Exploring inflammatory status in febrile seizures associated with urinary tract infections: a Two-Step cluster approach

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Study conducted in the Pediatric Research and Telemedicine Center in Neurological Diseases- Pediatric Clinical Hospital Sibiu
Introduction

- Febrile Seizure (FS): = most common childhood neurological disorders; an important health problem with potential short and long-term complications [1]:
- International League Against Epilepsy (ILAE) definition of FS: seizures occurring in childhood after one month of age,
  1. Associated with a febrile illness not caused by an infection of the central nervous system,
  2. Without previous neonatal seizures or a previous unprovoked seizure,
  3. Not meeting criteria for other acute symptomatic seizures [2].
- There is a lack of studies regarding the association between febrile seizures and other bacterial etiologies, such as urinary tract infections (UTIs).
Objective:

- The goal of our study was to identify specific patterns of UTIs, using a combination of inflammatory biomarkers, in order to differentiate UTIs from other bacterial diseases associated with FS.
Materials and Methods

• This study was conducted at the Sibiu Pediatric Clinical Hospital, approved by the Ethics Committee of the hospital.
• 136 patients with a recent history (<24 hours) and 197 distinct febrile seizure events were studied.
• Aged between 1 month-5 years.
• Simple febrile seizures = generalized seizures, < 15 minutes and no recurrence within 24 hours.
• Complex febrile seizures = at least one criterion from the following: 1. focal appearance, 2. > 15 minutes and 3. multiple seizures within 24 hours [1].
• The possible predictors for the UTIs status of febrile seizures children were considered:
  - Data on patient's general characteristics, seizures' pattern, infectious etiology, biological parameters (PDW, P-LCR, PCT, MPV, CRP and NLR).
• Analysis was conducted using SPSS v.20 (SPSS Inc, Chicago, IL, USA). Statistical difference was considered for p<0.05.
Results (1)

- 136 children, mean age (23.23 ± 12.43 months)
- Balanced gender distribution (50.8% boys).
- There were 197 distinct seizures events:
  - 156 (79.2%) with a simple febrile seizures
  - 41 (20.8%) with a complex pattern.
  - 58.3% febrile seizures events preceded by temperatures > 39 °C
  - Seizure duration between 1-5 minutes and.
  - Only in a small number of cases (4.1%) a higher than 72 hours time interval from fever occurrence to seizure onset.
  - Complex febrile seizures distribution:
    - UTIs children (35%)
    - non-UTIs children:
      a) gastroenteritis subgroup (25%),
      b) acute upper respiratory tract infections (URTIs) subgroup (21.43%),
      c) acute lower respiratory tract infections (LRTIs) group (19.01%)
Results (2)

• No significant statistical differences between UTIs and non-UTIs groups in clinical, demographical and laboratory predictors except for the higher levels of CRP values in UTIs group p<0.05

• Two Step Cluster analysis for the whole cohort of patients- using as segmentation variables the inflammatory biomarkers: CRP, neutrophil to lymphocyte ratio (NLR), plachetocrit (PCT), platelet large cell ratio (P-LCR), platelet distribution of the population (PDW), mean platelet volume (MPV), platelet counts (PLT).

• The clustering method identified four distinct groups of patients
**Results**

Cluster 1 and Cluster 2 - URTIs (viral or bacterial) and Gastroenteritis

Cluster 1: Lowest PDW, P-LCR, MPV values

Cluster 3 - URTIs + LRTIs (bacterial)

Female gender predominance

The maximum age group incidence is between 13-24 months

Most patients moderate febrile rise at seizure onset (between 38-39 C),

Most seizures lasted between 1 and 5 minutes,

21.43% of patients in cluster 3 have prolonged seizures (duration > 15 minutes).

Higher PDW, P-LCR, MPV, CRP and NLR inflammatory profile

Cluster 4 - UTIs (bacterial)

Male gender predominance

The maximum age group incidence is between 13-24 months

Most patients moderate febrile rise at seizure onset (between 38-39 C),

Most seizures lasted between 1 and 5 minutes,

14.29% of patients in cluster 4 have prolonged seizures (duration > 15 minutes).

UTIs were highly unlikely in the patients with significantly increased CRP values and normal values of platelet indices (PDW, PCT, P-LCR, PLT) in cluster 4

Simple febrile seizures 64.29% in both clusters (3,4) ≈ seizures recurrence 14.29% in the first 24 hours in both clusters.
Discussion and Conclusions

• UTIs prevalence of 10.7% and the predominance of enteric UTIs bacteria were in line with other studies reports [3-10].

• The analysis of individual clinical symptoms and inflammatory parameters provided limited knowledge on distinctive features for the UTIs in febrile seizure.

• The cluster analysis however identified four clusters with distinct inflammatory pattern in relation to the etiology of the infectious context.

• A distinctive inflammatory pattern have emerged: higher PDW, P-LCR, MPV, CRP and NLR inflammatory profile

• This pattern with higher CRP but with normal platelet indices associated mainly with bacterial lower respiratory infections and a highly unlikely UTIs bacterial etiology is suggesting the practical importance of the unsupervised machine learning in hastening the etiology diagnosis in children with febrile seizures.
Bibliography

1. International League against Epilepsy, Guidelines for epidemiologic studies on epilepsy, Commission on Epidemiology and prognosis, Epilepsia 1993, 34, 592–596.


