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Circulating CD89-IgA complex does not predict progression of IgA nephropathy

[1]Department of Internal Medicine, Yonsei University College of Medicine

Jong Hyun Jhee MD[1], Su-Young Jung MD[1], Seohyun Park MD[1], *Chang Hyun Lee, MD[1], Hyoungnae Kim MD[1], Hae Ryong Yun MD[1], Youn Kyung Kee MD[1], Chang-Yun Yoon MD[1], Young Eun Kwon MD[1], Hye-Young Kang MD[2], Jung Tak Park MD, PhD[1,2], Shin-Wook Kang MD, PhD[1,2], Tae-Hyun Yoo MD, PhD[1,2], and Seung Hyeok Han MD, PhD[1,2]

Background: Pathogenesis of IgA nephropathy is a complicated multi-step process involving generation of galactose-deficient IgA1 and autoantibodies against the misglycated IgA1, deposition of immune complex within the mesangiaum, and complement activation. CD89 is a soluble receptor for circulating IgA and CD89-IgA facilitates the formation of immune-complex. However,there is lack of evidence supporting circulating levels of CD89-IgA complex is associated with disease progression. This study aimed to delineate whether circulating CD89-IgA levels can predict the future renal outcome in patients with IgAN. **Methods:** A total of 344 patients with biopsy-proven IgAN between 2005 and 2014 were included. Demographic and laboratory data were recruited from the Glomerulonephritis Registry of Yonsei University Health System. Sera of these patients were obtained at the time of biopsy and stored at -80℃. Circulating CD89-IgA complex levels were determined by sandwich ELISA method. The study outcome was a 30% decrease of estimated GFR during the follow up. **Results:** The median value of CD89-IgA complex was 7.20 ng/ml[Inter quartile range 4.25 to 12.98]. Patients were categorized into 3 groups by tertiles of circulating CD89-IgA levels. There were no significant differences in baseline eGFR and proteinuria among 3 groups. In addition, circulating CD89-IgA complex levels were not correlated with eGFR at the time of biopsy and did not differ among CKD stages. During follow-up, 23 (34.3%), 25 (37.3%), and 19 (28.4%) patients in the lowest, middle, and highest tertiles reached the study endpoint, respectively ($p=0.59$). In a multivariable Cox models adjusted for age, sex, mean arterial pressure, IgA levels, eGFR, and proteinuria, circulating CD89-IgA complex levels were not associated with developing a 30% decrease in eGFR [Lowest versus Middle, Hazard ratio 0.95, 95% Confidential interval 0.44-2.07, $p=0.89$ and Lowest versus Highest, HR 1.14, 95% CI 0.49-2.61, $p=0.76$]. A receiver operating curve analysis showed that area under the curve for CD89-IgA was 0.55. **Conclusions:** Although CD89-IgA complex mediates formation of immune complex, our findings suggest that its circulating level is not a predictor of adverse renal outcome in IgAN

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Mesangial IgA Deposits Associated Development of Long term Adverse Outcomes in Adult IgA Nephropathy

Department of Internal Medicine, Eulji General Hospital, Seoul, Korea

*Ki young LEE, Sung Woo LEE

Background: Immunoglobulin A (IgA)-containing immune complexes have a pivotal role for the pathogenesis of IgA nephropathy (IgAN). However, there are no studies that explored the association between the degree of IgA-containing immune complexes seen in immunofluorescence (IF) staining and clinical outcomes. **Methods:** We retrospectively analyzed 340 patients diagnosed with primary IgAN at a tertiary care hospital between 2003 and 2013. The intensity of mesangial IgA deposits were assessed by classic direct IF technique. The primary outcome was composite of creatinine doubling, end-stage renal disease, and all-cause mortality. **Results:** During a median 4.8 years` follow-up, the composite outcome occurred in 16.2% of patients. The intensity of mesangial IgA deposits was 1+ in 3.2%, 2+ in 25.3%, and ≥ 3+ in 71.5% of patients. The intensity of mesangial IgA deposits was inversely associated with the development of the composite outcome (P-trend = 0.004). This was confirmed in multivariate Cox proportional hazard regression (P-trend = 0.018), mostly affected by the association between 1+ vs. ≥ 3+ [hazard ratio (95% confidence interval), 0.230 (0.068 - 0.775); $p=0.018$]. In subgroup analysis by the status of immunosuppressive drug (ISD) use, the inverse association between the intensity of mesangial IgA deposits and the development of the composite outcome was valid only in patients not using an ISD. **Conclusions:** The risk for the development of the composite outcome decreased as the intensity of mesangial IgA deposits increased. Future studies are needed to confirm our results.