

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

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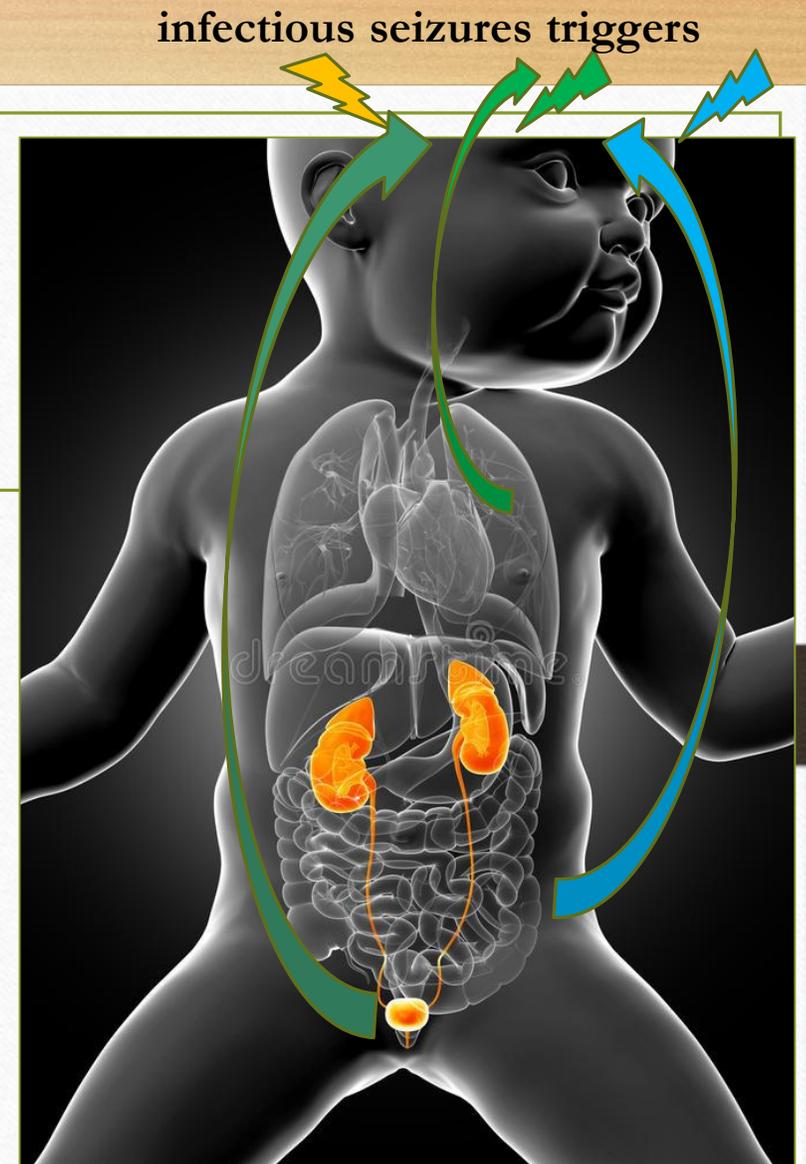
Study conducted in the Pediatric Research and Telemedicine Center in Neurological Diseases- Pediatric Clinical
Hospital Sibiu

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



Adapted from

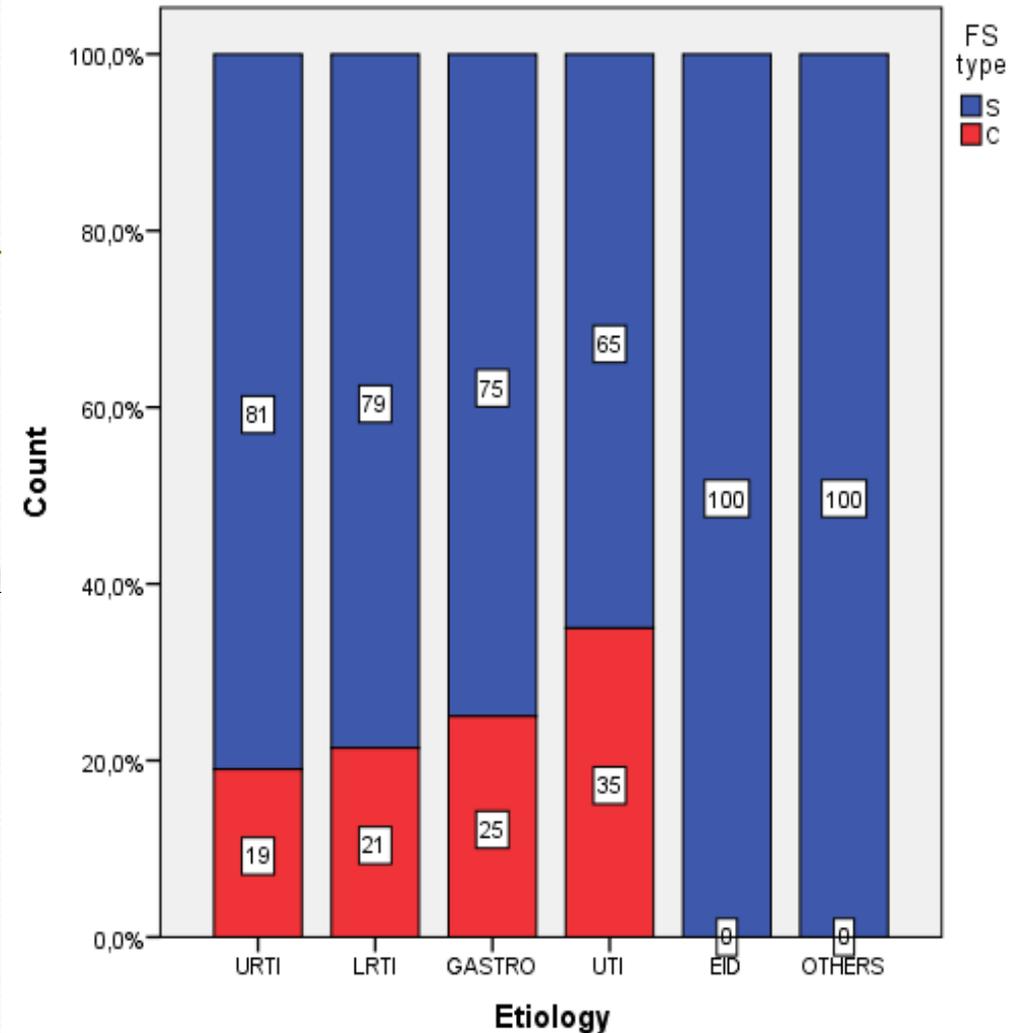
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Materials and Methods

- 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(3)

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

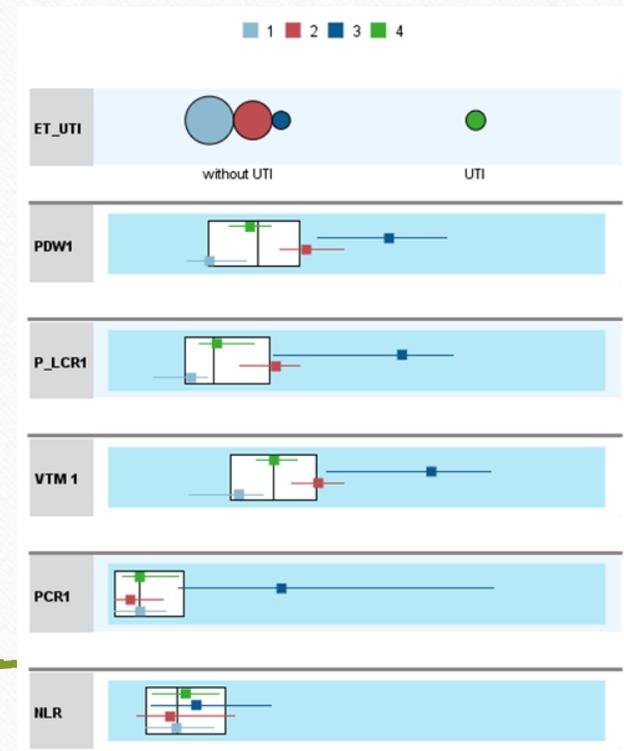
The maximum age group incidence is between 13-24 months

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 hasting the etiology diagnosis in children with febrile seizures.*

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