

Credibility of American Academy of Pediatrics Guidelines 2011 in Evaluating Apparent First Simple Febrile Seizures

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Abstract: Fever with seizures is a common presentation in pediatric emergency department. In apparent first simple febrile seizures (FSFS) acute bacterial meningitis (ABM) should always be considered as a differential diagnosis. American academy of Pediatrics (AAP) guidelines of FSFS 1996 strongly recommended lumbar puncture (LP) in 3-12 months infants and advised to consider LP in children of 12 to 18 months age as signs and symptoms of meningitis are absent or subtle. In 2011 AAP changed the guidelines and LP was made an option in these children based on Hemophilus influenza type b (HIB) and Pneumococcal vaccine (PCV) status. Present study was intended to evaluate the credibility of AAP guidelines 2011 in developing / underdeveloped countries. 226 children of 3-18 months of age with apparent FSFS were evaluated by meningeal signs and LP findings. Among 3-12 months children 13 had meningitis but only 5 (38%) presented with meningeal signs and 8 (62%) had no meningeal signs. In 12-18 months of age, meningitis was noticed in 11 children and 6 (55%) presented with meningeal signs and 5 (45%) had no meningeal signs. LP findings of 3-12 months children with meningitis (N-13) were suggestive of ABM in 10 (77%) and viral meningitis in 3 (23%) cases. Comparatively in 12-18 months children with meningitis (N-11) LP was suggestive of ABM in 8 (73%), viral meningitis in 2 (18%) and tuberculous meningitis in 1 (9%) of cases. Therefore, LP detected meningitis in remaining 62% infants in 3-12 months and 45% children in 12-18 months age group who could not be picked up by meningeal signs. Overall immunization coverage of HIB/PCV in our study was 64 (28.3%) and 11 (4.9%). In developing/under developed countries implementation of AAP recommendations 2011 need to wait till immunization coverage of HIB / PCV reaches more than 90 percent.

Keywords: AAP, 2011 guidelines, credibility, meningitis, febrile seizures, diagnosis.

INTRODUCTION

Simple Febrile seizure (FS) is the most common type seizure disorder occurring in children 3 months to 5 years of age with a peak incidence around 18 months, associated with a fever of 38.0°C or higher and presents without evidence of any definite causative diseases, such as central nervous system (CNS) infection or metabolic cause. Most cases of FS are benign and self-limiting, and in general need no specific treatment [1]. On the other hand suspected bacterial meningitis common in children of similar age group is a medical emergency, and immediate diagnostic steps must be taken to establish the specific cause so that appropriate antimicrobial therapy can be initiated. The mortality rate of untreated acute bacterial meningitis (ABM) approaches 100 percent and even with optimal therapy, morbidity and mortality may occur [2]. FS occurs more often in the Asian population, affecting 3.4% to 9.3% of Japanese children and 5% to 10% of Indian children, but only 2% to 5% of children in the

United States (US) and Western Europe [3]. Probability of acute ABM in these children varies from 0.6% to 6.7%. But number of studies in developing countries where immunization coverage of Hemophilus influenza type b (HIB) and Pneumococcal vaccines (PCV) is poor, revealed higher incidence (4.2% to 30.9%) of meningitis [4, 5].

Apparent first simple febrile seizures (FSFS) could be due to FS or ABM. In the diagnostic evaluation of these children it is of prime importance to ABM in all children less than 18 months presenting with apparent first simple febrile seizures (FSFS) either clinically if uncertain by doing lumbar puncture (LP) because out of 6 children with ABM one develops seizures and in one third of them meningeal signs and symptoms are lacking. The American Academy of Pediatrics (AAP) practice parameters for diagnosis and evaluation of simple febrile seizures 1996 recommended that LP be strongly considered in less

than 12 months infants because clinical signs and symptoms of meningitis may be minimal or absent and lumbar puncture should be considered in children of 12 to 18 months old as signs and symptoms of meningitis are subtle. These recommendations were changed in 2011 where in the committee made LP an option, left to the discretion of treating physician, in children of less than 12 months and 12-18 months in view of wide coverage of HIB and PCV during the period from 1996-2011 [6, 7]. Now the developing countries are at cross roads and not able to decide which way to go – follow AAP guidelines 2011 or to go with routine LP in dealing with apparent FSFS cases in children below 18 months of age. In view of this existing controversy, the present study was undertaken in the Department of pediatrics, of a tertiary care hospital in South India, to find out the incidence of ABM, determine the role of LP in differentiating ABM from simple FS and to evaluate how far the FS evaluation guidelines published by AAP in 1996 and revised in 2011 are applicable to developing countries like India, where Hemophilus influenza type b (HIB) and streptococcus pneumoniae are the common organisms responsible for ABM and HIB and PCV vaccination status is very low.

PATIENTS AND METHODS

A consecutive 226 infants and young children of 3-18 months of age with first episode of apparent simple febrile seizures who presented to the pediatric emergency department (PED) within 24 hours of seizures were included in the present study. Children less than 3 months or more than 18 months of age and children with past history of febrile seizures or disorders of central nervous system and those with prior antibiotic use or presented with complex febrile seizures were excluded from the study. This prospective study was conducted over a period of one year from October 2016 to September 2017 in a tertiary care teaching hospital in South India. 226 children were divided in to two age groups: 3 to less than 12 months and 12 to 18 months of age. In these children, a complete history was taken upon hospitalization, and then a physical examination was performed by the duty resident in charge giving special attention to following factors: age, gender, duration of seizure, postictal drowsiness, lethargy, irritability, vomiting, bulging fontanel, nuchal rigidity, Kernig sign, Brudzinski sign, and neurological deficit. LP was performed in all cases. The data was documented in a proforma and transferred to EXCEL software. In collaboration with Biochemistry, Pathology and Microbiology departments, laboratory tests including CBC, x-ray chest, electrolytes, urinalysis, urine culture, blood culture, and lumbar puncture were done. Also CSF tests for sugar, protein, WBC, and CSF culture were carried out in all patients. The child was considered as a case of meningitis if: WBC >5 cells/cu mm, sugar level < 2/3 rds of blood glucose, protein >40mg/dL and or positive CSF and blood culture. Children with apparent FSFS with meningitis (n=24) served as cases and those with

no meningitis (n=202) served as controls. Statistical analysis of various clinical and etiological factors was carried out by Chi-square test and P-value of less than 0.05 was considered significant. Ethical clearance was obtained from Institutional Ethical Committee. No source of funding and no conflict of interest involved in the study.

RESULTS

During the study period a total of 6982 children were admitted in the wards of Pediatric Department of this institution. Of these 3520 children presented to the PED. Among them apparent FSFS cases were 248. After applying exclusion criteria 226 cases remained in the study. Of these 103 were 3 to <12 months age and 123 were 12-18 months of age. Male to female ratio in each group was 1.4:1 and 1.5:1 respectively and there is no statistically significant disparity between the two groups. (P value = 0.8674) (Table-1) Out of 226 infants and children with apparent FSFS 24 turned out as meningitis (Cases) and 202 as non meningitis (Controls). Among the meningitis cases (from now on called as cases) 13 (54%) were between 3-12 months and 11 (46%) between 12-18 months of age. In the control group 90 (46%) were in 3 to <12 months age and 112 (54%) in 12-18 months age. The difference between the two groups was not significant statistically. (P Value = 0.37130). Gender wise distribution among cases and controls was 14 (58%) males/10 (42%) females and 119 (59%) males/83 (41%) females respectively. Difference is again not significant statistically. (P Value = 0.9566). Meningitis was the cause of fever among cases while respiratory tract infections (59%), gastroenteritis (17%) and urinary tract infections (5%) were leading causes of fever among controls (Table-2 & 3).

Among cases 11 (46%) had meningeal signs and 13 (54%) had no meningeal signs. Comparatively 24 controls (12%) had meningeal signs without meningitis and 178 (88%) had no meningeal signs. The difference was highly significant. (P = Value 0.0000) In 3 to <12 months of age 13 cases had meningitis but only 5 (38%) presented with meningeal signs and 8 (62%) had no meningeal signs. Among children of 12 to 18 months of age, meningitis was noticed in 11 children and of these 6 (55%) presented with meningeal signs and 5 (45%) had no meningeal signs. The difference between the two groups was not significant statistically. (P Value = 0.4307) Amid 3 to <12 months age group controls 90 children had FSFS without meningitis, but meningeal signs were present in 9 (10%) cases and in the remaining 81 (90%) children had no meningeal signs. Similarly among 12 to 18 months age group 112 children with FSFS without meningitis, 15 (13%) children presented with meningeal signs and 97 (87%) presented with no meningeal signs. The difference between the two groups was not significant statistically. (P-Value = 0.4588) (Table-3).

Table-1: Incidence of meningitis

| | |
|---------------------------------|-----------|
| Study period | 12 months |
| Total pediatric admission (TPA) | 6982 |
| Children presented in PED | 3520 |
| Apparent FSFS cases | 226 |
| Meningitis cases | 24 |
| Acute bacterial meningitis | 18 |
| Viral meningitis | 5 |
| Tuberculous meningitis | 1 |
| Incidence of meningitis | 10.6% |
| Incidence of ABM | 7.9% |

Table-2: Causes of fever in first apparent FSFS

| Etiology | Number (%) |
|-----------------------------------|------------|
| Upper respiratory tract infection | 85 (37.6%) |
| Lower respiratory tract infection | 48 (21.2%) |
| Gastroenteritis | 38 (16.8%) |
| Acute bacterial meningitis | 18 (7.9%) |
| Urinary tract infection | 12 (5.3 %) |
| Acute otitis media | 05 (2.2%) |
| Viral meningitis | 05 (2.2%) |
| Malaria | 04 (1.7%) |
| Dengue | 04 (1.7%) |
| Tubercular meningitis | 01 (0.4%) |
| Non specific without focus | 06 (2.6%) |

CSF analysis of all 226 children with apparent FSFS confirmed 24 cases of meningitis. 13 (54%) were among 3 to <12 months and 11 (46%) among 12 to 18 months age group. LP findings of 3 to <12 months infants with meningitis (N=13) revealed ABM in 10 (77%) cases, viral meningitis in 3 (23%) cases. In 12-18 months children with meningitis (N=11) LP confirmed ABM in 8 (73%), viral meningitis in 2 (18%) and tubercular meningitis in 1 ((9%) cases. All the cases of meningitis (N=24) were subjected to CSF and blood culture. 18 (75%) were CSF culture positive, where as 7 (29%) were blood culture positive and both CSF and blood cultures were positive in 4(17%). ABM was observed in 10 (77%) cases among 3 to < 12 months and 8 (78%) cases in 12 to 18 months age group. (P-value=0.4137) The organisms isolated from CSF among 3 to <12 months (N=10) age group were like this: *Hemophilus influenza type b* 4(40%), *Streptococcus pneumonia* 2 (20%), *Escherichia coli (E.coli)* 2 (20%), *Beta-hemolytic streptococci* 1 (10%), *Coagulase negative Staphylococci (CNS)* 1 (10%). Comparatively the organisms isolated among 12-18 months (N=8) were: *Hemophilus influenza type b* 2 (25%), *Streptococcus pneumonia* 3 (37.5%), *E.coli* 1 (12.5%), *Beta-hemolytic streptococci* 1 (12.5%), *CNS* 1 (12.5%). Overall immunization coverage of HIB/PCV was 64 (28.3%) and 11 (4.9%). Immunization coverage of HIB/PCV among 3 to <12 and 12 to 18 months age groups was 38 (36.8%) / 3 (2.9%) and 26 (21.1%) / 8 (6.5%) respectively. The difference was statistically significant. (P-value=0.0481) (Table-3).

DISCUSSION

The AAP in its consensus statement 1998 strongly recommended performing LP in infants younger than 12 months of age who present with apparent FSFS because the clinical signs and symptoms associated with meningitis may be minimal or absent in this age group and to consider it in children 12 to 18 months because clinical signs and symptoms may be subtle. In the revised AAP guidelines 2011: 1) LP is made an option in infants less than 12 months of age i.e., recommended when child is not immunized against *Hemophilus influenza* and *Streptococcus pneumonia* vaccines and 2) in children more than 12 months LP is made an option left to the discretion of the clinician. These recommendations were based on the assumptions: 1) Wide spread immunization against *Hemophilus influenza* and *Streptococcus pneumonia* the 2 most common causative organisms of meningitis in USA 2) Physician can diagnose meningitis easily between 12 to 18 months of age and his clinical experience will help him in making right judgment.

The present study was conducted on infants and young children of 3 to 18 months of age attending the PED of a tertiary care teaching hospital. The research question prior to the study was: How far the febrile seizure evaluation and diagnostic guidelines published by AAP in 1996 and revised in 2011 are applicable to developing countries like India, where the immunization against *Hemophilus influenza* and *Streptococcus pneumonia* are not wide spread as the former is introduced recently in the routine

immunization schedule and the later is still an optional vaccine? The primary objective was to find out the incidence of ABM and to determine the role of CSF in differentiating meningitis from apparent FSFS and the secondary objective was to formulate evidence-based recommendations for healthcare professionals about the diagnosis and evaluation of a simple febrile seizure in infants and young children 3-18 months of age that suits better to developing and underdeveloped countries

Number of studies from developed countries were of the opinion that the risk of ABM presenting solely as apparent FSFS is very low, whatever age are features of seizure. Hence they felt, performing routine LP in the absence of meningeal signs is likely to be of low utility in febrile young children presented with first seizure. Equal number of studies from developing world reported higher incidence of ABM and significant number of children presenting with no meningeal signs

in spite of having meningitis, especially in the age group of 3-18 months (Table-4 & 5). In the present study incidence of apparent FSFS among total pediatric admissions (TPA) was 3.6% and among cases presented to PED it was 7%, whereas incidence of meningitis and ABM among apparent FSFS cases was 10.6% and 7.9% respectively. Overall incidence of meningitis was similar to Owusu-Ofori *et al.*, (10.2%) and Tinsa *et al.*, (10%) studies [13, 21] while other studies reported variable incidence (4.2% to 30.9%), [4, 5] ABM incidence of our study was in correlation with Joshi Batajoo *et al.*, (4.5%) and Heydarian *et al.*, (6.25%) studies [17, 18], while others showed variable incidence (0% to 10.2%) [19, 13]. The study population was divided into two different age groups: 3 to <12 months and 12-18 months, to know in which age group meningitis is presenting more often without meningeal signs and cases were compared with controls to study the influence of various parameters (Table-3).

Table-3: Parameters – Cases Vs Controls

| S. No | Parameter | | Cases (N=24) | Controls (N=202) | P-Value | |
|-------|------------------------------|---------------|---------------------------------------|---------------------------------------|---------|--------|
| 1 | Age | 3 – 12 Mo | 13 (54%) | 90 (46%) | 0.3713 | |
| | | 12 – 18 Mo | 11 (46%) | 112 (54%) | | |
| 2 | Gender | Male | 14 (58%) | 119 (59%) | 0.9566 | |
| | | Female | 10 (42%) | 83 (41%) | | |
| 3 | Etiology | Meningitis | 24 | 0 | 0.0000 | |
| | | Others | 0 | 202 | | |
| 4 | Meningeal signs (overall) | Present | 11 (46%) | 24 (12%) | 0.0000 | |
| | | Absent | 13 (54%) | 178 (88%) | | |
| 5 | Meningeal signs (age group) | Age Group | Present/Absent | Present/Absent | 0.4307 | |
| | | 3 – 12 Mo | 5 (38%) 8 (62%) | 9 ((10%) 81 (90%)) | | 0.4588 |
| | | 12 – 18 Mo | 6 (55%) 5(45%) | 15 (13%) 97 (87%) | | |
| 6 | CSF analysis (overall) | Positive | 24 (100%) | 0 (0%) | 0.0000 | |
| | | Negative | 0 (0%) | 202 (100%) | | |
| 7 | CSF analysis (age group) | 3 – 12 Mo | Positive/Negative 13 (100%) 0 (0%) | Positive/Negative 0 (0%) 90 (100%) | - | |
| | | 12 – 18 Mo | 11 (100%) 0(0%) | 0 (0%) 112 (100%) | | |
| 8 | Immunization overall HIB PCV | Immunized | 64 (28%) | - | 0.0000 | |
| | | Not immunized | 162 (72%) | - | | |
| | | Immunized | 11 (5%) | - | | |
| | | Not immunized | 215 (95%) | - | | |

Table-4: Incidence meningitis among FSFS cases

| S. No | Author | Age | FSFS | Meningitis |
|-------|----------------------------------|----------|------|------------|
| 1 | Akpede <i>et al.</i> , [4] | 1-6yrs | 522 | 4.2% |
| 2 | TavasoliA, <i>et al.</i> , [8] | 1mo-6yrs | 422 | 4.5% |
| 3 | Ghotbi,F,Shiva [9] | 6mo-5yrs | 254 | 4.7% |
| 4 | JaI krishin <i>et al.</i> , [10] | 6mo-5yrs | 125 | 4.8% |
| 5 | Laditan AA [11] | 6mo-6yrs | 95 | 6.3% |
| 6 | Rana MN [12] | 1-5yrs | 444 | 10% |
| 7 | Owusu-Ofori [13] | 1m-15yrs | 186 | 10.2% |
| 8 | Belbase RH [14] | 1-5Yrs | 157 | 10.9% |
| 9 | Mustafa Ciftci [15] | <12mon | 33 | 12.2% |
| 10 | Shrestha SK [16] | 5mo-5yrs | 110 | 14.5% |
| 11 | Joshi Batajoo [17] | 6mo-5yrs | 175 | 17% |
| 12 | Heydarian, <i>et al.</i> , [18] | 6-18mo | 453 | 17.6% |
| 12 | Imran Moosa [19] | 6mo-18m | 105 | 26.6% |
| 14 | Surya wanshi [5] | 6m0-6yrs | 55 | 30.9% |
| 15 | Present study | 3-18 mo | 226 | 10.6% |

Table-5: Incidence ABM among FSFS cases

| S. No | Study | Age | Sample | Meningitis | ABM |
|-------|---------------------------------|-------------|--------|------------|-------|
| 1 | Kimia [20] | 6 mo -18 mo | 271 | 3.8% | 0.0% |
| 2 | Imran Moosa [19] | 6 mo -18 mo | 105 | 26.6% | 0.0% |
| 3 | Tavasolia,et al [8] | 1 mo -6yrs | 422 | 4.5% | 1.7% |
| 4 | Ghotbi F Shiva [9] | 6mo - 5yrs | 254 | 4.7% | 1.9% |
| 5 | Mustafa Ciftci [15] | < 12mo | 33 | 12.2% | 3.0% |
| 6 | Joshi Batajoo [17] | 6 mo -5yrs | 175 | 17.0% | 4.5% |
| 7 | Heydarian, <i>et al.</i> , [18] | 6 mo -18mo | 453 | 17.6% | 6.3% |
| 8 | Tinsa <i>et al.</i> , [21] | < 12 mo | 106 | 10.0% | 10.0% |
| 9 | Owusu-Ofori [13] | 1mo-15yrs | 186 | 10.2% | 10.2% |
| 10 | Present Study | 3 mo -18 mo | 226 | 10.6% | 7.9% |

Out of 226 infants and children 24 turned out as meningitis (cases) and 202 as non meningitis (Controls). Among the cases 54% were in 3 to <12 months age and 46% in 12-18 months of age. In the control group 46% were in 3 to <12 months age and 54% in 12-18 months age. Gender wise distribution among cases and controls was 58% males/42% females and 59% males/41% females respectively. Age and gender wise cases and controls were matching. Respiratory tract infections, gastroenteritis and urinary tract infections were common causes of fever among control group. Shretha SK *et al.*, [16], Sangeeta *et al.*, [22] and Batra *et al.*, [23] reported similar findings as our study.

Among 3 to < 12 months of age a total of 13 cases had meningitis but only 38% presented with meningeal signs and 62% had no meningeal signs. Amidst children of 12 to 18 months of age, meningitis was noticed in 11 children and of these 55% presented with meningeal signs and 45% had no meningeal signs. By subjecting 226 children presenting with apparent FSFS to routine LP and analyzing CSF all 13 cases of 3 to <12 months and 11 cases of 12-18 months age group revealed positive results with raised leukocyte /neutrophil count (>5 cells /cu mm), decreased CSF glucose (<2/3 rds of blood sugar) and increased protein content (>40 mg/dl). Therefore CSF analysis detected meningitis in remaining 62% infants in 3 to <12 months and 45% in 12-18 months age group who could not be picked up by meningeal signs, showing the importance of LP in both age groups. Among 3 to <12 months age group controls 90 children had FSFS without meningitis, but meningeal signs were present in 10% cases and in the remaining 90% children had no meningeal signs. Similarly among 12 to 18 months age group 112 children with FSFS without meningitis 13% children presented with meningeal signs and 87% presented with no meningeal signs. This data shows the unreliability of meningeal signs in diagnosing meningitis. If cases for LP were selected based solely on meningeal signs many cases of meningitis could have been missed and cases with no meningitis could have been unnecessarily treated as meningitis. John C. Ratcliffe *et al.*, study on 325 children with meningitis

revealed that in 35% of cases meningeal signs can be lacking and absence of signs of meningeal irritation was more common in younger children, but was also seen in children even after 2 years of age [23]. Incidence of meningitis /ABM in 3 to <12 months was 12.6% /9.7% and in 12 to 18 months 8.9% /6.5% respectively. Incidence was almost similar in both age groups. Though meningeal signs were more commonly observed among 12-18 months children still 45% had no meningeal signs, supporting the role of routine LP in both the age groups.

Overall immunization coverage of HIB/PCV was 28.3% and 4.9%. Immunization coverage of HIB/PCV among 3 to <12 and 12 to 18 months age groups was 36.8% / 2.9% and 21.1%/6.5% respectively. The difference was statistically significant. Our data is in correlation with WHO immunization coverage report 2015. Though Hemophilus influenza type B and Streptococcus pneumonia were the common organisms of meningitis in these children other organisms like Escherichia coli, Beta-hemolytic streptococci and Coagulase negative staphylococci accounted for meningitis in 40% of cases in both the age groups which is not the case in developed countries like USA. Our findings are in correlation with those reported by Joshi Batajoo *et al.*, [17]

CONCLUSIONS

In conclusion it was found that bacterial meningitis is still a common presentation in the pediatric emergency department in children presenting with apparent FSFS. If cases for LP were selected based solely on meningeal signs around 60% of meningitis cases in 3 to <12 months infants and 40% of meningitis cases in 12-18 months children are unlikely to be picked up. We conclude that LP should be strongly recommended in infants of 3 to <12 months and should be considered in children of 12-18 months age group as incidence of ABM is high, immunization status is poor and ABM is caused by other organisms other than Hemophilus influenza type b and Streptococcus pneumonia. We recommend to follow 1996 AAP guidelines till HIB / PCV immunization coverage reaches more than 90% as is existing now in united

states based on which these guidelines were revised in 2011.

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