liverpool Outcome Score. Although statistically non-significant (p>0.05) a higher number of deaths was reported in females (20.6%) in comparison to males (9.7%). Maximum number of deaths was seen in 0-1 year age group (23.5%) and maximum severe sequelae was seen in age group 1-5 (16.8%). A significant association was found between social class and sequelae (p=0.0019). Table 1 depicts the outcome and extent of sequelae among AES cases. Among 147 live cases studied in the follow up study. The sequelae was more in forms of behavioral problems (77.6%), low intellect in school or routine task (57.2%), poor speech (20.4%), hearing (14.3%), motor and locomotion (8.9%). 22.4% of the cases were either on anti- epileptic drugs or still having seizures. 21.1% cases had partial or complete loss of control of bladder and bowel, 18.3% could not be left alone, 6.2% had feeding difficulty and about 5.4% needed some help while dressing themselves. 7.5% had either abnormal walking or needed some support like crutches or sticks for walking while 1.4% were not able to walk at all. 3.4% needed help for standing, 2% needed help for sitting while 0.7% bed ridden. Table 2 shows that behavioural problems were the most common sequelae in both JE (85.7%) and non JE (78.2%) AES cases. Severe abnormal behaviour was seen in 11.9% non JE and 9.5% JE AES cases. Speech abnormalities were seen more in JE (38.1%) as compared to non JE (17.5%) AES cases (p=0.06).A higher number of JE cases needed help while feeding (9.5% JE vs.5.6% non JE), dressing (19% JE vs. 12.7% non JE) and can't be left alone (19% JE vs. 14.3% non JE).50% JE and 20.8% non JE school-going children had not been doing as well at school or work as before illness. 33.3% JE as compared to 41.5% non JE school-going children had dropped a school grade or no longer attending school or work. 23.8% JE as compare to 22.2% non JE AES cases had seizures or on antiepileptic drugs (p=0.87). 33.3% JE as compare to 19% non JE AES cases were urinary or fecal incontinent (p=0.23). 14.3% JE as compare to 7.9 % non JE AES cases had not been able to walk or walk abnormally independently or with crutches.

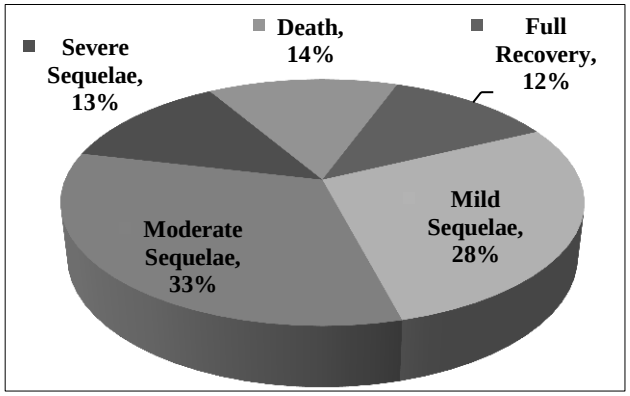

Figure 1: Outcome of AES cases on the basis of Liverpool outcome score.

Table 2: Comparison of sequelae among JE and non JE AES cases, Gorakhpur, Uttar Pradesh, India (N=147).

Characteristics	JE (N=21)		Non JE (N=126)		P value
	No.	%	No.	%	
Reduction in speech	8	38.1	22	17.5	0.06*
Need help while feeding	2	9.5	7	5.6	0.61#
Can't be left alone	4	19	18	14.3	0.52#
Not able to recognize	1	4.8	8	6.3	>0.05#
Get angry easily	8	38.1	38	30.2	0.64*
Other Behaviour problems	8	38.1	43	34.1	0.9*
Severe abnormal behaviour	2	9.5	15	11.9	>0.05#
Need help for dressing	4	19	16	12.7	0.5#
Reduced hearing	2	9.5	21	16.7	0.53#
Had seizure or on anti-epileptic drugs	5	23.8	28	22.2	0.87*
Bladder or bowel incontinent	7	33.3	24	19	0.23*
Can't sit or sitting with help	1	4.8	3	2.4	0.46#
Can't stand or standing with help	1	4.8	5	4	>0.05#
Not able to walk or walk abnormally independently or with crutches	3	14.3	10	7.9	0.41#
Abnormal hand on head	0	0	4	3.2	>0.05#
Abnormal pincer grasp	0	0	4	3.2	>0.05#

*Chi square test with yate's continuity correction; # Fisher's exact test.

DISCUSSION

Estimates of the extent of disability following AES have differed from country to country and in different studies based on multiple factors, including the methodology used for the assessment, the age group, and the type of patient group examined. Nevertheless, data have consistently shown, as in this study, that there is a significant burden from AES disability and mortality, as well as a wide spectrum of sequelae including physical, intellectual, and psychological problems. Our study shows that more than one quarter of the children who suffered AES either died or were left with disabilities that were sufficiently severe to result in the child being unlikely to lead an independent life. Children with severe sequelae frequently scored poorly on multiple assessment

questions. Several children were noted to be totally incapacitated, including one child in vegetative state. Maha et al in a similar study among Indonesian children reported 17 % death in hospital and eight percent death after discharge. Severe sequelae, moderate sequelae, minor sequelae and full recovery were reported respectively in 25%, seven percent, 18% and 25% children.[9] In another study Pieper and Kurland followed the survivors of a 1947 JE outbreak in Guam and found that 40% had neurologic sequelae; 11% were considered severe.[10] Wang and Chen followed 54 patients and of those 23 (43%) exhibited neurologic sequelae, 24 (44%) showed psychiatric abnormalities, and 34 (63%) had mental deficit.[11] Goto reported neurologic sequelae in 76% of 43 JE cases at 5 years of follow-up.[12] In another study in Hong Kong among the 41 survivors, 24% had neurological sequelae with focal neurological deficit in 29%; personality changes in 6%; moderate mental retardation in 2%; severe mental retardation in 4%; hyperactivity in 4% and epilepsy in 4%.[13]Baruah et.al in a study showed that out of 30 patients, 13 (43.3%) showed complete recovery at the end of 421 days. Residual problems persisted in 9 (30%) cases till the end of study.[14] Ooi et.al, 1997-2005**,** Central Sarwak, Malaysia, reported at hospital discharge, 44 (41%) of the 108 patients who survived had apparent full recovery; 3 (3%) had mild, 28 (26%) had moderate, and 33 (31%) had severe neurological sequelae. Eighty six of the 108 patients were followed up for a median duration of 52.9 months (range, 0.9–114.9 months). During follow-up, 31 patients experienced improvement, but 15 patients experienced deterioration in their outcome grade.[15] Japanese Encephalitis (JE) disability assessment, Cambodia, 2007-2008, reported that out of 54 survivors five (10.6%) had severe sequelae, eighteen (38.3%) and twenty one (44.7 %) of children had moderate and mild sequelae, respectively. Only three children (6.4%) were considered to have recovered completely to a comparable condition as prior to illness.[16]

Comparison of sequelae among JE and non JE AES cases– Both JE and non JE AES cases have shown similar outcome and extent of disability. Behaviour problems were the leading sequelae in both groups, almost three fourth of JE and two third of non JE cases have shown mild to moderate form of behaviour problems. Severe behaviour problems were seen in about one-tenth of both JE and non JE cases. Reduction of speech and aphasia is more in JE cases as compared to non JE cases which is marginally non significant (p=0.06). Physical dysfunctions like difficulty in sitting, standing or walking were higher in JE as compare to non JE but these are not statistically significant (p=0.4).

CONCLUSION

Mental & behavioural problems were more frequently encountered sequel in patients with JE and non-JE AES.

Recommendations

To ensure best outcomes for the children, follow-up is extremely important to assess recovery, identify new problems that may develop, and manage the rehabilitation process. In addition, routine documentation of the extent of disability after AES could be very useful as part of disease surveillance programme conducted by health departments, to help better understanding of the extent of AES disease burden, and enable advocacy for support measures for these children.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Shrivastava P, Shrivastava DK, Tiwari HC, Kushwaha KP, Gore M. A study of sequelae of acute encephalitis syndrome in district Gorakhpur, Uttar Pradesh, India. Int J Res Med Sci 2016;4:1062-7.