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Role of cerebro spinal fluid analysis among the children between 6 to 18 months age group presented with first episode of febrile seizure

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ABSTRACT:

Background: Febrile seizure is the most common type of seizure among the children which may be due to acute bacterial meningitis. Early diagnosis and treatment of acute bacterial meningitis among children with first febrile seizure is utmost necessity. In this study, we evaluated role of cerebrospinal fluid analysis among children with first episode of febrile seizure.

Methods: Children aged between 6 to 18 months with first episode of febrile seizure admitted within 24 hr of seizure onset were enrolled. Clinical history, physical findings and vital parameters were noted. Cerebrospinal fluid was analyzed for cell count, sugar, protein, microbiological examination. Acute bacterial meningitis was diagnosed based on cell count>5/mm^3, protein >100mg/dl and sugar <40 mg/dl or<50% of serum glucose in the cerebrospinal fluid.

Results: Seven (14%) out of 50 children were diagnosed as acute bacterial meningitis. Other causes for febrile seizure were: upper respiratory infection (48%), diarrhea (18%), urinary tract infection (8%) and fever of unknown origin (12%). Three children with acute bacterial meningitis showed positive meningeal sign. In one case of acute bacterial meningitis, organism *klebsiella* was isolated. Body temperature; hear rate and respiratory rate were found significantly elevated among the cases with acute bacterial meningitis as compared to other cases.

Conclusion: In children first febrile seizure, cerebrospinal fluid examination is important to rule out acute bacterial meningitis as the incidence was 14% in this study. Whenever meningeal signs are present with first episode of febrile seizure, there is a significant possibility of acute bacterial meningitis.

KEY-WORDS: Febrile seizure, Convulsions, Meningitis, Lumbar puncture, Children

INTRODUCTION:

A seizure is a transient occurrence of abnormal excessive or synchronous neuronal activity in the brain characterized by convulsions. Fever with seizures also known as the febrile seizures is the most common type of seizures in children.[1,2] It may be due to simple febrile seizure, complex febrile seizure or secondary to some serious underlying etiology like neuro-infection. By the age of 5 years, 2-5% of children experience one or more episodes of febrile seizure.[2-4] Febrile seizure is a convulsions associated with an elevated temperature > 38^{o} C occurring in children between the age group of 6 months and 5 years. Exclusion to the diagnosis include a history of a previous afebrile seizures, infection or inflammation of the central nervous system or acute systemic metabolic abnormalities that may also produce the convulsions.[5] In children with febrile seizure, probability of acute bacterial meningitis (ABM) ranges from 0.6 to 6.7%.[1] ABM can lead to considerable mortality, morbidity and serious long term sequealae during early childhood hence, it is essential to diagnosis early and provide prompt treatment.[6] Cerebrospinal fluid (CSF) analysis is an important diagnostic tool for diagnosis of ABM.[4] In children between 6 to 18 months of age who present with a first "simple febrile seizure", possibility of ABM is very low.[3,7] In the developed countries, the issue of whether a well-appearing child with a first febrile seizures is at high risk for ABM is controversial, because of a scarity of quantitative data and data inclusion prior to availability of *Haemophilus influenza* b (Hib) vaccine.[7] In 1996, the American Academy of Pediatrics consensus statement recommended that CSF analysis should be done for children of 6 to 18 months age presenting with a first simple febrile seizure.[7] In guidelines for the Neuro-diagnostic Evaluation of the Child with a Simple Febrile Seizure, it has been suggested to include ABM in the differential diagnosis, and lumbar puncture should be performed if there are clinical signs or symptoms of concern and it is option in: (i) an infant of 6 to 12 months who are deficient or unknown status of Hib or *Streptococcus pneumoniae* immunizations and (ii) children who are pre-treated with antibiotics.[2] However, in India, the use of Hib and Pneumococcal vaccines is not yet extensive.[8] Therefore, in our conditions, these guidelines probably require some modification. So, we conducted the present study to determine the relevance of routine lumbar puncture, in children aged 6 to 18 months having first episode of febrile seizures.

METHODS

The present cross-sectional study was started after the approval from the ethics committee and Informed consent was obtained from the parents of children before their enrolment. Children of the age group 6 to 18 months with a history of first episode of seizure with associated febrile illness admitted within 24 hours of first seizure in Pediatric Medical Ward, New Civil Hospital, Surat were included in the study. Children with history of previous intracranial infections, previous neurological deficits, cases for whom already lumbar puncture has been done before for the current episode, and any contraindication to the lumbar puncture procedure such as signs of raised intracranial tension; bleeding disorder – coagulopathy or decreased platelet count (<50,000/cmm); any local skin infection; mental retardation; vertebral deformity (scoliosis or kyphosis); cerebral palsy were excluded from the study.

For included children, clinical history, physical findings, respiratory rate, heart rate, axillary temperature, were noted at the admission. A detailed neurological examination was done. Lumbar puncture was performed with full aseptic precautions and CSF was collected and sent to the laboratory for cell count, differential count, sugar, protein, Gram's stain, Ziehl Neelsen stain and culture.ABM was diagnosed if child had combination of all three of the following:(1) CSF cells >5/mm^{3}, (2) protein > 100mg/dl and (3) Sugar <40 mg/dl or<50% serum glucose.[9] Growth of bacteria in the CSF and/or positive Gram's stain was considered as culture proven ABM. Other causes for first febrile seizure were also noted. Descriptive statistics was used for summarizing the data. Categorical data were compared using Chi square test and continuous data were compared using the un-paired t test. $P < 0.05$ was considered as significant.

RESULTS

In present study, 50 eligible children were enrolled and evaluated for the presence of ABM. The mean age of presentation was 11.98± 3.51 months. Demographic details are shown in table 1.

As shown in table 2, the most common cause for the first febrile seizure was the upper respiratory infection, followed by diarrhea and ABM. Forty one (82%) patients were finally diagnosed to have febrile seizure whereas; seven (14%) patients were diagnosed with ABM. Two (4%) patients had the hypocalcaemia.

In present study, 7 out of 50 patients were diagnosed as acute bacterial meningitis after performing the CSF examination. Of seven, 5 children were from the 6 to 12 month age group while 2 children were from the 13 to 18 month age group. Out of 7 confirmed ABM cases, 3 were male and 4 were female. In ABM confirmed case 5 children presented with simple febrile seizure while 2 children presented with complex febrile seizure. In ABM confirmed cases 3 children had meningeal sign positive while 4 children had meningeal sign absent. Only 1 case had CSF culture positive and the organism was *klebsiella*. CSF examination details for each ABM patient are shown in table 3.

Among 40 cases presented as simple febrile seizures, 5cases had ABM whereas; Out of 10 cases of complex febrile seizures, 2 cases had ABM. This difference in proportions was not statistically significant (Table 4).

Meningeal signs were found to be significantly associated with ABM with a specificity of 100%. (Table 5)

The difference in the mean temperature, heart rate and respiratory rate at admission between ABM group and non ABM group was statistically significant. More temperature, tachycardia and tachypnea were noted in cases with ABM as shown in table 6.

DISCUSSION

In this study, we evaluated the proportion of acute bacterial meningitis using CSF analysis among the children presented with first episode of febrile seizure. Fifty cases of first episode of febrile seizure were evaluated of which 31(62%) were male and 19 (38%) were female with Male: Female ratio of 1.63:1. Such observation of male preponderance was similar to other studies.[1,10,11] Lumbar puncture was performed in all 50 children and based on CSF analysis, 14% children were found to have ABM. In present study, there were 32 (64%) children in 6 to 12 months and 18 (36%) in 13months to 18 months age group out of 50 cases. Five (15.6%) of 32 children had ABM in 6 to 12 month age group while 2 (11.1%) of 18 children had ABM in 13 to 18 month age group. Thus, 6 to 12 month age group had higher risk of ABM as compared to 13 to 18 month age group when they present with first episode of febrile seizure. This finding is comparable with other studies.[1,10]

In our study, the most common cause of fever among the study group was URTI 24(48%). Similar findings were seen in other studies.[12,13] Etiology of fever was either urinary tract infection or upper respiratory tract infection in a study done by Gunduz et al and was viral infection in a study conducted by Ehsanipour et al.[14,15] Viruses are the most common cause of illnesses in children admitted to the hospital with febrile seizure.[16] URTI was the most common cause of febrile seizure in our study. The second most common cause of fever in our study was diarrhea 9 (18%) which is higher than found by Jun-Hwa Lee et al 8 (3.2%).[12] The cause of fever was undetermined in 6 (12%) in our study and was 62 (25%) in the study by Jun-Hwa Lee et al.[12] ABM should not be missed in any child with fever and seizures. Among the 50 cases presenting in the emergency room with apparent febrile seizures 7 children (almost 1 in 7) had ABM. 7 cases had ABM based on CSF cytological and biochemical criteria.[1] In another study done in Kathmandu, 10.9% of patients with apparent first febrile seizure had ABM. Other studies on ABM in apparent febrile seizure have found the incidence of ABM to vary from 2-7%.[17-19] Our finding was comparatively higher than from studies done outside India. The culture yield of CSF was 14.28%, which is comparable to other studies of febrile seizure.[20-23] Our study showed children with ABM had significantly higher heart rate, respiratory rate and temperature compared to children in non ABM group. The younger children had the more risk of the ABM. In 6-12 months age group, 15.6% had ABM as compared to 11.1% in 13-18 months age group. Other studies have also come to the same conclusion.[18, 20-22, 24] Therefore, it is likely that, younger the age more is the chance that a child presenting with fever and seizure may have ABM.

In our study, meningeal signs were found to be significantly associated with ABM with sensitivity 42.8%, specificity of 100%, positive predictive value of 100% and negative predictive value of 91.4%. However as the sample size is small in our study we advocate further studies with larger sample size. The high risk of ABM in the presence of meningeal sign in a patient with fever and seizure is found to be comparable to other studies.[13] Meningeal signs may occur in other disorders like cervical spine injury, spinal epidural hematoma, subarachnoid hemorhage, peri-tonsillar and deep neck abscess and epidural abscess. Being a fatal disorder unless treated, it is important to confirm ABM. In this regard lumbar puncture and CSF analysis become relevant. It was seen that in children aged 6-12 months there was more probability of having ABM without signs of meningeal irritation than in children aged 12-18 months but the difference was not statistically significant. 4 out of 7 children altogether had ABM without meningeal sign. Around 60% of children in the age group of 6-12 months had ABM without meningeal signs. This is comparable to other studies.[17,25] Incomplete myelination in this age group causes absence of meningeal signs in ABM.[26] Therefore, our observation highlights the importance of performing lumbar puncture and CSF examination even in the absence of meningeal signs in children aged 6-12 months, considering the urgency of diagnosing ABM.

In conclusion, 14% children with first episode of febrile seizure had acute bacterial meningitis. Hence, CSF examination should be performed to rule out acute bacterial meningitis in children with first febrile seizure. Whenever meningeal signs occur in children with first episode of seizure with febrile illness, there is significant possibility of acute bacterial meningitis.

DECLARATIONS

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Table 1: Demographic details of included children

Variables	**Number (%) (n=50)**
Age group	
6-12months	32 (64)
13-18months	18 (36)
Gender	
Male	31 (62)
Female	19 (38)
Presenting symptoms	
Fever	50 (100)
Convulsions	50 (100)
Cold and Cough	24 (48)
Loose stool	09 (18)
Vomiting	05 (10)
Altered consciousness	19 (38)
Type of seizure	
Simple febrile seizure	40 (80)
Complex febrile seizure	10 (20)

Table 2: Causes of fever with first febrile seizure among the study group

Causes	**Number (%) (n=50)**
Upper respiratory tract infection	24 (48)
Diarrhoeal disease	9 (18)
Acute Bacterial Meningitis	7 (14)
Urinary tract infection	4 (8)
Cause of fever unknown	6 (12)

Table 3 : Details of 7 children found to have ABM on routine lumbar pucture

No.	Age (Months)	Sex	Length of convulsion (min)	Type of seizure	Meningeal sign	CSF cell count	CSF protein (mg/dl)	CSF sugar (mg/dl)	Organism
1.	7	M	15	Simple febrile seizure	Absent	110	118	7	*Klebsiella*
2.	15	M	45	Complex febrile seizure	Absent	48	145	23	No growth
3.	17	F	3	Simple febrile seizure	Present	99	102	18	No growth
4.	8	F	10	Simple febrile seizure	Present	362	117	32	No growth
5.	9	M	20	Complex febrile seizure	Absent	150	132	20	No growth
6.	9	F	3	Simple febrile seizure	Absent	131	116	22	No growth
7.	9	F	10	Simple febrileseizure	Present	271	104	29	No growth

Table 4: Distribution of ABM cases among different types of febrile seizure

Type of seizure	ABM (n=7)	Non ABM (n=43)	p value
Simple febrile seizure (n=40)	5	35	**0.92**
Complex febrile seizure (n=10)	2	8	

Table 5: Association of meningeal sign with ABM

Meningeal signs	ABM (n=7)	No ABM (n=43)	P value
Present	3	0	0.0018
Absent	4	43	

Table 6: Comparison of vital signs, at admission, between ABM and non ABM cases

Vital signs	ABM (n=7)	Non ABM (n=43)	P value
Temperature (^{0}C)	38.92±1.59	37.67 ± 0.70	<0.0008
Heart rate (beats/min)	158.71 ±11.82	123.06 ± 16.87	<0.00004
Respiratory rate(breaths/min)	44.57 ± 12.09	31.6 ± 6.13	<0.02

Data expressed as mean ± SD; P value is for unpaired t-test.