IgAN severity, including eGFR, hypertension and Oxford-T scores. In addition, ACR, but not PCR and 24h UPE, presented with positive association with Oxford-S scores. In univariate survival analysis, ACR, PCR, as well as 24h UPE were significantly associated with long term renal outcome. When comparing the performance of ACR, PCR and 24h UPE in predicting IgAN prognosis, ACR had consistently better performance than the other two measurements, as represented by higher AUC using time-dependent survival analysis. When adjusted for well known risk factors for IgAN progression, including eGFR, hypertension, histological lesions and therapy, only ACR was still significantly associated with poor renal outcome of IgAN (HR: 2.230 (1.452–3.424), \( P < 0.001 \)). On contrary, PCR and 24h UPE were not associated with long term renal outcome after adjusting.

**Conclusion:** In IgAN, ACR, PCR and 24h UPE had comparable association with severe clinical and histological findings. Compared to PCR and 24h UPE, ACR showed better performance in predicting IgAN progression.

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**Synthetic Double-stranded RNA Poly(I:C) Aggravates IgA Nephropathy by Triggering IgA Class Switching Recombination Through TLR3-BAFF Axis**


**Objective:** Immunoglobulin class-switch recombination (CSR) is crucial for the expression of IgA, and plays a vital role in the physiopathology of IgA nephropathy (IgAN). The aim of the study is to investigate the effect of poly(I:C) in modulating TLR3-BAFF axis activation in promoting IgA CSR of IgAN patients and IgAN rat model.

**Methods:** Blood samples and tonsillar tissue specimens were obtained from 24 patients with IgAN and 26 patients with chronic tonsillitis (CT) as control. We also used the IgAN rat model to investigate the relationship between viral infection and IgA CSR.

**Results:** Immunohistochemical and ELISA Western blotting examination revealed that TLR3/BAFF axis are activated in IgAN patients compared with controls. Synthetic double-stranded RNA Poly(I:C) stimulation up-regulated TACI/TLR3/TRIF/TRAF6 expression, promote IgA CSR and BAFF productions in tonsil-mononuclear cells. TLR3 or BAFF siRNA decreases IgA expression. In IgAN rat models, TLR3/BAFF signaling was highly activated. With 200 \( \mu \)g Poly(I:C) sodium salt into the left naris for 8 weeks, IgA was highly deposited on glomeruli. It also revealed that Poly(I:C) activated TLR3/BAFF axis and IgA CSR in vivo.

**Conclusion:** These data points towards the role of TLR3/BAFF axis in IgA CSR of IgAN, and the data also supports the notion that mucosal immunization with virus infection results in impaired mucosal and systemic IgA responses.