An aetiological study of acute encephalitis syndrome in children in Karnataka State, South India

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Background:

Acute encephalitis syndrome (AES) is an important problem in children throughout Asia. AES is often viral, with Japanese encephalitis (JE) the most frequent diagnosis in Asia. During a cohort study on the role of immunity in JE pathogenesis in South India, we found few cases of acute JE, however the number of cases of AES remained high. Therefore, we analysed clinical data, and samples collected during the study, to determine the clinical features and causes of AES in South Indian children.

1. Methods:

Inclusion criteria

Fever, plus one of:

- Clouding of consciousness
- Seizures
- Focal neurological signs

Diagnostic testing

Serology:

- Dengue, Zika, Chikungunya, Scrub typhus, hepatitis E (JEV)

Viral PCR:

- HSV1 & 2, VZV, mumps, enterovirus, parechovirus

Bacterial PCR:

- *Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae*

Age		Sex		Length of illness prior to admission	
Median	4 years	Male	211 (64%)	Median	1 day
IQR	2 - 6 years	Female	116 (35%)	IQR	0 - 3 days
Range	1 - 15 years	Not recorded	1 (0.3%)	Range	0 - 30 days

Table 1. Demographic details and time to presentation

2. Results

Three hundred and sixty AES cases were recruited over the period September 2011 - February 2013, of whom 328 fitted the case definition and had data available for analysis (table 1). Only 176 patients (52%) had lumbar puncture performed.

Clinical diagnoses

Based on clinical features, LP, JE and dengue testing available locally at the time of admission, diagnoses could be made on 176 patients (53.7%, table 2). Ninety patients had seizures before presentation, but had no further seizures nor neurological abnormalities and were diagnosed as febrile seizures.

Diagnosis	Number (%)	
Dengue	25	(7.6%)
JE	11	(3.4%)
Febrile seizures	90	(27.4%)
Bacterial meningitis	17	(5.2%)
TBM	20	(6.1%)
Fever & Hydrocephalus	1	(0.3%)
Fever & stroke	1	(0.3%)
No diagnosis (AES)	163	(49.7%)

Table 2. Clinical diagnoses, and diagnostics available locally. AES = acute encephalitis syndrome, agent not diagnosed.

3. Further diagnostic tests

The number of patients with a microbiological diagnosis or treatable syndrome was only 73. Therefore, we attempted to improve upon this using stored samples, in the 238 patients who did not have febrile seizures (table 3). Excluding these patients, the number of patients with a diagnosis rose from 73 to 99, though a number of patients were also re-classified by diagnostic testing. Several patients tested positive for multiple pathogens (figure 1). A number of additional pathogens tested positive, no single positive cases Zika and hepatitis E were identified (table 4).

Diagnosis	Number (%)	
Encephalitis, cause unknown	137	(57.6%)
JE	11	(4.6%)
Chikungunya	12	(5.0%)
Dengue	31	(13.0%)
Enterovirus	1	(0.4%)
Varicella zoster virus	1	(0.4%)
Bacterial meningitis	17	(7.1%)
TBM	17	(7.1%)
Scrub typhus	3	(1.3%)
Multi pathogen positive	6	(2.5%)
Other	2	(0.8%)

Table 3. Final diagnoses made in 238 children with acute encephalitis syndrome, excluding those with febrile seizures. Other = once case of hydrocephalus, and one cerebral infarct
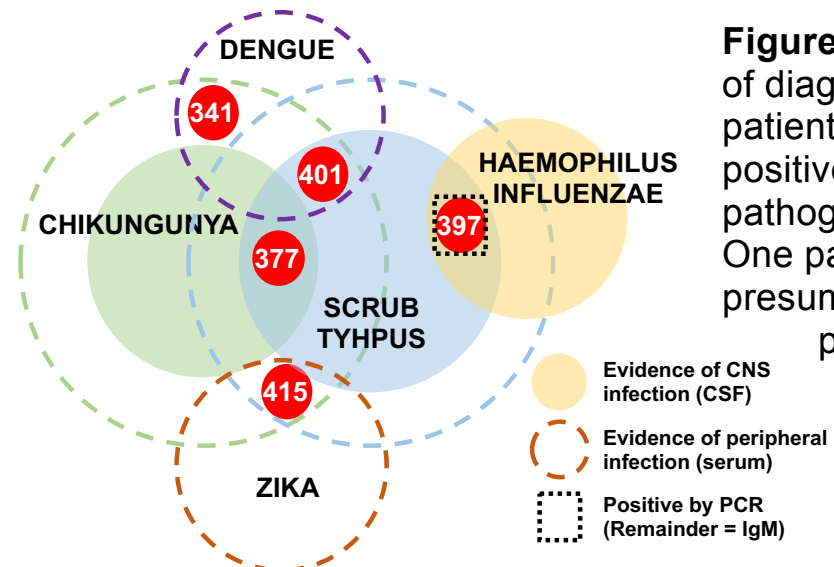

Figure 1. Distribution of diagnostic tests in 5 patients testing positive for multiple pathogens. One patient who was presumed false positive on all tests run has been omitted

Evidence of CNS infection (CSF)

Evidence of peripheral infection (serum)

Positive by PCR (Remainder = IgM)

Pathogen	Number
Dengue	33
Chikungunya	16
Scrub typhus	8
H influenzae	4
Zika	2
Varicella zoster virus	1
N meningitidis	1
Enterovirus	1
Hepatitis E	1

Table 2. Number of individual tests positive for each pathogen in the diagnostic panel. *H. influenzae, N meningitidis,* eneterovirus and varicella zoster were PCR, the remainder IgM assays. Some patients had more than one test positive.

Conclusions:

Excluding patients who had febrile seizures, the number of patients with a diagnosis rose from 73 to 99 (41.6%), though a number of patients were also re-classified by diagnostic testing. The number of diagnoses remained low. Prospective studies of novel diagnostic strategies are needed.