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Research Article

Seizure

The utility of Lumbar Puncture in the first episode of Simple Febrile Seizure in Children between 6 to 18 months of age

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Introduction: Febrile seizures are the most common seizures occurring in children and are exclusive to childhood. It is the most common pediatric emergency and the most common type of seizure every pediatrician is dealing with. It accounts for 2.5% of all seizures in children. Despite progress in the understanding of febrile seizure and development of consensus statement about diagnostic evaluation and management there exists a diversity of opinion regarding blood investigations, neuro-imaging, Electro Encephalogram (EEG) and the need for routine lumbar punctures (LP)during a febrile seizure. **Aim & objectives**: To determine the utility of lumbar puncture in identifying the group of children aged 6 to18 months having the first episode of fever with seizures that would benefit from the procedure. **Observation:** Most common cause of fever in febrile seizures was found to be upper respiratory tract infection (38%) in children followed by AGE(15%). Family history was present in 12.77% of cases of SFS. The most common symptom is cough and cold apart from fever and seizure saw in children. Most common clinical sign was transient lethargy lasting less than <15 minutes seen in 18% of cases. In 11.7% of cases of SFS a diagnosis of meningitis was made at the time of admission. Out of these only 1 case (2.4%) was suggestive of meningitis in the age group of 6 to 12 months. **Conclusion:** Lumbar puncture is necessary to rule out meningitis in all children between the ages of 6 months to 12 months presenting with the first episode of fever with seizure to rule out meningitis.

Keywords: Febrile Seizure, Cerebrospinal Fluid, Bacterial Meningitis, Electroencephalography.

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Introduction

Seizures are a common problem in pediatric practice. The approximate prevalence of seizures in children is around 10% [1]. They are more common than in the adult population as the brain is still developing. Childhood seizures differ from adult seizure since the brain is developing organ. Many types of seizures are exclusive to childhood. The clinical picture is not static and pattern and type of seizures keep changing with age and brain development unlike adults, most seizures in children are provoked by somatic disorders originating outside the brain such as high fever, infection, syncope, head trauma, hypoxia, and toxins etc [1].

Febrile seizures are the most common convulsive phenomenon seen in humans. Febrile seizures are a form of acute symptomatic seizures that occur in 2-5% of all seizures in children [2]. Febrile seizures are the most common seizures occurring in children and are exclusive to childhood [2]. It is the most common pediatric emergency and the most common type of seizure every pediatrician is dealing with. Much ignorance prevails in the general public about febrile seizures. There is a lot of fright and parental anxiety when faced with an episode of a febrile seizure. Many studies are being done on understanding mechanisms, genetics and long term outcome of febrile seizures.

There has been a changing view of the management and role of Anti-Epileptic Drugs(AED) on these common and largely benign [3]. Febrile seizures are generally benign and have an excellent prognosis [4,5] but sometimes fever with seizure may also signify a serious underlying acute infectious disease such as sepsis or bacterial meningitis. Therefore each febrile seizure must be carefully examined and investigated and appropriately investigated for the cause of fever, especially when it is the first episode [6,7].

Despite progress in the understanding of febrile seizure and development of consensus statement about diagnostic evaluation and management there exists a diversity of opinion regarding blood investigations, neuro-imaging, Electro Encephalogram (EEG) and the need for routine lumbar punctures (LP)during a febrile seizure [8,9]. Febrile seizure diagnosis is an essential clinical diagnosis and needs proper clinical evaluation. Routine lab testing is not required in all cases10.

Laboratory evaluation is indicated in a clinical situation where the source of fever is uncertain or the diagnosis is unclear. The laboratory, radiographic, neurologic evaluation should be aimed at a diagnosis of the cause of fever. The American Academy of Pediatrics (AAP) in 1996 issued practice parameters regarding the neurodiagnostic evaluation of children with a first simple febrile seizure (FSFS) who present within 12 hours after the seizure [10].

Simple Febrile Seizure (SFS) was defined as the first episode of seizure accompanied by fever, manifested as a primary generalized seizure lasting <15 minutes and not recurring within 24 hours. The term febrile seizure is not intended for use among children with evident central nervous system infections or underlying seizure disorders [11]. The AAP practice parameters recommended that lumbar puncture (LP) be strongly considered for patients <12months of age and be considered for patients 12 to 18 months of age, to diagnose bacterial meningitis among children with FSFS as their sole clinical manifestation of infection.

These recommendations were based on the knowledge that seizure is a common presenting symptom of bacterial meningitis [12,13] clinical skills and experience vary widely among examiners, and clinical assessment of children at this age for subtle signs can be difficult. However, the issue of whether a well-appearing child presenting with an FSFS is at increased risk for bacterial meningitis has remained controversial [14,15,16,] because of a lack of quantitative data and the inclusion of data from the pre-Haemophilus influenza type B vaccine era [17].

Although seizure is a common symptom among patients presenting with bacterial meningitis, it is quite uncommon for a simple, brief, non-focal seizure to be the sole manifestation of bacterial meningitis [18]. With the introduction of a 10-valent, pneumococcal conjugate vaccine the incidence of bacterial meningitis has decreased significantly, which further affects the probability of this condition in young patients with simple febrile seizures [19-21].

Although there are quantitative data regarding the LP yield among patients presenting with FSFS [18,8,22] no data from a large cohort of patients that specifically address patients 6 to 18 months of age (the focus of the AAP practice recommendations) have been presented.

Hampers et al [23] reported decreases in rates of LP performance in these patients, to <10%, in community hospitals. Hence this study was planned to evaluate the rate of bacterial meningitis and the need for routine LP among otherwise healthy infants 6 to 18 months of age who presented to a pediatric emergency department (ED) with FSFS.

Aim and Objectives

Aim: To determine the utility of lumbar puncture in identifying the group of children aged 6 to18 months having the first episode of fever with seizures that would benefit from the procedure.

Objectives: The main objectives of the study are to study the clinical profile of febrile seizures in this group of children 6 to 18 months of age, whether lumbar puncture is to be done routinely for all cases of simple febrile seizures in 6 to 18 months of age &to assess the number of actual cases meningitis masquerading the clinical picture of SFS in this age group.

Materials & methods

After obtaining institutional ethical committee clearance this hospital-based non-randomized prospective observational study was conducted in the department of pediatricsSCB & SVPPGIP, Cuttack from May 2018 to April 2020.

Inclusion criteria: All children in the age group 6 to 18 months admitted in pediatrics medical ward, SCB MCH &SVPPGIP, Cuttack with Fever present before onset of seizure, first episode of GTCS type convulsion lasting less than 15 minutes & not more than 1 episode of convulsion in 24 hr period with a normal postictal period.

Exclusion criteria:1.Obvious evidence of Central Nervous System (CNS) infection (via history &physical examination) & metabolic disturbances, 2. Complex febrile seizure or those with prior neurological deficits, 3. Any contraindication for LP, 4. History of afebrile seizures, previous seizures and syndromes associated with seizures, recent trauma, neurodevelopment delay, brain tumours & ventriculoperitoneal shunts.

Method of collection of data: Children were considered as having fever if axillary temperature >101.5 F or with h/o fever in the past 24 hrs. In all children of 6 to18 months of age with non-focal, generalized seizure, single episode lasting less than 15 minutes with fever before the onset of seizure were included in the study. Cases were selected based on inclusion & exclusion criteria.

Cases were studied about the clinical history and physical findings. Respiratory rate, heart rate, axillary temperature, weight, height, head circumference and weight for height were measured at admission. A detailed neurological examination was done. An LP was performed and Cerebrospinal fluids (CSF) was collected and was sent for cell count, differential count, sugar, protein, Gram's stain, ZN stain and culture.

Acute bacterial meningitis (ABM) was diagnosed if the child had the combination of all three of the following: CSF cells >5/mm3, protein more than 100mg/dl and Sugar <40 mg/dl or <50% serum glucose.12 Growth of bacteria in the CSF and/or positive Gram's stain was considered as culture-proven ABM. Informed consent was taken from the parents or the guardians before enrolment into the study.

INVESTIGATION 1. CBC, 2.MP-ICT, Urine & stool (a. routine, b.microscopic),3.CSF analysis,4. Other investigations will be done as per need basis and clinical presentation like Chest X-ray, EEG, Transcranial ultrasound, C T Scan of the brain (plain, contrast).

Statistical analysis:

Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at a 5 % level of significance.

The following assumptions on data are made:

01. Dependent variables should be normally distributed.
02. Samples drawn from the population should be random; cases of the samples should be independent.

Student t-test (two-tailed, dependent) has been used to find the significance of study parameters on the continuous scale within each group. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on a categorical scale between two or more groups.

3. Significant figures: Suggestive significance (P value: 0.05<P<0.10)

Observations

Table-1: Distribution of Febrile Seizure (n=94)

VARIABLE		NUMBER	PERCENTAGE
Age	6-12months	50	42.6
	13-18months	54	47.4
Sex	Male	64	68
	Female	30	32
Focus of fever	Without focus	54	57.4
	With focus	40	42.6
Family history	Present	12	12.76
	Absent	82	87.23

There was a higher frequency of febrile seizures above 1 year. A higher incidence is seen in the 13-18 month's group [57.4%].In our study febrile seizures are more common in males, with M: F ratio of 2.4:1.In 57.4% of cases even after history and investigations no focus of fever could be found in them. Family history of febrile seizure among one parent, both parents or siblings was present in 12(12.76 %) cases. In the majority (87.2%) cases, no family history of febrile seizure was found.

Table-2: Cuases Of Febrile Seizure (n=94)

Cause	Number	Percentage
URTI	36	38%
AGE	14	15%
UTI	2	2%
ASOM	2	2%
No focus	40	42.6%
Total	94	100%

The most common cause of fever in febrile seizure was found to be upper respiratory tract infection (URTI) in 38% of Cases followed by AGE in 15%. No focus was found in 42.6%.

Table-3: Clinical Symptoms in Cases (n=94)

Symptoms	Frequency(n=94)	percentage
Fever	94	100%
Convulsion	94	100%
Cough and cold	36	38.2%
Irritable	17	18%
Loose stools	14	15%
Ear discharge	2	2.1%
Red eyes	5	5.31%
Rash	2	2.1%
Neck stiffness	0	0%

In our study, all cases presented with fever and convulsion(100%) as these were the inclusion criteria.

In addition to this, the most common associated symptom was cough and cold which was found in 36(38.2%) cases followed by irritability and loose stools found in 18% and 15% cases respectively. Not a single case presented with neck stiffness.

TABLE-4: Clinical signs In SFS Cases (n=94)

Signs	Frequency(n=94)	Percentage
Transient lethargy	17	18%
Bulged fontanelles	2	2.12%
Pallor	4	4.2%
Microcephaly HC<-3SD	3	3.1%
Tachypnoea	1	1%
Organomegaly	5	5.3%
Focal neurological deficits	0	0%
Loss of consciousness	0	0%

The above table depicts the presence of clinical signs in 32(33.7%) cases which was about 1/3rd of the total cases. Most common clinical sign was lethargy seen in 18% cases, which was transient in nature, lasting for around 10-15 minutes followed by regain of normal sensorium. Signs of meningial irritation ,focal neurological deficits or loss of consciousness were not found in any of the cases.

Table-5: Clinical diagonosis at the time of admission (n=94)

Clinical diagnosis	Frequency(n=94)	percentage
SFS	21	22.3%
SFS with viral fever	7	7.4%
SFS with URTI	36	38%
SFS with AGE	14	15%
SFS with ASOM	2	2%
SFS with malaria	3	3.2%
Meningitis	11	11.7%
Total	94	100%

Clinical diagnosis of meningitis was made in 11.7% cases of SFS at the time of admission.

Table-6: Investigation Results

Investigations	Frequency [n=94]	(%)	Frequency of abnormal	% of abnormal
CBC	84	89.3%	41	48.8%
MP Slide/ICT	76	80.8%	1	1.3%
Urine	56	59.5%	2	3.57%
EEG	11	11.8%	4	36.3%
TC-USG	2	2.1%	0	0%
CT Scan	2	2.1%	0	0%
CSF Study	41	43.6%	1	2.4%

Most investigations in SFS are found to be normal. CBC is the most common investigations done, found abnormal in 48.8% in the form of mild anemia and

EEG was abnormal in 4 out of 11 cases(36.3%).CSF study was abnormal in only 1 case(2.4%) suggestive of meningitis.

Table-7: C S F study report (n=41)

CSF study	Frequency	Percentage
LP done	41	43.6%
LP<12Months	30	73.1%
LP>12Months	11	26.9%
CSF pleocytosis [WBC>5/mm3]	1	2.43%
CSF Gram stain abnormal	0	0
CSF C/S Growth[+ve]	0	0

LP was done only in 41(43.6%) cases out of 94 cases as valid informed consent was not given by parents in the rest of the cases. In the age group 6-12 months,30 (73.1%)cases had undergone LP whereas 11(26.9%) cases in the age group 12-18 months. Only 1 case had pleocytosis. None of the cases came out to be gram stain or culture positive.

TABLE-8: C S F PARAMETER IN SFS

CSF PARAMETER	MEAN ± S.D	95% C.I
WBC count [/mm3]	2.56 ± 2.72	1.73 to 3.39
Protein [mg/dl]	70.29 ± 11.08	66.9 to 73.68
Sugar[mg/dl]	56.73 ± 11.55	53.19 to 60.27

Reports of C S F shows within normal limits

TABLE-9: DISTRIBUTION OF ABM AMONG DIFFERENT AGE GROUP OF SFS (n=41)

Age	ABM	Non ABM	P value
6 to 12 months	1	29	0.5398
12 to 18 months	0	11	

Out of 30 cases clinically diagnosed as simple febrile seizure (6-12 months age group), only 1 case had CSF findings suggestive of meningitis while in the age group of 12 to 18 months, none of the 11 cases turned out to have meningitis. This was not statistically significant (p=0.5398). Though the association between febrile seizure and meningitis came out to be statistically insignificant, meningitis being a rapidly deteriorating disease, we should not miss even a single case as it is highly preventable.

In our study,1 out of 30 cases in the age group of 6-12 months came out to be ABM, equivalent to about 33/1000 cases proportionately, which can contribute to significant morbidity and mortality. However, in the age group of 12-18 months, not a single case of meningitis was detected. So our aim should be not to miss even a single case of meningitis. Hence, LP should be mandatory in the age group of 6-12 months to rule out meningitis.

TABLE-10: OUTCOME OF SFS(n=94)

Outcome	Frequency	Percentage
Discharge	68	72%
LAMA	10	10.6%
Discharge on request	16	17%
Death	0	0
Recurrence	6	6.3%

There was no death. No focal neurological deficits and sequelae were noticed following the seizure. Recurrence of seizure was seen in 6.3% of cases during a hospital stay. So, SFS has a good prognosis but long term follow up study is needed to find any neurological abnormality in future.

Discussion

This was a hospital-based non-randomized prospective study conducted in the department of pediatrics SCB MCH & SVPPGIP, Cuttack from May 2018 – April 2020. In all 94 children of 6-18 months with non-focal, generalized seizure, single episode lasting less than 15 minutes with fever before the onset of seizure were included in the study. In all children detailed history, examination and relevant investigation were done. Finally Lumber puncture could be done in 41 (43.6%) cases after taking informed consent.

There was a higher frequency of febrile seizures above 1 year. Higher incidence [57.4%] of febrile seizures is seen in the 13-18 months age group. Heijbel J [24] in their study found the median and mean age for the first FS was for boys 16 and 19.9 months respectively. Offringa et al [25] have done a Dutch study and found the median age at onset FS was 18 months. Nguefack et al [7] in their study found the peak age of these patients was 12-17 months. In my study also SFS more common above 1 year like in most other studies.

In our study SFS are found to be more common in males than the female with M: F ratio of 2.4:1, probably because of preference towards the male child in our region.

Heijbel J et al [24] in their study found FS was more common among boys, with a male to female ratio of 1.72 to 1. Nguefack S et al [7] in their study found the sex ratio (M: F) was 1.5. Yoldi- Petri ME et al in their study found the sex ratio (M: F) was 1.98:1. Nelson KB et al [26] found the sex ratio 1.12:1 for whites and 1.20:1 for black. Shah SS et al found a sex ratio of 1.34:1. Millar J S et al [27] found a sex ratio of 1.4:1.

Most studies show a male preponderance may be due to genetic reasons. In our study also there is an increased incidence in males compared to other studies.

In 40 (42.6%) cases even after history, examination and all relevant investigations no focus of fever could be found in these cases. The most common cause of fever in febrile seizures was found to be upper respiratory tract infection (38%) similar to most other studies. Family history among one parent, both parents or sibling was present in 12.77% of cases of SFS.

Martin Offringa et al [25] have done a dutch study and found that of all the children,5.4% had a positive first-degree family history of febrile seizures. B Rharucha et al [28] in their study found the familial prevalence was 20% and the commonest relative was a sibling. In my study familial prevalence was 12.77% in between the studies. Variation is due to genetic differences and other regional factors.

B Rharucha et al [28] showed URTI was the most common infection in SFS. Kodah IH found viruses are the most common cause of illness presenting in the form of URTI in children admitted to the hospital with a first febrile seizure.

Jun-Hwa Lee et al [29] & Margaretha et al [30], both studies showed URTI was the most common infection in SFS. Aetiology of fever was either UTI or URTI in a study done by Gunduz et al[31]. Viruses are the most common cause of illnesses in children admitted to the hospital with SFS[32,33]

The second most common cause of fever in our study was ADD 14(15%)which is similar to a study done by Margaretha et al [30] 5 (20%). The cause of fever was undetermined in 40(42.6%) in our study and was 62 (25%) in the study by Jun-Hwa Lee et al [29].

Since the most common cause of SFS was URTI, the commonest clinical symptom was cough and cold seen in 38.2% of cases. Clinical signs are minimal present in 34%cases only. The most common clinical sign was lethargy seen in 18% of cases which were transient, lasting for around 10 to 15 minutes followed by normal sensorium.

None of the patients had focal neurological deficits and loss of consciousness following the seizure. No studies could be found for comparison in this regard.

We have incidentally found three cases of microcephaly (<-3SD) among FSFS and they were included in our study because these cases did not have development delay, neonatal seizure or afebrile seizure earlier. They presented as SFS for the first time. Therefore follow up study is required to estimate the probability of these cases going into future epilepsy. Two cases had bulged fontanelles but on LP meningitis was ruled out. Here, bulged fontanelle may be a false interpretation for meningitis by a physician due to excessive cry.

In 11.7% of cases of SFS a diagnosis of meningitis was made at the time of admission. Lorber J, Sunderland R [34] in their study, an initial diagnosis of meningitis was made in 9.53% of cases. W Shrestha S et al [35] study shows 14.54% of children were diagnosed to have meningitis, 21.4% in the age group 6-12 months, 21.4% in 12-18 months, 7.8% in more than 18 months age group.

Our study is comparable to the above 2 studies with 11 cases (11.7%) diagnosed as meningitis at the time of admission. On the contrary, only one case out of the 11 cases turned out to be meningitis proven by LP.

Results of various investigations CBC, urine, malarial studies, EEG and other investigations are depicted. Most investigations done in SFS cases are found to be normal.CBC was the most common investigation ordered in 89.3% of cases. It was abnormal in 48.8% of cases in form of mild anaemia followed by EEG abnormality in 4(36.3%) cases among 11 patients.

Mean Hb was 10.5±1.13 gm%.In 48.8% of cases anaemia was present of mild grade. The most common type of blood picture was normocytic hypochromic anaemia seen in 69% of cases. Gerber MA, Berliner BC6...Reviewed the routine diagnostic tests measurement of blood glucose, serum calcium, serum electrolyte and BUN levels, blood cell count, urinalysis and EEG performed on 100 consecutive children.

Most investigations [95%] were normal. Maytal J et al [36] showed abnormalities in an early postictal EEG performed on otherwise normal children with febrile seizures is 8.6% or less.

Out of 30 cases in the age group of 6 to 12 months of simple febrile seizure, 1 case was found to be actual meningitis confirmed by LP while in the age group of 12 to 18 months, none of the 11 cases turned out to be meningitis.

This difference in proportion was not statistically significant. (p=0.5398) Lumbar punctures were more frequently done in less than 1 year age group in 30(73.1%) cases as compared to 11(26.9%) cases above 1 year age group. Mean CSF values were 2.56±2.72 cells/mm3, CSF protein 70.29±11.08 mg /dl and CSF sugar 56.73±11.55 mg/dl.

Gram stain and cultures were normal in all the cases. Out of these only one case (2.4%) had meningitis in the form of CSF pleocytosis (WBC >5/cumm), increased CSF protein (110 mg/dl), decreased CSF sugar (40mg/dl) in the age group 6-12 months.

Though the association between febrile seizure and meningitis came out to be statistically insignificant, meningitis being a rapidly deteriorating disease, we should not miss even a single case as it is highly preventable. In our study,1 out of 30 cases in the age group of 6-12 months came out to be ABM, equivalent to about 33/1000 cases proportionately, which can contribute to significant morbidity and mortality.

However, in the age group of 12-18 months, no single case of meningitis was detected. So our aim should be not to miss even a single case of meningitis. Hence, LP should be mandatory in the age group of 6-12 months to rule out meningitis.

Table-11: Comparison of incidence of ABM and possible occult bacterial meningitis following a febrile convulsion.

Authors	Number of children with febrile seizure	Number with ABM	Number with signs of meningitis
Batra P et al [36]	199	5	Not recorded
Shreshta SK et al [37]	110	16	Not recorded
Teach et al [22]	243	0	0
Anderson et al [3]	100	0	0
Gerber and Berliner [6]	100	0	0
Heijbel et al [24]	119	4	4
Lorber and Sunderland [34]	452	3	3
Amir A Kimia et al [36]	271	0	0
Present study	94	1	0

It is clear from pooled data of various studies that the incidence of meningitis after the first episode of febrile seizure is very low. Despite progress in understanding febrile seizures and the development of consensus statements about their diagnostic evaluation and management there is considerable variation in interpretation, evaluation, treatment in febrile seizures.

There was no death. There are no long term effects. Recurrence was observed in only 6.3% of cases. Further long term follows up study is needed in this regard. Chugach M, Shorvon S [39] found that simple febrile seizures do not carry a risk of death. There is no evidence of any risk of hippocampal or mesial temporal sclerosis in association with simple febrile seizures.

Knudsen FU, Paerregaard A, Andersen R, Andersen J et al [3]. found in their study on longterm follow up the occurrence of epilepsy, neurological, motor, intellectual, cognitive and scholastic achievements in a cohort of children with febrile convulsions randomized in early childhood. Children with simple febrile convulsions had a benign outcome.

Conclusion

It was found that meningitis is a presentation in a few cases of apparent simple febrile seizure mainly in the age group 6 to 12 months, so meningitis should always be considered as a differential diagnosis.

Lumbar puncture is necessary to rule out meningitis in all children between the ages of 6 months to 12 months presenting with the first episode of fever with seizure to rule out meningitis, even in the absence of meningeal signs so that we may not miss a single case of meningitis which has significant morbidity and mortality.

What does the study add to the existing knowledge?

Lumbar puncture is necessary to rule out meningitis in all children between the ages of 6 months to 12 months presenting with the first episode of fever with seizure to rule out meningitis.

Author's Contribution

All authors were involved in research design, data analysis, and manuscript preparation and editing.

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