DIAGNOSTIC VALUE OF PHOSPHOLIPASE A2 RECEPTOR, IGG4, ALDOSE REDUCTASE AND SUPEROXIDE DISMUTASE IN DETERMINATION OF PRIMARY VERSUS SECONDARY MEMBRANOUS GLOMERULONEPHRITIS.

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Background

Membranous glomerulonephritis (MGN) is the most common cause of t he nephrotic syndrome in adults. Most cases of MGN are primary but s econdary cause of MGN are frequently encountered. Determination of secondary MGN is crucial to initiate appropriate treatment. We investig ated the diagnostic yield of 4 putative markers of primary MGN such as phospholipase A2 receptor (PLA2R), IgG4, aldose reductase (AR), and superoxide dismutase (SOD). We compared immunohistochemical (IH C) expressions of four markers between primary and secondary MGN a nd analyzed those expressions with clinicopathologic parameters.

Materials and Methods

We enrolled 119 patients who were diagnosed as primary MGN in 59 pati ents and secondary MGN in 64 patients. We analyzed clinical characterist ics of the patients and performed immunohistochemical stainings for PLA 2R, IgG4, AR, and SOD. We performed the immunofluorescent (IF) staini ngs for AR and SOD on the frozen sections of the 4 primary and 4 second ary MGN cases.

Results

The immunohistochemical stainigs of PLA2R, IgG4, and AR expressions were dominantly positive in primary MGN ($p<0.05$, all of three). However, the SOD expression did not differ between primary and secondary MGN ($p=0.686$). The sensitivity and specificity of each marker for detection of pri mary MGN were 81% and 86% for PLA2R, 76% and 87% for IgG4, and 7 2% and 60% for AR. There was no correlation between PLA2R, IgG4, AR, and SOD expressions and clinicopathologic parameters of primary MGN.

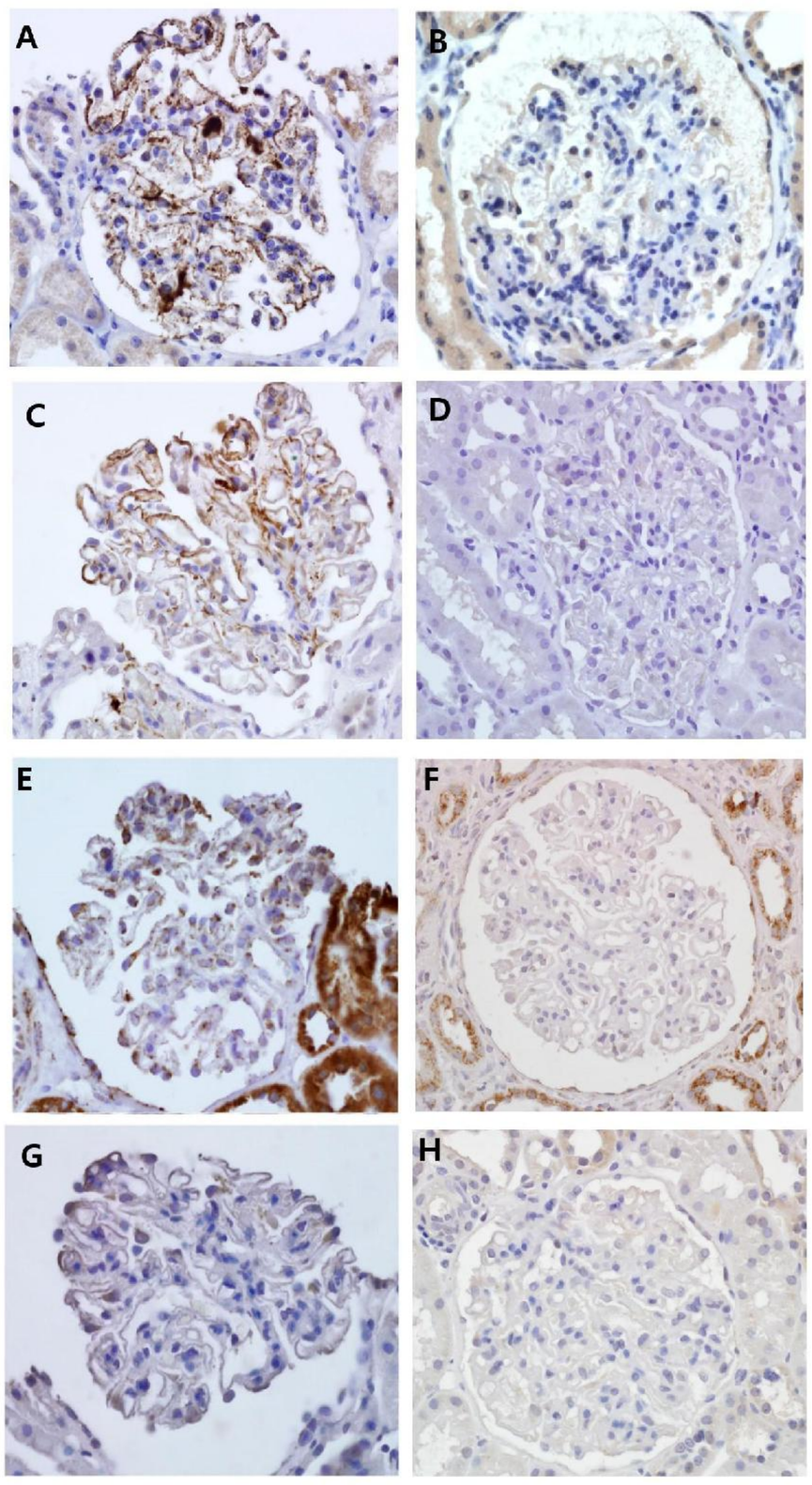

Fig 1. A. The IHC stains for PLA2R showed diffuse and strong granular staining along the glomerular capillary loops and visceral epithelial cells of primary MGN cases. C. IgG4 showed diffuse and strong granular staining along the glomerular capillary loops of primary MGN cases. E & G. SOD and AR showed diffuse and weak granular staining along the glomerular capillary loops of primary MGN cases. B, D, F, H. The PLA2R, IgG4, SOD, and AR were negative for secondary MGN cases.

Both SOD and AR was all positive in 4 primary MGN cases. Three were negative and one was weak expression of SOD and one was negative and two were weak expression of AR in secondary MGN cases.

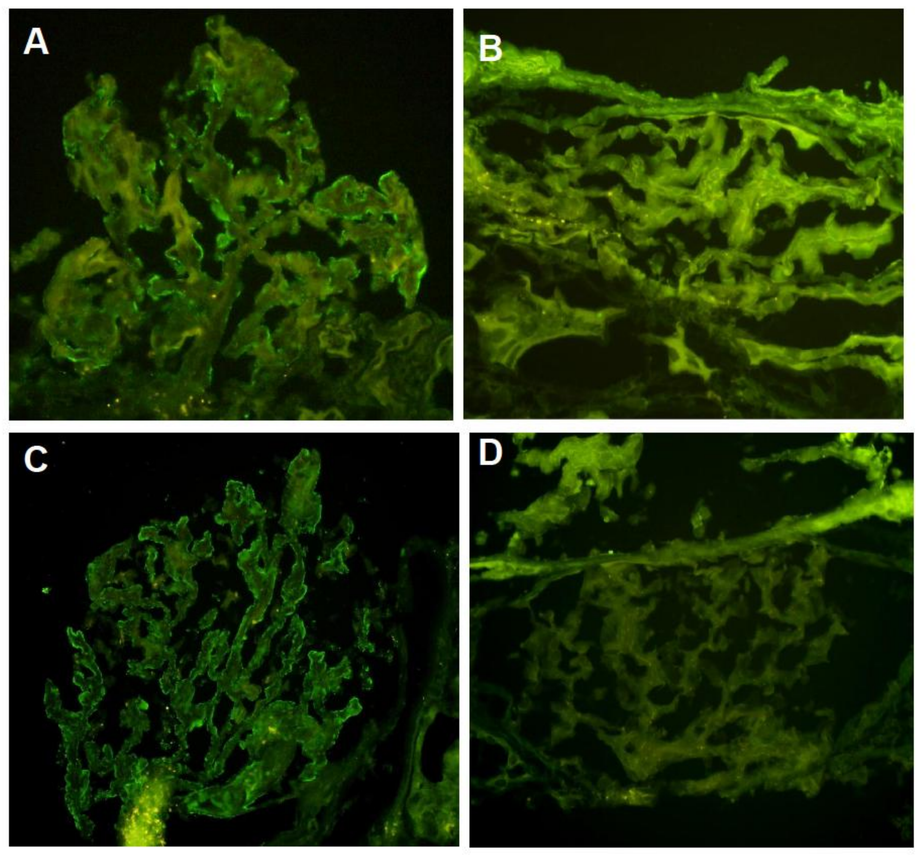

Fig 2. A. The IF stains for SOD showed diffuse granular staining along the glomerular capillary loops C. The AR showed diffuse granular staining along the glomerular capillary loops of the primary MGN. B, D. The SOD and AR were negative for secondary MGN.

Six studies including our study were included in the meta-analysis of specificity and sensitivity of the PLA2R. The mean sensitivity of PLA2R was 79% (95% CI= 75% -83%, $I^{2=}$85.0%) and ours was 81%. B. The mean specificity of PLA2R was 86% (95% CI =80% -91%), $I^{2=}$22.9%) and ours was 86%. C. Eight studies were included in the meta-analysis of specificity and sensitivity of the IgG4. The mean sensitivity of IgG4 was 83% (95% CI= 79% -87%, $I^{2=}$77.9%) and ours was 76%. D. The mean specificity of IgG4 was 68% (95% CI =61% -75%), $I^{2=}$73.9%) and ours was 87%.

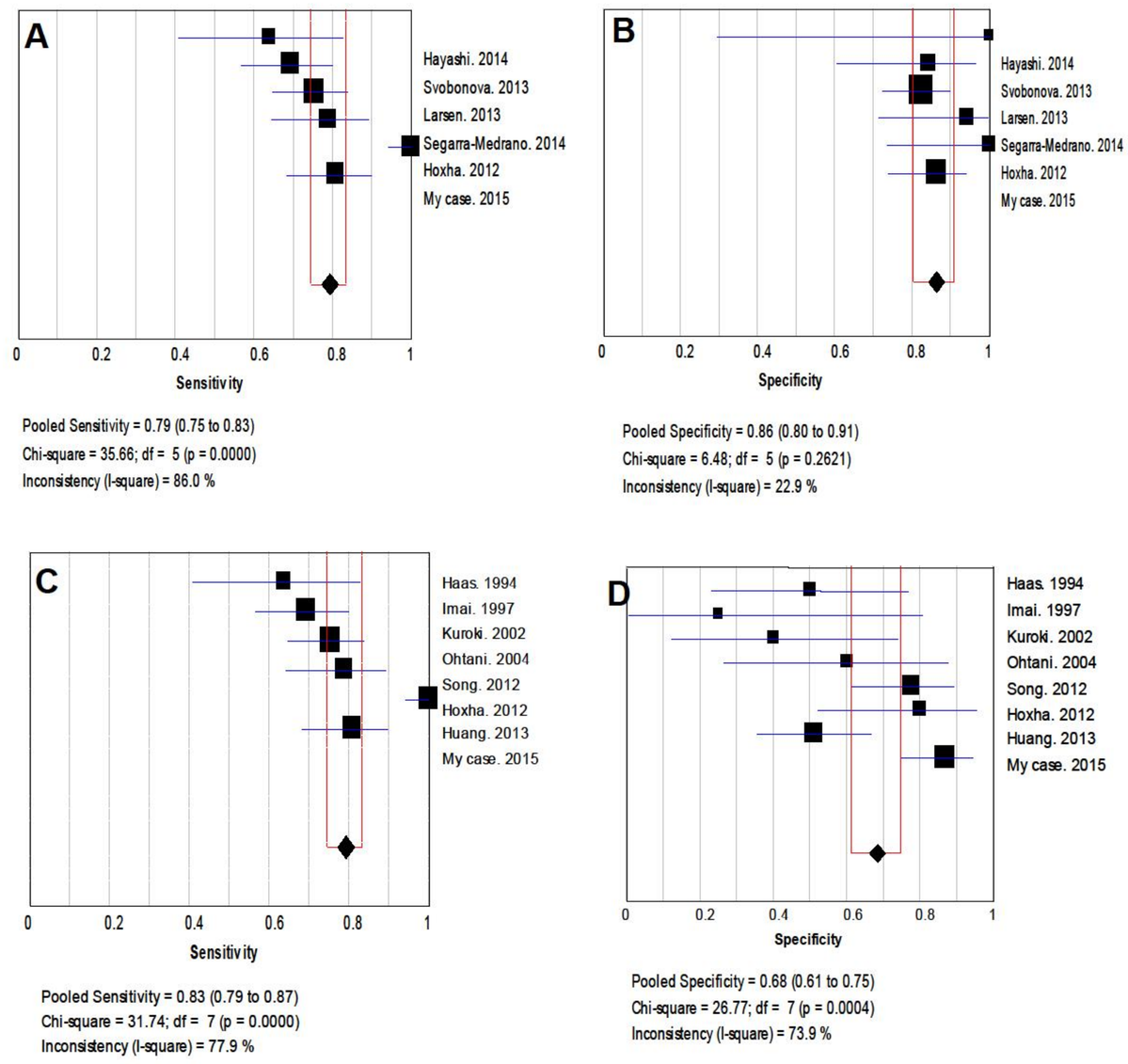

Fig 3. Forest plots of the sensitivity and specificity of PLA2R and IgG4 expressions on the renal biopsy specimens. A. The mean sensitivity of PLA2R B. The mean specificity of PLA2R . C. The mean sensitivity of IgG4 D. The mean specificity of IgG4

Conclusion

It could be considered that immunohistochemical staining of both PLA2R and IgG4 could be useful in differentiating primary MGN from secondary MGN with high sensitivity and specificity.

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