TOLL-LIKE RECEPTORS EXPRESSION AND SWITCH FROM PROTEASOME TO IMMUNEPROTEASOME IN CHILDREN WITH HENOCH-SCHOENLEIN PURPURA AND PRIMARY IGA NEPHROPATHY.

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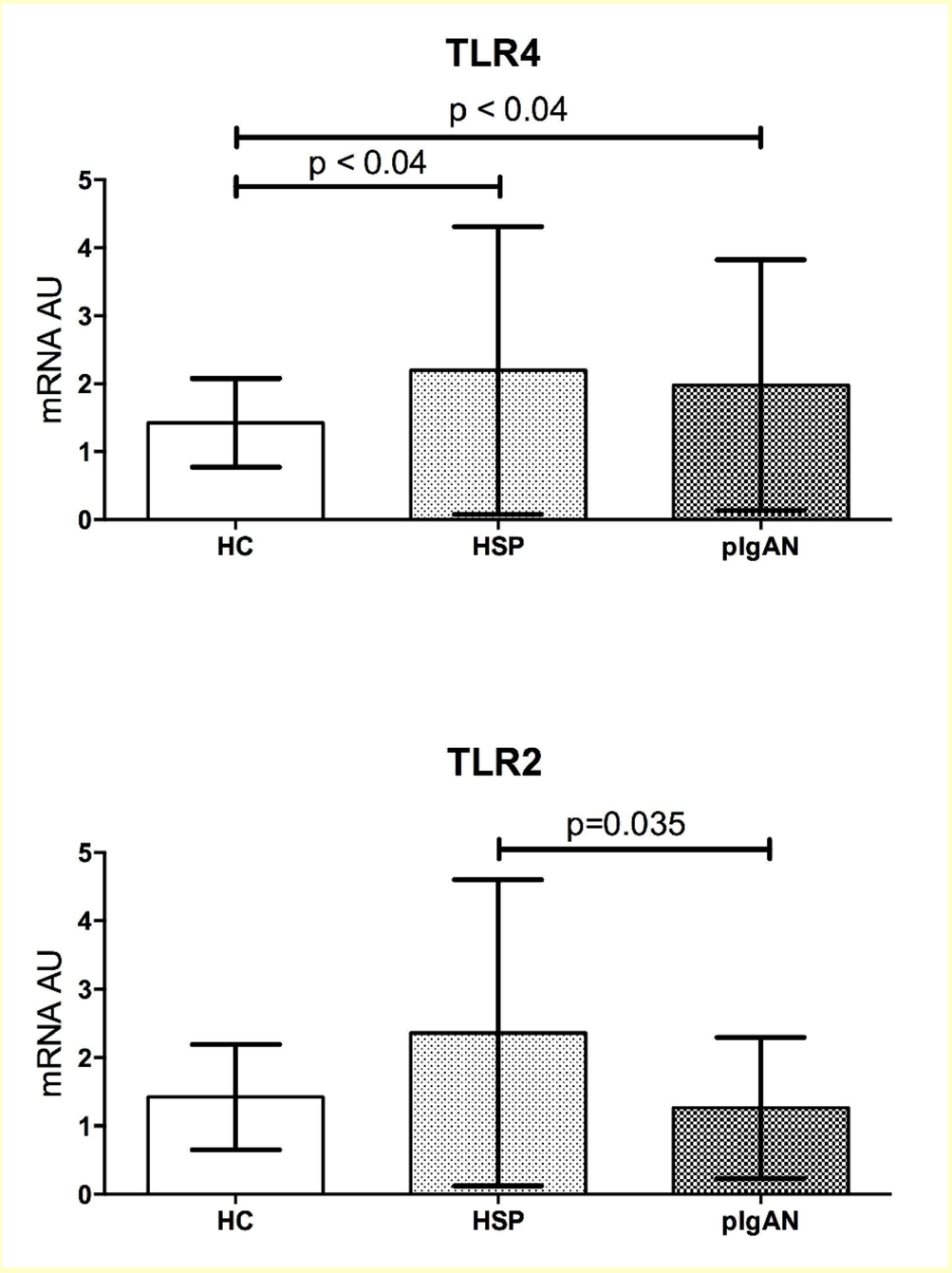
OBJECTIVES

Henoch Shoenlein Purpura (HSP) nephritis and primary IgA Nephropathy (pIgAN) present with glomerular IgA deposits, but differ for clinical features. The suspected involvement of different immune system pathways is largely unknown. Innate immunity is mostly activated through Toll-Like Receptors (TLR) ligation, which activates the interferons pathway, with dendritic cell maturation with switch of the proteasome (PS) to immuneproteasome (iPS), by substituting 3 catalytic units beta1, 2 and 5 with 3 new ones LMP2, LMP7 and MECL-1. This modification confers an optimal catalytic property for peptide presentation to MHC Class I, leading to T lymphocyte activation.

METHODS

This study was aimed at investigating TLR expression and PS/iPS switch in 63 children with HSP with/without renal involvement and in 25 pIgAN. Real time PRC (Taqman) was used to quantify mRNA levels in peripheral blood mononuclear cells (PBMC).



RESULTS

The expression of mRNAs encoding for TLR4 in both HSP and pIgAN was higher than in controls (HC) (HSP 2.20 ± 0.27; pIgAN 2.0 ± 0.39; both p<0.04 vs HC 1.42 ± 0.08), without significant difference between the two diseases. Conversely, a significant difference was found the expression of TLR2mRNA, higher in children with HSP than in those with pIgAN (HSP 2.36 ± 0.31; pIgAN 1.27 ± 0.23, p=0.035).A switch from PS to iPS was detected only in PBMC of HSP (LMP2/β1) (HSP 1.23 ± 0.66; HC 0.91 ± 0.42, p=0.008) and it was correlated with the increase in TLR2mRNA (p<0.01).

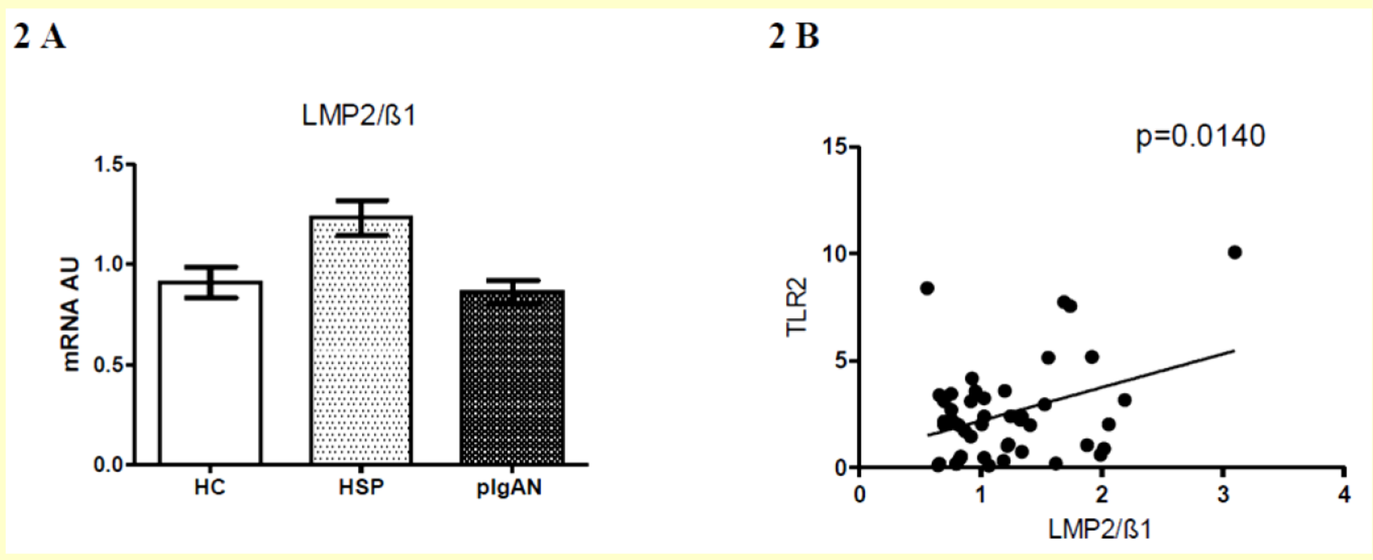


FIG.1. TLR4 mRNA and TLR2 mRNA expressions in PMBC of patients with Henoch-Shoenlein Purpura (HSP), primary IgA Nephropathy (pIgAN) and in healthy controls (HC).
Results are expressed as arbitrary units (AU)

Figure 2 A: The switch from proteasome (PS) to immunoproteasome (iPS) in PBMC of patients with Henoch-Shoenlein Sindrome (HSP), rimary IgA Nephropathy (pIgAN) and in healthy controls (HC).
Results are expressed as arbitrary units (AU).
Figure 2 B: correlation between TLR2 mRNA and LMP2/β1 mRNA values.

CONCLUSIONS

Children with HSP and pIgAN present with similar signs of engagement of TLR4 in PBMC.
The increased immuneproteasome switch, correlated with TLR2 activation may suggest an innate immunity pathway peculiar to HSP vasculitic presentation.

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