



BMH Medical Journal 2016;3(2):37-42 **Research Article**

## Outbreak of Enterovirus - 71 Meningitis in Calicut

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### Abstract

**Objective:** Enterovirus 71(EV 71) causes wide spectrum of infections ranging from asymptomatic conditions to clinical syndromes like diarrhea, rash, hand-foot-and mouth disease (HFMD), herpangina, aseptic meningitis, encephalitis, myocarditis, acute flaccid paralysis, bulbar and brainstem encephalitis Guillain Barre syndrome, pulmonary haemorrhage. This study deals with an outbreak of aseptic meningitis in children caused by EV 71 virus.

**Methods:** The authors report an outbreak of aseptic meningitis in children in and around Calicut in June 2008. Clinical and laboratory study was done in collaboration with National Centre for Disease Control, New Delhi. 149 children with aseptic meningitis were studied and followed up from June 2008 to May 2009.

**Result:** All children had clinical features suggestive of aseptic meningitis and serology showed the rising antibody titre against EV 71 virus infection. CSF analysis also showed four fold rise in antibodies in one and  $\geq 1:2$  neutralising antibodies titer against EV- 71 in four samples indicating meningitis due to EV-71.

**Conclusion:** EV 71 was identified as the causative agent of the outbreak of aseptic meningitis in the study and the fact that the EV 71 infection has evolved from minor illness like HFMD to major illness like aseptic meningitis from the same locality is truly alarming.

**Keywords:** Aseptic Meningitis, Enterovirus 71

### Introduction

Enterovirus 71(EV-71) infection, first recognized in California in 1969, appears to be giving rise to

large epidemics with much fatality among young children [1-4]. EV -71 infection like other enteroviruses are usually asymptomatic or may be associated with various clinical syndromes like diarrhea, rash, hand-foot and mouth disease, herpangina, aseptic meningitis, encephalitis, myocarditis, acute flaccid paralysis, bulbar and brainstem encephalitis, Guillain Barre Syndrome and pulmonary haemorrhage/edema [5-9]. Increasing attention is now being paid to the study of this virus. There is continuing activity of EV-71 in our neighbourhood for the last 3 decades. It has emerged as an important public health problem causing serious clinical illness. Its invasion caused hand foot and mouth disease (HFMD) in Calicut, India for the first time in 2005 [10]. Subsequently we were in search of other clinical syndromes caused by this virus and we came across children with aseptic meningitis which prompted us to conduct this prospective study.

Enterovirus 71 infection usually occurs by the fecal, oral or respiratory route leading to viremia and invasion of various organs of the body. Meningitis usually presented with fever, irritability, photophobia, malaise, headache, nausea, anorexia, vomiting and lethargy. Occasionally, they may have rash, rhinitis, pharyngitis, cough and diarrhea. Myalgia, neck stiffness and other signs of meningeal irritation are encountered with less intensity in children [11].

### Material and Methods

A prospective observational study was conducted for aseptic meningitis from June 2008. All patients came from within a radius of 70 kilometers. The study continued till May 2009 and was approved by the Institutional Review Board. Sudden increase in the number of children and adults with meningitis were noted during the study period.

Aseptic meningitis was characterized by fever, headache and vomiting with clinical signs of meningeal irritation, confirmed by CSF study. The CSF pressure was normal or minimally raised, cell count varied with lymphocytic preponderance. Absence of microorganisms, normal / slightly decreased CSF glucose, normal or mildly elevated protein were also noted.

History and clinical examination findings of all the patients were recorded. Routine investigations of blood, urine and cerebrospinal fluid were done along with throat swabs, rectal swabs. Blood samples as well as CSF of patients were collected on the day of admission and at discharge or two weeks later. Sera was separated and stored in the cold, till they were examined together at National Centre for Disease Control (NCDC), New Delhi as per the protocol [12].

All patients were given standard care for meningitis and patients were discharged in good condition after 7-10 days. They were periodically assessed for any complication of the illness or the treatment during hospital stay. All of them were followed up to six months for any neurological sequelae.

Magnetic Resonance Imaging (MRI) was done at random in 40 children and they were followed up for 2 months for any neurological sequelae.

### Results

A total of 149 patients with aseptic meningitis were studied, 92 were males and 57 were females. Monthly incidence and gender distribution is shown in (Figure 1). Youngest patient was 7 month old and oldest 14 years. Majority of them belongs to the age group of 3-12 years (Figure 2). The presenting symptoms and signs are shown in (Figure 3). There were 30 adult patients admitted in the hospital during the same period. 9 of them were mothers of children with meningitis. One mother had Herpangina. From a single household, there were 4 children and their mother admitted with meningitis. There were 10 sibling with meningitis in this series. Another interesting findings was 31 of the patients had biphasic illness, manifested as recurrence of high fever on 6th or 7th day of the illness, while on treatment. All of them had conjunctival and mucosal congestion with macular rash over the body. All symptoms subsided on 12-14 days. Only one child had HFMD

while on treatment for meningitis. There were no deaths or any other complications pertaining to this illness. Routine blood examination showed leucocytosis, raised ESR and elevated CRP. The CSF analysis values showed normal sugar and mildly elevated protein and pleocytosis. Gram stain did not show any organism except for occasional pus cells. CSF culture was Negative for bacteria. MRI brain was reported normal in 40 children selected at random. Serology report (Table 1) showed the rising antibody titres against EV 71 virus infection. CSF analysis showed four fold rise in antibodies in one, and four samples showed  $\geq 1:2$  neutralising antibodies titer against EV- 71 indicating meningitis due to EV-71.

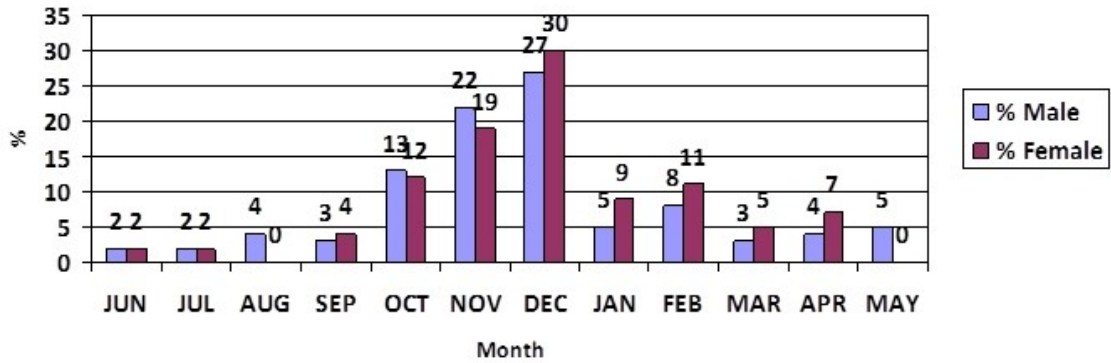


Figure 1: Monthly incidence and gender distribution

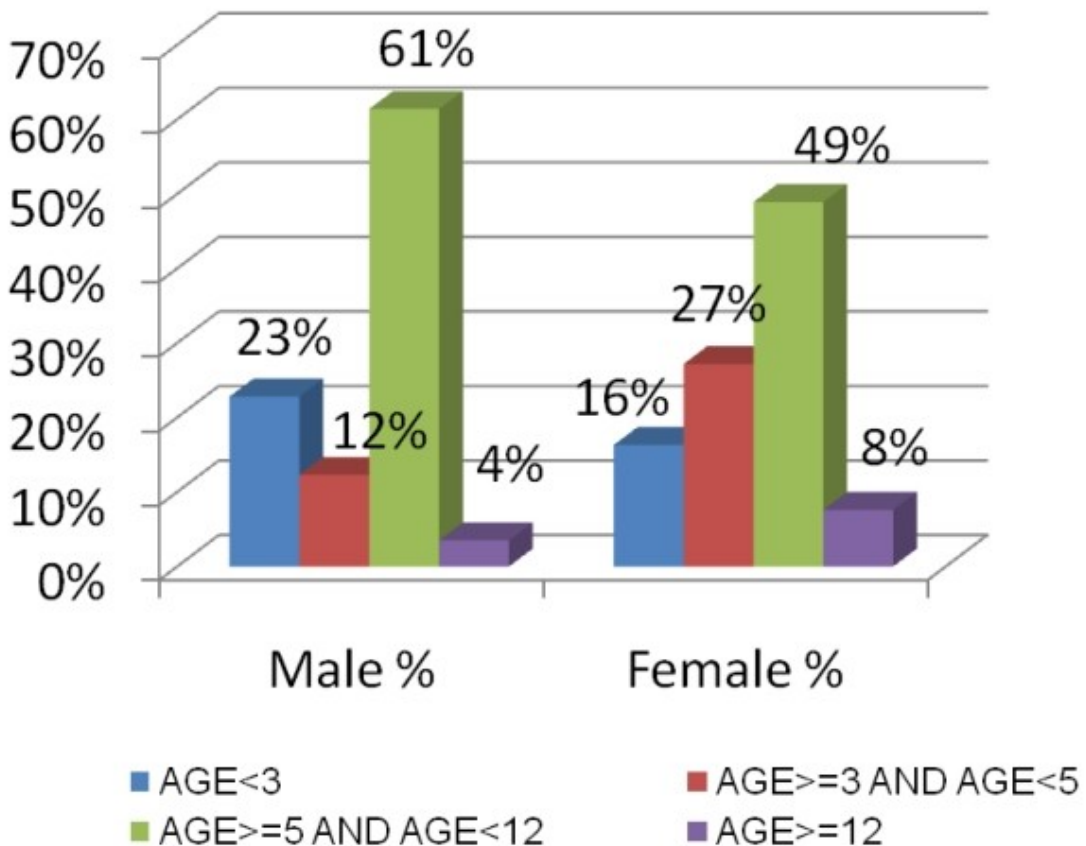


Figure 2: Age and gender distribution

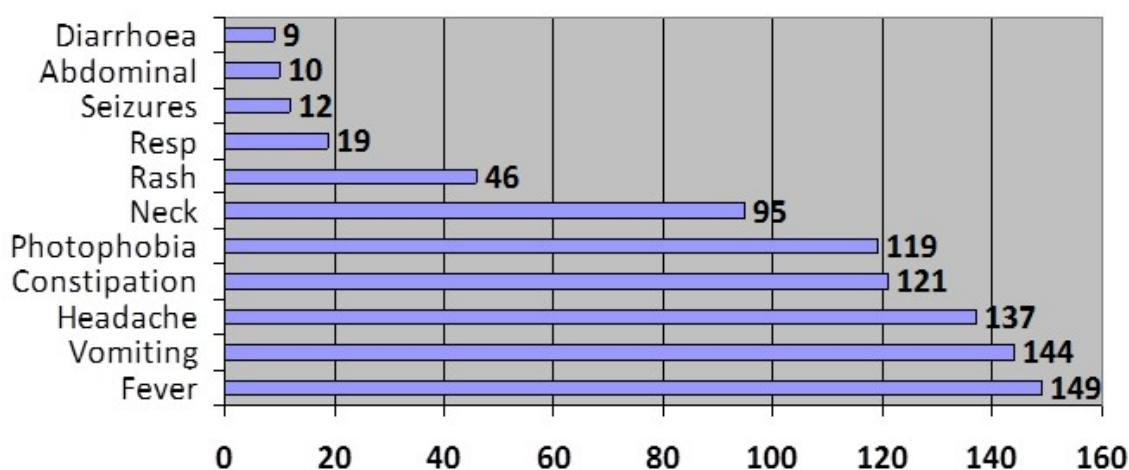


Figure 3: Presenting symptoms and signs

Table 1: Enterovirus 71 serology results

Age distribution (n=149)	Total No. of samples	Samples showing four fold rise in the Nt. Antibodies titer	Samples showing two fold rise in the Nt. Antibodies titer *	Both the samples showing high antibody titer >1:128**
<3yrs(30)	18	6(33.3%)	3(16.7%)	9(50%)
3-<5yrs(29)	19	6(33%)	3(33%)	7(34%)
5-<12yrs(82)	24	9(37%)	8(33.3%)	7(29%)
>12yrs(8)	4	1(25%)	2(50%)	1(25%)
Total	65	22	19	24

\* Second blood samples were collected at discharge on 7th day

\*\*Admitted after one week of onset of illness

## Discussion

Emergence and re - emergence of infections is causing significant public health problems in various countries. EV71 infection has undergone transformation from a minor illness like HFMD to epidemics causing several deaths and neurological complications. Asian countries had experienced the burnt of attacks by this infection [13-15]. EV71 infection causes a number of different clinical syndromes [5]. Successive epidemics have shown different genotypes [14,16].

There has been few documented reports showing isolates of EV71 infection in India, which deals with HFMD only [17,18]. The first report of outbreak of HFMD in India was from Calicut in 2005 [10].

This study deals with 149 children admitted with meningitis, spread over a period of one year with peak incidence in October to December 2008. Reports of outbreaks of isolated EV71 meningitis in India is scant [19, 20]. CNS involvement has been documented by various studies from other

countries [8,9,15]. PCR remains the gold standard of confirmation of viruses. Serological confirmation is also equally important where rise in titer is demonstrated [12].

In the present study findings of paired sera samples from patients showed 4 fold rise in antibody titer against EV 71 in specific microneutralization test confirms the fact that the virus was the causative agent.

MRI brain done on 40 children at random was reported as normal. Studies done elsewhere had reported abnormalities in MRI but majority of children in these studies had neurological complications like brain stem encephalitis, acute parencephalitis, acute flaccid paralysis and encephalomyelitis which were not seen in the present study [15,21].

There is no specific treatment for this disease. Recent researches show the development of first inactivated EV71 whole virus vaccine for preventing severe HFMD [22]. This vaccine could be tried in children susceptible to develop EV 71 meningitis after further Randomised Control Trials.

This study reiterates the fact that EV 71 had made its presence in India in 2005 in Calicut and the present outbreak from the same locality with more severe form of illness like meningitis is alarming.

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