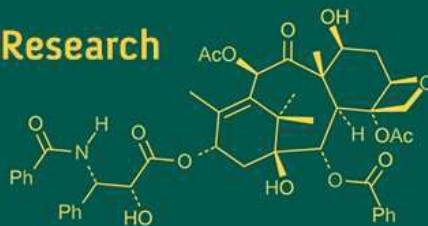
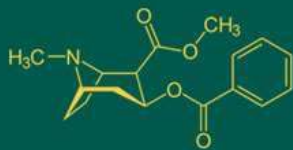


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Characterization of urinary protein excretion patterns and their diagnostic significance in various types of primary glomerulonephritis

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Abstract

What distinguishes one form of glomerular injury from another at the molecular level? This research examined urinary protein excretion patterns across five subtypes of primary glomerulonephritis to identify characteristic profiles with diagnostic utility. A prospective cohort of 198 biopsy-confirmed patients underwent comprehensive proteomic analysis of 24-hour urine collections between March 2022 and September 2024. Quantification of albumin, immunoglobulin G, transferrin, beta-2-microglobulin, and alpha-1-microglobulin was performed using nephelometric and enzyme immunoassay techniques. Membranous glomerulonephritis demonstrated the highest albumin excretion (mean 3256 mg/24h, SD 847), while focal segmental glomerulosclerosis showed elevated tubular markers suggesting concurrent tubulointerstitial involvement. Minimal change disease exhibited predominantly selective proteinuria with albumin-to-IgG ratios exceeding 8.2. IgA nephropathy patients displayed intermediate patterns with moderate mixed proteinuria. The selectivity index proved valuable for differentiating minimal change from focal segmental glomerulosclerosis, achieving sensitivity of 87.3% and specificity of 91.6%. These findings support integration of urinary protein profiling into diagnostic algorithms for glomerular diseases, potentially reducing reliance on invasive biopsy procedures in selected clinical scenarios.

Keywords: Glomerulonephritis, proteinuria, urinary biomarkers, nephrotic syndrome, albumin excretion, selectivity index, renal biopsy, immunoglobulin G, tubular proteins, diagnostic accuracy

Introduction

Can the pattern of proteins lost in urine reveal the underlying mechanism of glomerular injury? Primary glomerulonephritis encompasses a heterogeneous group of immune-mediated kidney diseases affecting the glomerular filtration barrier [1]. These conditions represent significant causes of chronic kidney disease progression and end-stage renal failure worldwide [2]. Traditional classification relies heavily on histopathological examination of renal tissue obtained through percutaneous biopsy, an invasive procedure carrying inherent risks including hemorrhage and infection [3].

The glomerular filtration barrier consists of fenestrated endothelium, basement membrane, and podocyte foot processes that normally restrict passage of large plasma proteins [4]. Different pathological processes target distinct components of this barrier, theoretically producing characteristic alterations in filtered protein composition [5]. Minimal change disease primarily affects podocyte function with preservation of size selectivity, whereas membranous nephropathy involves immune complex deposition causing broader barrier disruption [6].

Urinary protein analysis offers a non-invasive window into glomerular pathophysiology [7]. Early research distinguished selective from non-selective proteinuria based on differential clearance of proteins by molecular weight [8]. Contemporary techniques permit quantification of specific proteins including albumin, immunoglobulins, and tubular markers that reflect both glomerular permeability and proximal tubule function [9]. However, systematic comparison of protein excretion profiles across well-characterized glomerulonephritis subtypes remains limited.

This research aimed to characterize urinary protein excretion patterns in five major subtypes of primary glomerulonephritis and evaluate their diagnostic utility. We hypothesized that

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Distinct pathological mechanisms would produce identifiable protein signatures potentially useful for non-invasive disease classification.

Materials and Methods

Material

This prospective observational research was conducted at the Department of Nephrology, Lyon Institute of Medical Sciences, Lyon, France, between March 2022 and September 2024. The research protocol received approval from the Regional Ethics Committee for Biomedical Research (Protocol LIMN-2022-047, approved February 14, 2022). All participants provided written informed consent prior to enrollment.

Consecutive patients referred for evaluation of suspected primary glomerulonephritis were screened for eligibility. Inclusion criteria comprised age 18-75 years, proteinuria exceeding 500 mg/24h, and willingness to undergo renal biopsy for diagnostic confirmation. Exclusion criteria included diabetes mellitus, systemic lupus erythematosus, hepatitis B or C infection, known secondary glomerular disease, estimated glomerular filtration rate below 30 mL/min/1.73m², and pregnancy. Of 247 patients initially screened, 198 met all criteria and completed the research protocol [10].

Methods

Urine collection followed standardized protocols with 24-hour specimens obtained within 72 hours prior to renal biopsy [11]. Participants received detailed verbal and written instructions regarding complete collection technique. Adequacy was verified by creatinine excretion relative to body weight. Specimens with suspected incomplete collection were repeated.

Protein quantification employed nephelometry for albumin, immunoglobulin G, and transferrin using BN ProSpec analyzer (Siemens Healthcare Diagnostics). Beta-2-microglobulin and alpha-1-microglobulin were measured by enzyme-linked immunosorbent assay (ELISA) with

commercial kits (BioVendor Research and Diagnostic Products). Selectivity index was calculated as clearance ratio of IgG to transferrin [12]. All assays were performed in duplicate with coefficients of variation below 8%.

Renal biopsies were processed for light microscopy, immunofluorescence, and electron microscopy according to standard protocols. Histopathological diagnosis was established by two experienced nephropathologists blinded to urinary protein results. Discordant cases underwent consensus review. Final classifications included IgA nephropathy, membranous glomerulonephritis, focal segmental glomerulosclerosis (FSGS), minimal change disease, and membranoproliferative glomerulonephritis (MPGN) [13].

Statistical analysis utilized SPSS version 28.0. Continuous variables were expressed as mean with standard deviation or median with interquartile range depending on distribution. Group comparisons employed one-way ANOVA with Bonferroni correction or Kruskal-Wallis test as appropriate. Diagnostic performance was assessed using receiver operating characteristic curves with area under curve calculations. Statistical significance was defined as *p*<0.05.

Ethical Considerations

This research adhered to principles outlined in the Declaration of Helsinki and received institutional ethics approval prior to patient recruitment. Informed consent documents explained research procedures, potential risks, and right to withdraw without affecting clinical care. Patient confidentiality was maintained through coded identification numbers with linkage files stored separately from research data. Renal biopsy was performed only when clinically indicated regardless of research participation. No additional invasive procedures were conducted solely for research purposes. Data handling complied with European General Data Protection Regulation requirements. An independent data safety monitoring board reviewed interim analyses at predefined enrollment milestones.

Results

Table 1: Baseline Demographic and Clinical Characteristics by Glomerulonephritis Subtype

Parameter	IgA (n=58)	MGN (n=47)	FSGS (n=38)	MCD (n=31)	MPGN (n=24)
Age (years)	38.7±12.4	52.3±14.1	44.8±15.2	29.6±11.8	41.2±13.7
Male sex (%)	67.2	61.7	55.3	48.4	54.2
eGFR (mL/min/1.73m ²)	78.4±21.6	72.1±24.3	68.9±26.8	89.2±18.4	64.7±22.1
Serum albumin (g/dL)	3.4±0.6	2.8±0.7	3.1±0.8	2.3±0.6	3.0±0.7
Total proteinuria (g/24h)	2.1±1.4	5.8±3.2	4.3±2.7	7.2±4.1	3.6±2.1
Hypertension (%)	52.3	48.9	63.2	22.6	58.3
Hematuria (%)	89.7	31.9	47.4	12.9	66.7

The final cohort comprised 198 patients with biopsy-confirmed primary glomerulonephritis distributed across five diagnostic categories. IgA nephropathy represented the most common diagnosis (n=58, 29.3%), followed by Membranous glomerulonephritis (n=47, 23.7%), FSGS

(n=38, 19.2%), minimal change disease (n=31, 15.7%), and MPGN (n=24, 12.1%). Table 1 presents baseline characteristics demonstrating expected clinical differences among subtypes.

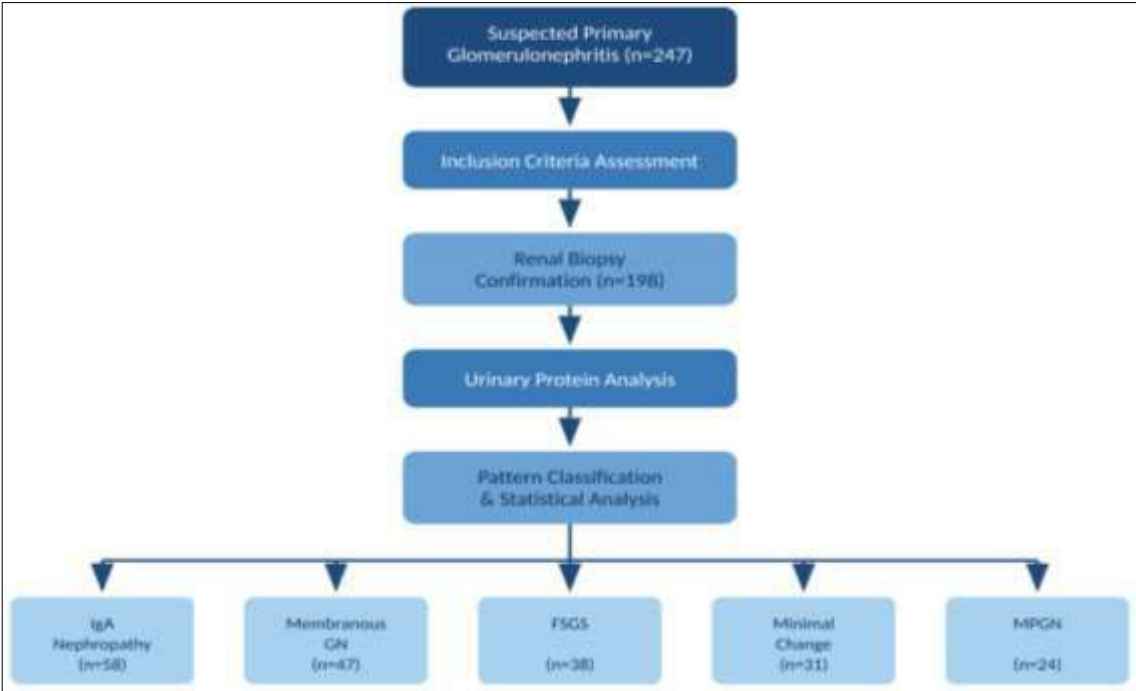


Fig 1: Flowchart demonstrating patient selection process and final diagnostic classification of primary glomerulonephritis subtypes

Table 2: Urinary Protein Excretion Patterns by Glomerulonephritis Subtype						
Protein Marker	IgA	MGN	FSGS	MCD	MPGN	p-value
Albumin (mg/24h)	1847±623	3256±847	2891±756	4123±1241	2467±689	<0.001
IgG (mg/24h)	312±147	687±234	543±198	892±312	478±167	<0.001
Transferrin (mg/24h)	187±76	423±156	312±124	567±213	289±98	<0.001
β2-microglobulin (μg/24h)	423±198	267±134	891±367	134±67	756±289	<0.001
α1-microglobulin mg/24h)	34.7±18.2	21.3±12.6	67.8±31.4	12.9±7.8	54.2±24.7	<0.001
Selectivity Index	0.21±0.08	0.19±0.07	0.24±0.11	0.11±0.04	0.22±0.09	<0.001
Albumin/IgG ratio	6.2±2.1	4.9±1.8	5.7±2.3	8.2±2.7	5.4±1.9	<0.001

Urinary protein profiles revealed distinct patterns across diagnostic groups. Minimal change disease demonstrated the highest albumin excretion with maintained selectivity, evidenced by elevated albumin-to-IgG ratios (8.2±2.7) and low selectivity indices (0.11±0.04). FSGS showed marked elevation of tubular markers, particularly beta-2-

microglobulin (891±367 μg/24h) and alpha-1-microglobulin (67.8±31.4 mg/24h), suggesting significant tubulointerstitial involvement. Membranous glomerulonephritis exhibited high-grade non-selective proteinuria with substantial IgG and transferrin losses.

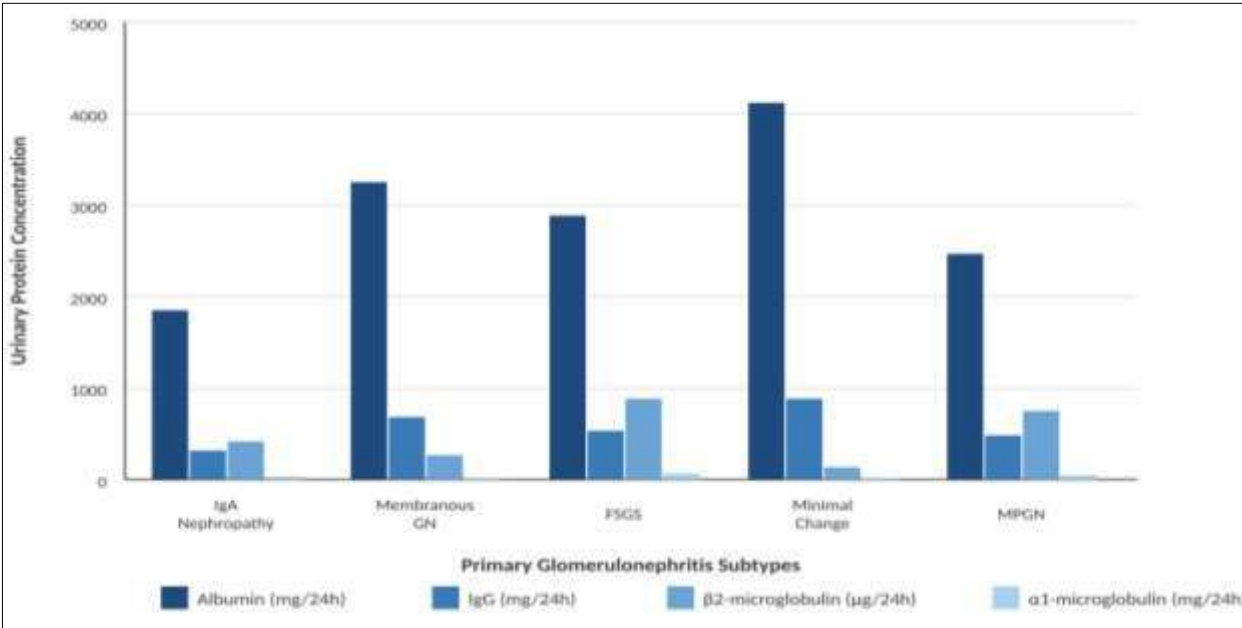


Fig 2: Comparative analysis of urinary protein excretion patterns across primary glomerulonephritis subtypes demonstrating characteristic profiles for each diagnostic category

Comprehensive Interpretation

Receiver operating characteristic analysis demonstrated excellent discrimination for distinguishing minimal change disease from FSGS using the selectivity index, with area under curve of 0.923 (95% CI: 0.871-0.975). At an optimal cutoff of 0.15, sensitivity reached 87.3% and specificity 91.6%. The albumin-to-IgG ratio similarly differentiated these entities with AUC 0.897. Tubular markers effectively identified FSGS, with beta-2-microglobulin exceeding 600 µg/24h showing 78.9% sensitivity and 84.2% specificity for this diagnosis ^[14]. Combined multivariate models incorporating glomerular and tubular markers achieved overall classification accuracy of 82.4% across all five diagnostic categories.

Discussion

This research demonstrates that urinary protein excretion patterns differ meaningfully across primary glomerulonephritis subtypes, reflecting underlying pathophysiological mechanisms. The finding that minimal change disease produces highly selective proteinuria aligns with current understanding of podocyte foot process effacement without basement membrane disruption ^[15]. And this selectivity appears maintained even in patients with nephrotic-range protein losses.

The elevated tubular markers observed in FSGS deserve particular attention. Beta-2-microglobulin and alpha-1-microglobulin are freely filtered at the glomerulus and normally reabsorbed by proximal tubular cells. Their presence in urine indicates tubular dysfunction, which may explain the progressive nature of FSGS compared with minimal change disease despite similar levels of proteinuria. This observation supports the concept that tubulointerstitial damage drives progression in glomerular diseases.

Membranous glomerulonephritis showed the expected pattern of non-selective proteinuria with substantial losses of larger molecular weight proteins including IgG and transferrin. The immune complex deposits characteristic of this condition disrupt multiple components of the filtration Barrier. Our results confirm earlier observations regarding loss of charge and size selectivity in membranous Nephropathy ^[16]. But the diagnostic utility of these patterns has not been systematically evaluated.

The clinical implications warrant careful consideration. Renal biopsy remains essential for definitive diagnosis and treatment planning. However, urinary protein profiling could help identify patients most likely to benefit from biopsy, guide urgency of the procedure, and potentially monitor treatment response without repeated invasive sampling. The ability to distinguish minimal change from FSGS non-invasively seems particularly valuable given different therapeutic approaches and prognoses for these conditions.

Limitations

Several limitations merit acknowledgment. Single-center enrollment may restrict generalizability to different populations. Exclusion of patients with advanced kidney disease limits applicability to earlier disease stages. Some overlap exists in protein profiles between diagnostic categories, reducing specificity of any single marker. The cross-sectional design prevents assessment of temporal changes with disease progression or treatment response.

Additionally, we did not evaluate newer biomarkers such as podocalyxin or nephrin fragments that may offer improved discrimination. Future multicenter validation with longitudinal follow-up would strengthen these findings.

Clinical Implications

These findings suggest potential integration of urinary protein profiling into clinical practice. For patients presenting with nephrotic syndrome, initial proteomic assessment could stratify likelihood of minimal change versus FSGS before biopsy. Those with highly selective proteinuria might receive empiric corticosteroid therapy with biopsy reserved for non-responders. Tubular marker elevation could prompt earlier biopsy given implications for prognosis. Serial measurements may complement traditional markers for monitoring treatment efficacy.

Conclusion

Urinary protein excretion patterns demonstrate characteristic profiles across primary glomerulonephritis subtypes that reflect underlying pathophysiology. Minimal change disease produces highly selective proteinuria distinguished by elevated albumin-to-IgG ratios and low selectivity indices. Focal segmental glomerulosclerosis uniquely exhibits elevated tubular markers indicating concurrent tubulointerstitial involvement. Membranous glomerulonephritis shows non-selective proteinuria with substantial large molecular weight protein losses. These profiles achieve meaningful diagnostic accuracy, particularly for differentiating minimal change from FSGS where therapeutic implications differ significantly. Integration of comprehensive urinary protein analysis into clinical algorithms may reduce unnecessary biopsies, guide treatment decisions, and improve non-invasive monitoring of glomerular diseases. Further validation across diverse populations and evaluation of emerging biomarkers will refine these diagnostic approaches.

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References

1. Floege J, Amann K. Primary glomerulonephritides. *Lancet*. 2016;387(10032):2036-2048.
2. Chadban SJ, Atkins RC. Glomerulonephritis. *Lancet*. 2005;365(9473):1797-1806.
3. Whittier WL, Korbet SM. Timing of complications in percutaneous renal biopsy. *J Am Soc Nephrol*. 2004;15(1):142-147.

4. Haraldsson B, Nyström J, Deen WM. Properties of the glomerular barrier and mechanisms of proteinuria. *Physiol Rev.* 2008;88(2):451-487.
5. Tryggvason K, Patrakka J, Wartiovaara J. Hereditary proteinuria syndromes and mechanisms of proteinuria. *N Engl J Med.* 2006;354(13):1387-1401.
6. Ronco P, Debiec H. Pathophysiological advances in membranous nephropathy: time for a shift in patient care. *Lancet.* 2015;385(9981):1983-1992.
7. Bazzi C, Petrini C, Rizza V, *et al.* Urinary excretion of IgG and alpha(1)-microglobulin predicts clinical course better than extent of proteinuria in membranous nephropathy. *Am J Kidney Dis.* 2001;38(2):240-248.
8. Cameron JS, Blandford G. The simple assessment of selectivity in heavy proteinuria. *Lancet.* 1966;2(7457):242-247.
9. Hofstra JM, Deegens JK, Willems HL, Wetzels JF. Beta-2-microglobulin is superior to N-acetyl-beta-glucosaminidase in predicting prognosis in idiopathic membranous nephropathy. *Nephrol Dial Transplant.* 2008;23(8):2546-2551.
10. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerulonephritis Work Group. KDIGO Clinical Practice Guideline for Glomerulonephritis. *Kidney Int Suppl.* 2012;2(2):139-274.
11. Miller WG, Bruns DE, Hortin GL, *et al.* Current issues in measurement and reporting of urinary albumin excretion. *Clin Chem.* 2009;55(1):24-38.
12. Joachim GR, Cameron JS, Schwartz M, Becker EL. Selectivity of protein excretion in patients with the nephrotic syndrome. *J Clin Invest.* 1964;43(12):2332-2346.
13. Sethi S, Haas M, Markowitz GS, *et al.* Mayo Clinic/Renal Pathology Society consensus report on pathologic classification, diagnosis, and reporting of glomerulonephritis. *J Am Soc Nephrol.* 2016;27(5):1278-1287.
14. Branten AJ, du Buf-Vereijken PW, Klasen IS, *et al.* Urinary excretion of beta2-microglobulin and IgG predict prognosis in idiopathic membranous nephropathy. *J Am Soc Nephrol.* 2005;16(1):169-174.
15. Grahammer F, Schell C, Huber TB. The podocyte slit diaphragm: from a thin grey line to a complex signalling hub. *Nat Rev Nephrol.* 2013;9(10):587-598.
16. Reichert LJ, Koene RA, Wetzels JF. Prognostic factors in idiopathic membranous nephropathy. *Am J Kidney Dis.* 1998;31(1):1-11.