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A Pilot Study Exploring The Role Of Urinary Soluble CD163 As A Novel Biomarker In IgA Nephropathy

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Objectives : IgA nephropathy (IgAN) is the most common primary glomerulonephritis and a major cause of kidney failure. CD163 is produced by macrophages, with increased concentrations in acute inflammation. Elevated urinary (u-)CD163 may imply glomerular macrophage infiltration in active glomerulonephritis. We hypothesize that uCD163 can distinguish IgAN as a useful non-invasive biomarker compared to other nephropathies.
Methods : We conducted a single centre retrolective study and compared uCD163 levels in historical and prospective participants with IgAN, with corresponding levels in patients with quiescent lupus nephritis (LN), diabetic nephropathy (DN), and healthy controls (HC). Prospective IgAN patients were recruited from May 2023 to June 2024 and urine tested within 6 months of biopsy. uCD163 was measured using ELISA. We performed univariate, multivariate, discriminant ROC analysis; and calculated Youden's index to determine the cut-off of uCD163 for optimal classification of IgAN versus other nephropathies.
Results : We studied 90 patients, including 16 IgAN, 7 LN, 23 DN, and 44 HC. There were no significant demographic differences between patients with IgAN versus those with other nephropathies or HC; both groups had comparable eGFR (p=0.148) and proteinuria (p=0.056) at the point of uCD163 measurement. Median uCD163 was 0.367 (0.351-0.544) in IgAN and 0.345 (0.240-0.378) in LN, DN, or HC (p=0.015); uCD163 remained significantly higher in IgAN versus other nephropathies or HC when adjusted for urine protein creatinine ratio (p=0.010). uCD163 had an AUC of 0.695 (95% confidence interval: 0.555-0.835), with an optimal cut-off of 0.356 ng/mL that had a 75% sensitivity and 62% specificity for distinguishing IgAN versus other nephropathies or HC, including a negative predictive value of 92%.
Conclusions : Elevated uCD163 levels may be useful in distinguishing patients with IgAN from those with quiescent glomerulonephritis vs non-immune nephropathies.

Univariate and Multivariate Analysis Table.jpg

Table 1: Univariate analysis of baseline demographic parameters and kidney function between patients with IgAN (Group 1) and other nephropathies and controls (Group 2)

	Group 1 (n=16)	Group 2 (n=74)	p-value
Age, n (%) < 50 years ≥ 50 years	 11 (68.8) 5 (31.3)	 39 (52.7) 35 (47.3)	0.241
Gender, n (%) Male Female	 7 (43.8) 9 (56.3)	 43 (58.1) 31 (41.9)	0.295
Ethnicity, n (%) Chinese Malay Indian Others	 7 (43.8) 4 (25.0) 1 (6.3) 4 (25.0)	 37 (50.0) 15 (20.3) 15 (20.3) 7 (9.5)	0.436
eGFR, ml/min/1.73m² (Median, IQR)	73.8 (37.9-96.0)	96.4 (44.8-111.8)	0.148
Mean BP, mmHg (Median, IQR)	86.3 (79.2-91.0)	85.0 (78.2-93.3)	0.726
Urine Protein: Creatinine Ratio, mg/mmol (Median, IQR)	111.0 (26.7-375.5)	14.6 (8.1-286.8)	0.056
Urinary sCD163 (ng/ml)	0.367 (0.351-0.544)	0.345 (0.240-0.378)	**0.015**
Etiology, n (%) IgA Lupus Diabetic Controls	 16 (100.0) 0 (0.0) 0 (0.0) 0 (0.0)	 0 (0.0) 7 (9.5) 23 (31.1) 44 (59.5)	**<0.001**

Table 2: Multivariate analysis of predictive variables deemed potentially significant (p<0.10) in the univariate analysis between Group 1 and Group 2

Variable	IgA	Others	OR (95% CI)	p-value
Urine Protein: Creatinine Ratio mg/mmol (Median, IQR)	111.0 (26.7-375.5)	14.6 (8.1-286.8)	1.001 (1.000-1.002)	0.198
CD163, ng/ml, (median, IQR)	0.367 (0.351-0.544)	0.345 (0.240-0.378)	0.002 (0.000-0.218)	**0.010**

Univariate and Multivariate Analysis Table.jpg

Figure 1: Receiver-operating characteristics (ROC) curve of uCD163 in distinguishing between IgAN and Group 2 cohort (AUC 0.695, 95% CI: 0.555-0.835)