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FULLY VIRTUAL MEETING
September 02 (Thu) - 05 (Sun)

## Oral Communication Abstract
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**Oral Communications 3 Sep. 2 (Thu), 15:40-16:40**

# Acute pyelonephritis and urinary tract infections in pediatric patients: the diagnostic and prognostic role of High Mobility Group Box-1 (HMGB1)

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**Objectives:** Differentiation between urinary tract infection (UTI) and acute pyelonephritis (APN) is crucial for a prompt clinical management. High mobility group box-1 (HMGB1), belonging to the danger-/damage-associated molecular patterns (DAMPs) is produced in early phases by immune cells, amplifying the inflammatory process. We investigate whether HMGB1 could be a useful biomarker in discriminating children with UTI or APN, considering that, to date, not data are available.

**Methods:** 74 pediatric patients with suspected UTI/APN were enrolled. According to the positive or negative renal scintigraphy (DMSA) scan abnormalities, the studied cohort was divided into APN or UTI groups.

**Results:** APN group was characterized by higher serum (s) HMGB1 levels, when compared to UTI patients [13.3 (11.8 – 14.3) vs 5.9 (5.2 – 6.8) ng/ml; p= 0.02], whereas there were no differences between the two groups according to urine (u) HMGB1 values. HMGB1 directly correlated with C reactive Protein (CRP) (β = 0.47; P = 0.02).
ROC analyses were performed for identifying renal scars in APN group.
sHMGB1 area was significantly different than that of CRP (p: 0.01) and white blood cells (WBC) (p: 0.003). (Figure 1)
All children with APN underwent a second DMSA six months later.
To identify putative risk factors associated with renal scarring, we performed a Cox regression analysis inserting in the model all variables that were different at baseline in patients who had renal scars at DMSA evaluation after the follow-up period. After multivariate analyses, VUR (HR 4.81) and sHMGB1 (HR 1.16; p: 0.006) were independently associated with the development of renal scarring.

**Conclusions:** sHMGB1 could represent a useful marker to identify children with an increased risk of developing renal scarring, differentiating APN from UTI. (Figure 2)
Measurement of sHMGB1 could be useful in choosing children with UTI who may need early intervention, such as a precocious DMSA or long-term follow-up.

Figure 1

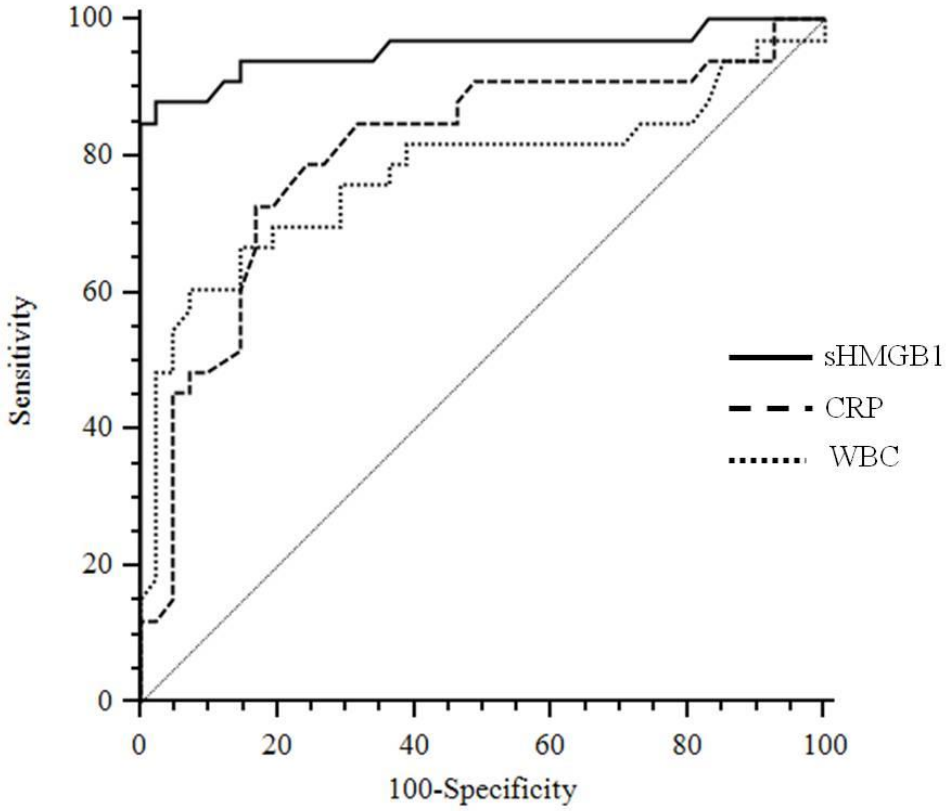
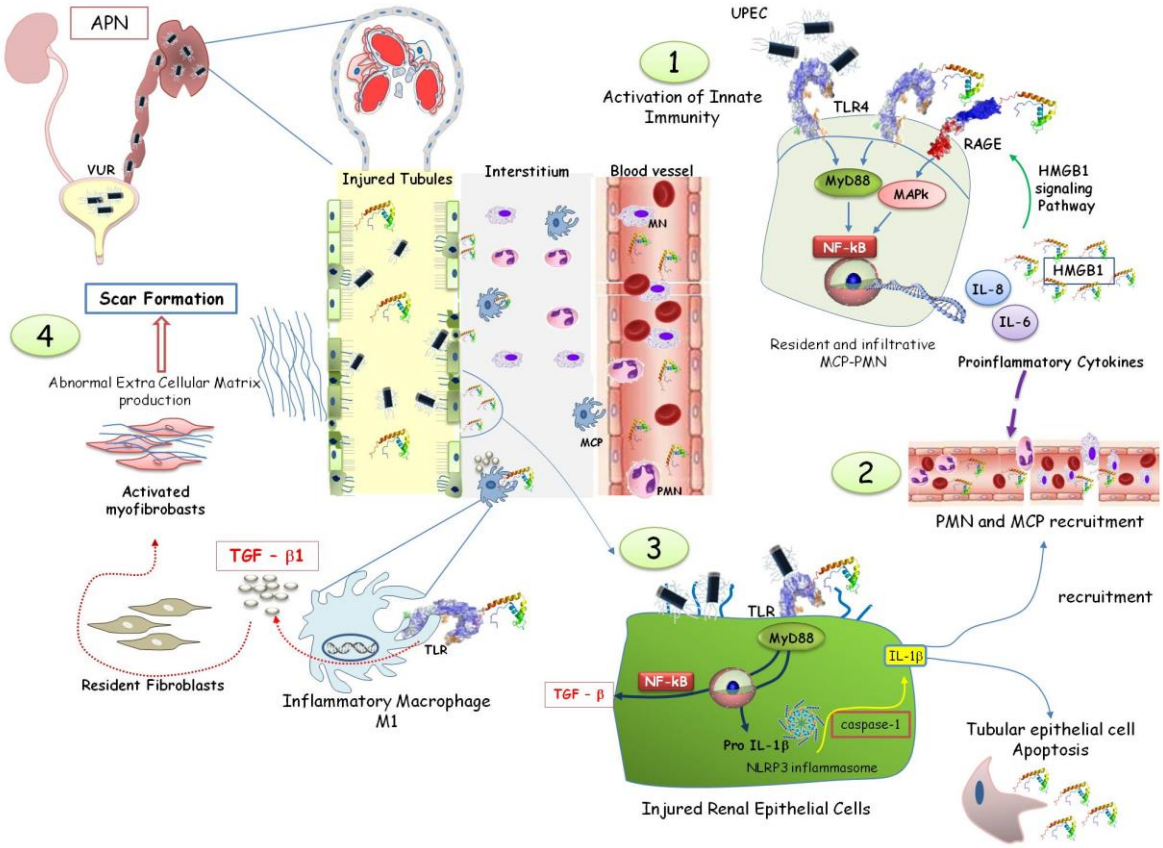


Figure 2


APN
VUR
Injured Tubules
Interstitium
Blood vessel
MN
MCP
PMN
UPEC
1
Activation of Innate Immunity
TLR4
RAGE
MyD88
MAPk
NF-kB
HMGB1 signaling Pathway
HMGB1
IL-8
IL-6
Resident and infiltrative MCP-PMN
Proinflammatory Cytokines
2
PMN and MCP recruitment
recruitment
Scar Formation
4
Abnormal Extra Cellular Matrix production
Activated myofibrobasts
TGF - β1
Resident Fibroblasts
TLR
Inflammatory Macrophage M1
3
TLR
MyD88
NF-kB
TGF - β
IL-1β
caspase-1
Pro IL-1β
NLRP3 inflammasome
Injured Renal Epithelial Cells
Tubular epithelial cell Apoptosis