Increase in Serum Galactose-Deficient IgA1 Level Measured by New Lectin-ELISA Predicts Progression to Kidney Failure in Adults with IgA Nephropathy

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INTRODUCTION

IgA nephropathy (IgAN) is the most common primary glomerular kidney disease in many countries and a leading cause of kidney failure. Its autoimmune pathogenesis begins with circulating galactose-deficient IgA1 (Gd-IgA1) — the initiating autoantigen — which is recognized by IgG autoantibodies, forming immune complexes that deposit in the glomerular mesangium and drive progressive kidney injury.

Prior lectin-based enzyme-linked immunosorbent assays (ELISAs) were limited by batch-to-batch variability and inconsistent reagent specificity, preventing cross-study comparison. The **GaID™ Assay** addresses this with standardized reagents and calibrated reference standards for reproducible measurements.

AIM

To assess whether percent change in serum Gd-IgA1 level, measured by the standardized **GaID™ Assay**, independently predicts progression to kidney failure in adults with biopsy-confirmed IgAN.

METHODS

Serum Gd-IgA1 level was measured using the **GaID™ Assay** in paired samples from **251 adults with biopsy-confirmed IgAN in CureGN**, a NIH-funded multicenter longitudinal observational cohort.

Paired samples had been collected nearest to the kidney biopsy date and ~1-year later (**median interval: 13 months**); **median follow-up, 7.4 years**.

Kidney failure was defined as chronic dialysis, transplantation, or two consecutive estimated glomerular filtration rate (eGFR) measurements <15 mL/min/1.73 m² ≥30 days apart (21% event rate).

Cox proportional hazards modeling assessed percent change in Gd-IgA1 as an independent predictor, adjusted for age, eGFR, urinary protein/creatinine ratio (UPCR), race, renin-angiotensin-aldosterone-system (RAAS) inhibitor use, and immunosuppressant use.

RESULTS

Baseline Patient Characteristics

Characteristic	Total (N = 251)
Demographics	
Age at first sample, years, Median (IQR)	42 (31, 55)
Male sex, n (%)	138 (55%)
Race, n (%)	
White / Caucasian	188 (75%)
Asian	36 (14%)
Black / African American	8 (3%)
Other / Unknown	16 (7%)
Hispanic ethnicity, n (%)	42 (17%)
Disease Characteristics at First Sample	
eGFR, mL/min/1.73 m², Median (IQR)	59 (42, 86)
UPCR, g/g, Median (IQR)	0.9 (0.2, 1.7)
Hypertension, n (%)	144 (57%)
Hematuria ≥1+, n (%)[1]	124 / 184 (67%)
Treatment at First Sample	
RAAS inhibitor, n (%)	201 (80%)
Immunosuppression, n (%)	74 (29%)
Study Timeline	
Time from biopsy to first sample, months, Median (IQR)	16 (5, 37)
Interval between paired samples, months, Median (IQR)	13 (11, 15)
Follow-up from second sample, years, Median (IQR)	7.4 (5.4, 8.4)
Outcome	
Kidney Failure events, n (%)	53 (21%)

[1] Hematuria data were unavailable for 67 participants (27%); percentage calculated from 184 with evaluable dipstick result.
IQR = interquartile range; Kidney failure = chronic dialysis, kidney transplantation, or two consecutive eGFRs <15 mL/min/1.73 m² ≥30 days apart.

BIDIRECTIONAL RISK · KIDNEY FAILURE

10% Rise in GaID™ (Gd-IgA1) *Serum level increases* ↑ **+11.7% Higher Risk** of kidney failure

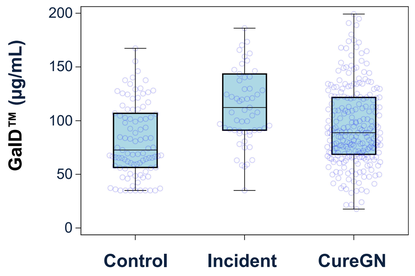
10% Fall in GaID™ (Gd-IgA1) *Serum level decreases* ↓ **−10.5% Lower Risk** of kidney failure

HR 1.011 per 1% rise [95% CI 1.002–1.021, p = 0.016]
Cox proportional hazards · Independent predictor

GaID™ Assay Values and Primary Outcomes

GaID™ Assay — Serum Gd-IgA1 Values (N = 251)	Median (IQR)
Absolute Serum Gd-IgA1 (µg/mL)	
First sample	88.8 (68.6, 121.6)
Second sample	90.1 (69.3, 119.0)
Change Between Paired Samples	
Absolute change, µg/mL	1.9 (−11.4, 11.5)
Percent change, %	2.2 (−13.4, 11.9)
Primary Result — Adjusted Cox Model	
Hazard ratio per 1% rise in Gd-IgA1 [95% CI]	1.011 [1.002, 1.021]
p-value	0.016
Covariates adjusted	Age, eGFR, UPCR, race, RAAS inhibitor, immunosuppression

Distribution Analysis: Control | Incident | CureGN



Distribution Analysis Data: Percentile values for Box and Whisker Plots						
Cohort	N	5%	25%	50%	75%	95%
Control	97	35.00	56.40	72.70	106.90	140.20
Incident	61	59.20	91.10	112.30	143.50	261.20
CureGN	251	41.58	68.59	88.79	121.58	172.89

Box and Whisker plots comparing distributions of serum Gd-IgA1 levels measured by **GaID™ Assay** of the initial measurement for the 251 CureGN IgAN patients in this study, with prior measurements sera from 97 healthy controls and incident samples from 61 patients with IgAN.

CONCLUSIONS

Percent change in serum Gd-IgA1 level, measured by the **GaID™ Assay**, was an independent predictor of kidney failure in adults with IgAN — after full adjustment for eGFR, proteinuria, age, race, and treatment.

A **10% rise** in the serum **Gd-IgA1** level corresponded to **11.7% higher risk** of kidney failure; a **10% fall** corresponded to **10.5% lower risk** of kidney failure — a bidirectional, clinically actionable signal.

These findings directly support **KDIGO 2025 Guideline** recommending monitoring of pathogenic IgA (Gd-IgA1) as a treatment target in IgAN.

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