Urinary Transferrin and Emerging Biomarkers for Early Detection of Diabetic Kidney Disease

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Abstract

Background: Diabetic kidney disease (DKD) can develop through glomerular, tubular, inflammatory, and fibrotic pathways, while albuminuria and estimated glomerular filtration rate may fail to reveal some early pathological changes. Urinary transferrin has emerged as a candidate marker of abnormal glomerular protein permeability and tubular protein handling. Objective: To critically evaluate urinary transferrin for early DKD detection and compare its potential diagnostic contribution with established and emerging urinary biomarkers. Methods: A narrative synthesis was developed from clinical studies, diagnostic evidence, recent reviews, and kidney disease guidance, with particular attention to urinary transferrin, glomerular and podocyte markers, tubular injury proteins, inflammatory mediators, and molecular signatures. Findings: Early observational research linked transferrinuria with subsequent microalbuminuria. A 2024 meta-analysis of six studies reported pooled sensitivity of 82%, specificity of 88%, and a summary area under the curve of 0.92, although variability in diagnostic definitions, thresholds, and populations limits clinical transportability. Transferrin reflects partly overlapping processes with albumin, while urinary nephrin, kidney injury molecule-1, neutrophil gelatinase-associated lipocalin, liver-type fatty acid-binding protein, and monocyte chemoattractant protein-1 capture complementary mechanisms. Multiplex strategies may therefore improve pathological characterization, but external validation and evidence of incremental clinical benefit remain limited. Conclusion: Urinary transferrin is a promising adjunctive investigational biomarker rather than a replacement for conventional surveillance. Prospective head-to-head studies using standardized assays, clinically relevant control groups, and longitudinal kidney outcomes are needed to establish its independent prognostic utility and role in precision DKD assessment.

Keywords: diabetic kidney disease, urinary transferrin, early detection, novel biomarkers

Introduction

Diabetic kidney disease (DKD) is among the most consequential complications of diabetes because progressive renal injury amplifies cardiovascular risk, limits pharmacological choices and increases the likelihood of kidney replacement therapy. The American Diabetes Association (ADA) 2026 Standards of Care estimate that chronic kidney disease occurs in approximately 20%–40% of people with diabetes. This burden includes diverse clinical phenotypes rather than a uniform sequence of albuminuria followed by glomerular filtration loss. The distinction matters because contemporary screening must identify both prevalent disease and individuals whose kidneys are undergoing injury before established functional abnormalities emerge. [1]

DKD arises from sustained metabolic and hemodynamic stress across the nephron. Chronic hyperglycemia modifies mitochondrial metabolism and increases oxidative stress; altered sodium delivery at the macula densa, intraglomerular hypertension and renin–angiotensin–aldosterone system activation promote mechanical strain. Podocyte damage, endothelial dysfunction and basement-membrane remodeling impair the glomerular filtration barrier, while tubular oxygen demand and inflammatory activation contribute to interstitial fibrosis. These mechanisms overlap, but their relative contribution differs across patients and disease stages. [2,3]

Classical diabetic glomerulopathy encompasses thickening of the glomerular basement membrane, mesangial expansion, podocyte depletion and, in advanced disease, nodular sclerosis. Yet tubulointerstitial injury can be substantial even when urinary albumin excretion is low. Altered proximal tubular protein reclamation, renal microvascular disease and local inflammation may also influence urinary biomarker concentrations. [4,5] Thus, interpreting any one protein as a uniquely glomerular or tubular signal can be misleading without considering the entire pathway between plasma, filtration and urinary excretion. [6]

DKD diagnosis in clinical practice is based principally on estimated glomerular filtration rate (eGFR), urine albumin-to-creatinine ratio (UACR), clinical history and exclusion of atypical causes. The 2026 ADA guidance recommends at least annual UACR and eGFR assessment in every person with type 2 diabetes and in those with type 1 diabetes of at least five years' duration. Those with established chronic kidney disease require more frequent monitoring based on stage and trajectory. These markers retain well-established associations with kidney and cardiovascular outcomes. [7]

Albumin excretion varies biologically and can rise with infection, severe hyperglycemia, exertion, uncontrolled blood pressure and other transient conditions; repeated measurements are therefore necessary to establish persistent abnormality. A separate challenge is normoalbuminuric renal impairment, in which filtration decreases without the expected increase in urinary albumin. Conversely, individuals can sustain early glomerular or tubular stress while both UACR and eGFR remain within apparently reassuring ranges. These observations support a search for adjunctive injury markers, not abandonment of established measures. [8-10]

The therapeutic landscape has changed with demonstrated renal benefits from sodium–glucose cotransporter-2 inhibition, renin–angiotensin blockade, nonsteroidal mineralocorticoid receptor antagonism and selected glucagon-like peptide-1 receptor agonists. Early recognition of kidney damage could widen opportunities for timely risk-factor modification and disease-modifying treatment. However, a new biomarker must prove that it improves classification, predicts relevant outcomes or changes decisions beyond UACR and eGFR; an elevated concentration alone does not establish clinical utility. [11-13]

Urine is an attractive investigative medium because repeated noninvasive sampling permits measurement of filtered plasma proteins, products of injured epithelial cells and molecules released by inflammatory and fibrotic processes. [14-15] Among these candidates, urinary transferrin occupies a distinctive position: its size and circulating origin make it a plausible marker of filtration-barrier dysfunction, while its tubular handling and iron-binding biology complicate a purely glomerular interpretation. The central question is where transferrin contributes information that existing tests cannot

capture reliably. [16,17]

2. Aim of the Review

This narrative review critically evaluates the biological basis, analytical measurement and diagnostic performance of urinary transferrin for early DKD, with emphasis on normoalbuminuric disease and its incremental value relative to established measures and emerging glomerular, tubular, inflammatory and molecular biomarkers. It also identifies methodological gaps that prospective studies must address before clinical implementation.

3. Literature Identification and Evidence Appraisal

A focused narrative literature search was undertaken using PubMed/MEDLINE and online sources from peer-reviewed journals and professional guideline organizations, with literature available through Search concepts combined “diabetic kidney disease” or “diabetic nephropathy” with “urinary transferrin”, “transferrinuria”, “early detection”, “albuminuria”, “podocyte biomarkers”, “nephrin”, “NGAL”, “KIM-1”, “L-FABP”, “cystatin C”, “MCP-1”, “TNFR”, “proteomics” and “extracellular vesicles”. Priority was given to 2024–2026 studies, systematic reviews, meta-analyses and major clinical guidance, supplemented by foundational longitudinal transferrin studies. Reports were considered for mechanistic relevance, diagnostic accuracy, comparison groups, assay methods, temporal prediction and practical applicability.

4. Established Indicators of Early Renal Damage and the Unresolved Diagnostic Gap

UACR is the most extensively validated urinary marker of DKD and a quantitative predictor of progression and cardiovascular risk. Albuminuria categories integrate with eGFR categories to guide monitoring and treatment, while longitudinal change in albumin excretion is clinically meaningful. Its chief limitation for early discovery is that pathological injury may not produce persistent albuminuria at the time of assessment, and modest results fluctuate for reasons unrelated to progressive diabetic structural damage. The problem is insufficient sensitivity for some phenotypes, not lack of diagnostic or prognostic value. [18,19]

Serum creatinine and creatinine-based eGFR summarize filtration rather than pinpointing the anatomic source of injury. Creatinine generation varies with muscle mass, diet and clinical context, so seemingly stable eGFR may obscure structural disease or meaningful early decline. Incorporating serum cystatin C into combined estimating equations can improve filtration estimation when clinical decisions require greater accuracy, but a more accurate filtration estimate still does not directly measure incipient glomerular permeability changes or epithelial injury. [20,21]

The presence of albuminuria and eGFR changes in distinct sequences creates a mismatch between a single-marker screening strategy and the heterogeneous biology of DKD. In nonalbuminuric diabetic CKD, vascular and tubulointerstitial pathways may be conspicuous; in albuminuric disease, filtration-barrier permeability dominates the clinical signal. Biomarkers derived from distinct nephron compartments might identify injury that is clinically silent using routine tests, yet their overlap and dependence on comorbidity require careful interpretation. [9]

Karimi et al 2024 synthesized human observational studies of emerging urinary and circulating candidates, including transferrin, NGAL and inflammatory proteins. Although many biomarkers have been linked to diabetic kidney disease, their additional benefit over UACR and eGFR remains unclear. Studies comparing patients with advanced DKD to healthy individuals may show good diagnostic results. However, the main clinical value lies in identifying patients with diabetes who are at risk of future kidney function decline, even when their current kidney function tests are still normal [19,22]

The main research gap is therefore operational: reliable cutoffs, interlaboratory harmonization, performance in normoalbuminuria, longitudinal prediction of sustained eGFR decline, independent validation and evidence that biomarker-guided testing changes care are not yet established for most urinary candidates. Comparative studies should account for age, diabetes duration, glycemic control, baseline UACR, eGFR, hypertension, medication exposure and competing kidney disorders. Disease-specificity and improved net clinical benefit are at least as important as a favorable receiver operating characteristic curve. [17,23]

5. Urinary Transferrin: Molecular Characteristics and Renal Handling

Transferrin is an approximately 80-kDa circulating glycoprotein that transports ferric iron to tissues through receptor-mediated uptake. Its origin in plasma permits urinary measurement to reflect passage across the renal filtration barrier, although urinary transferrin is also affected by the capacity of proximal tubular cells to reclaim filtered protein. This dual dependence makes transferrinuria potentially informative, but not anatomically exclusive to the glomerulus. [24- 26]

Transferrin and albumin have broadly comparable molecular sizes but differ in electrical and physicochemical properties. Historical observations suggested that early diabetic changes in the glomerular charge barrier could facilitate urinary transferrin loss in some patients before overt albuminuria. Modern understanding recognizes that barrier selectivity is multifactorial, involving endothelial glycocalyx, basement membrane and slit diaphragm integrity, and that charge-based explanations alone are insufficient to account for all observed protein flux. [27]

Podocyte injury and endothelial dysfunction can increase macromolecular permeability under diabetic conditions. At the same time, maladaptive proximal tubular endocytosis reduces the fraction of filtered protein returned to the circulation or metabolized intracellularly. Elevated transferrin excretion can thus emerge from increased filtered load, impaired tubular uptake or both; concurrent assessment of albumin and tubular proteins may aid biological interpretation. [28,29]

Iron delivery adds an additional mechanistic dimension. Transferrin-associated iron normally participates in tightly regulated cellular trafficking, but altered protein and iron handling under metabolic stress can favor oxidative damage. In the kidney, iron-related oxidative processes are plausible contributors to epithelial stress, yet current urine transferrin assays measure a potential injury signal rather than directly establishing that transferrin itself drives DKD progression. [24]

The early clinical observations linking transferrinuria with diabetic renal abnormalities predate contemporary renal-protective therapy. Kazumi and colleagues reported that greater urinary transferrin excretion predicted later microalbuminuria among individuals with type 2 diabetes. Kanauchi and coworkers subsequently connected transferrinuria with early nephropathy and tubulointerstitial injury, reinforcing the possibility that a single urinary protein signal integrates filtration and reabsorptive abnormalities. These studies remain important for biological plausibility but require reinterpretation in modern treated populations. [27,30]

Clinical measurement is commonly performed by immunological methods including enzyme-linked immunosorbent assay. Spot urine concentrations depend on hydration and should ideally be interpreted with a creatinine-normalized measure or carefully standardized specimen collection. Samples should be assessed for hematuria, urinary tract infection, acute illness and other sources of proteinuria; assay calibration, storage stability and between-platform comparability must also be reported. These technical issues substantially affect whether a promising research result can be reproduced clinically. [18,31]

6. Diagnostic Evidence and the Potential Value of Transferrinuria in Early DKD

Kazumi et al. reported that increased urinary transferrin levels could predict the development of microalbuminuria in patients with type 2 diabetes, suggesting its potential value in detecting early kidney damage. Similarly, Narita et al. found that urinary transferrin, immunoglobulin G, and ceruloplasmin may help predict microalbuminuria. These findings suggest that urinary transferrin could identify early diabetic kidney injury before albuminuria becomes detectable. Although these studies were conducted several years ago, they provide important evidence supporting the potential use of urinary transferrin as an early diagnostic biomarker. [32]

Kanauchi et al. examined transferrinuria in type 2 diabetes with early nephropathy and tubulointerstitial injury, drawing attention to the shared glomerular and tubular interpretation of the signal. Other investigations have compared several urinary markers across diabetes stages and reported relationships with albumin excretion and kidney function. Such findings support biological plausibility but need careful reading: cross-sectional differences between normoalbuminuric and albuminuric groups do not

establish that transferrin predicts subsequent disease, and correlations with UACR do not establish superiority over UACR. [33,34]

A 2024 meta-analysis by Li, Wang, and Ye pooled six studies assessing urinary transferrin for diabetic nephropathy and reported sensitivity of 0.82, specificity of 0.88, and summary receiver-operating characteristic area of 0.92. The pooled positive likelihood ratio was 7.07 and negative likelihood ratio 0.20. These estimates indicate meaningful diagnostic discrimination within the included research settings. Importantly, the synthesis does not resolve variation in case definitions, patient selection, assay methods, or study thresholds. A pooled result should not be generalized uncritically into a universal screening cut-off or assumed to predict kidney failure. [35]

Current clinical relevance depends on the populations tested. Studies that contrast established proteinuric nephropathy against healthy controls are likely to produce stronger apparent performance than studies restricted to normoalbuminuric patients with similar eGFR and cardiometabolic profiles. The most informative comparison would evaluate transferrin against UACR, eGFR, disease duration, retinopathy, blood pressure, and medication exposure in an unselected diabetes population. It would test whether transferrin identifies independently verified incipient injury, improves calibration of future kidney risk, or changes subsequent clinical decisions. [36]

Transferrin measurement may also be relevant to the discordance between retinal and renal microvascular disease. Diabetes-related endothelial dysfunction affects multiple organs, but the presence of diabetic retinopathy does not prove that a kidney lesion is diabetic, particularly in type 2 diabetes. Associations between transferrinuria and other microvascular outcomes should therefore be treated as potentially informative rather than organ-specific. Longitudinal work should determine whether the marker independently predicts kidney decline after adjustment for baseline retinal complications, glycemic exposure, and conventional renal risk markers. [37]

Urinary transferrin is commonly quantified using an enzyme-linked immunosorbent assay. Analytical platforms may differ in antibody specificity, calibration materials, measurable concentration ranges, precision, and matrix effects. Concentrations expressed in mass per volume are influenced by urinary dilution; a transferrin-to-creatinine ratio may reduce some variability, though creatinine excretion itself depends on muscle mass and other characteristics. Any report of diagnostic sensitivity or a cut-off is inseparable from its assay method, urine collection protocol, units, and reference population. 17,23

Preanalytical standardization is central to reproducibility. Collection at a consistent time, documentation of acute illness or vigorous activity, attention to hematuria and urinary infection, adequate processing, and appropriate storage reduce avoidable noise. Urinary blood contamination can elevate plasma-derived proteins and mislead interpretation. Investigators should report freeze–thaw handling, assay detection limits, intra- and inter-assay variation, blinded laboratory procedures, and whether the assay measures intact transferrin or immunoreactive fragments. These details are not cosmetic methodological additions: they govern whether a threshold can be replicated by another laboratory. [10]

A clinically usable threshold would require prospective derivation followed by validation using a separately recruited cohort and a prespecified assay. Receiver-operating characteristic analysis in the same sample used to select the threshold is optimistic, especially in modest case–control studies. Both sensitivity and specificity should be reported with confidence intervals, alongside predictive values at plausible real-world disease prevalences. Decision-curve analysis, net clinical benefit, and incremental performance relative to standard care would determine whether an additional test helps practitioners rather than merely separating already recognizable groups. [25,26]

Li, Wang and Ye published a 2024 meta-analysis including six studies of urinary transferrin for early diabetic nephropathy. Pooled sensitivity was 0.82 (95% CI 0.71–0.89), specificity 0.88 (0.84–0.92) and summary ROC AUC 0.92 (0.89–0.94). The pooled positive and negative likelihood ratios were 7.07 and 0.20, respectively. These results support discrimination within the included research settings; they should not be interpreted as proof of population-screening effectiveness, a universal cutoff or superiority over guideline-directed UACR and eGFR. [18]

A 2026 pilot study assessed type IV collagen, transferrin and L-FABP in first-morning urine and found higher levels in microalbuminuric than normoalbuminuric and control groups. Type IV collagen

achieved an AUC of 0.904 for early DKD in that sample; transferrin concentrations also differed substantially between groups and were higher among participants with diabetic retinopathy. Given the small study and cross-sectional comparisons, it cannot determine whether transferrin predicts future kidney outcomes or outperforms other markers in independent populations. [38]

The most compelling putative use of urinary transferrin is as an adjunct in individuals with type 2 diabetes whose UACR remains normal but who have prolonged metabolic exposure or additional risk factors. A transferrin result should prompt careful interpretation, repeat assessment and comprehensive evaluation rather than automatic classification of DKD. The significance of a positive test depends on baseline risk, prevalence of competing kidney disease and whether it changes preventive management or follow-up frequency beyond decisions already indicated by diabetes, blood pressure and eGFR. [18]

7. Comparative Evaluation: Urinary Transferrin Versus Established and Emerging DKD Biomarkers

Table 1. Comparison of urinary transferrin with established and emerging biomarkers for early diabetic kidney disease

Evidence-focused summary. Diagnostic and prognostic findings are distinguished; reported AUCs are study-specific and are not directly comparable across different cohorts.

Biomarker	Biological signal	Important clinical evidence	Comparison with urinary transferrin	Main limitation	Refs
Urinary transferrin (Tf)	Plasma-derived iron-transport protein; urinary rise reflects altered glomerular passage and/or proximal tubular reclamation.	2024 six-study meta-analysis: sensitivity 82%, specificity 88%, AUC 0.92. Elevated Tf may precede microalbuminuria in some patients.	Index marker; possible early signal despite normal UACR, but does not uniquely identify DKD.	Variable assay thresholds; scarce prospective external validation.	[18,32,33]
UACR + eGFR	UACR measures albumin excretion; eGFR estimates filtration function.	Standard screening, staging and risk assessment; validated prognostic and treatment decision thresholds.	Clinical baseline: Tf must add prediction beyond serial UACR and eGFR.	May miss early normoalbuminuric injury; UACR has within-person variability.	[1,21]
Urinary nephrin / podocalyxin	Podocyte slit-diaphragm and cell-surface components; shedding indicates podocyte damage.	Nephrin can increase before marked albuminuria in some observational cohorts.	More directly linked to podocyte injury than Tf, which reflects protein passage/handling.	Not specific to DKD; assays and clinical cut-offs not standardized.	[40,2]
Urinary IgG / ceruloplasmin	Circulating proteins indicating altered size/charge selectivity of the filtration barrier.	Narita et al. reported associations with later microalbuminuria alongside Tf.	Complementary leakage profile; larger proteins may suggest more extensive barrier dysfunction.	Small older studies; uncertain independent value over UACR/Tf.	[39]
KIM-1	Proximal tubular epithelial injury-response protein.	Associated with tubular stress and injury in DKD, including early stages.	Captures tubular epithelial injury rather than filtered plasma-protein loss.	Elevated in multiple renal insults; limited DKD specificity.	[27,42]
NGAL	Tubular epithelial stress and inflammatory-response protein.	May rise with diabetic renal injury but is also elevated in AKI and infection.	Adds tubular/inflammatory information distinct from Tf.	Strong confounding from infection, AKI and systemic inflammation.	[27,43]
L-FABP	Proximal tubular lipid/oxidative-stress response.	Studied as an early tubular marker; included in the 2026 Tf–type IV collagen–L-FABP pilot.	Reflects oxidative tubular stress rather than glomerular protein leakage.	Transient stress changes; small heterogeneous diagnostic cohorts.	[38,42]
Urinary cystatin C / RBP / β_2-microglobulin	Low-molecular-weight filtered proteins normally reclaimed by proximal tubules.	Urinary elevations may indicate impaired tubular reabsorption.	Helps contextualize Tf elevation due to defective reclamation vs increased filtration.	Sample handling and urine pH affect some analytes; urine cystatin C ≠ serum cystatin C.	[2,27]
Urinary type IV collagen	Glomerular/tubular basement-membrane matrix turnover and remodeling.	Terzić et al. (2026) pilot (80 T2D; 10 controls): reported AUC 0.904 for early DKD discrimination.	Structural matrix signal may complement Tf leakage signal.	Pilot, cross-sectional evidence; no accepted threshold or proven longitudinal benefit.	[38]
MCP-1 / CCL2	Chemokine associated with monocyte recruitment and intrarenal inflammation.	Associated with inflammatory renal injury and early histologic lesions in diabetes.	Inflammatory compartment complements Tf protein-permeability signal.	Inflammation in other renal/systemic conditions limits specificity.	[44,27]
Circulating TNFR1/TNFR2 / suPAR	Soluble inflammatory/receptor pathways associated with renal risk.	Some circulating markers have substantial prognostic literature for progression; they are not urine-specific tests.	May aid long-term risk prediction rather than detection of protein leakage.	Affected by systemic inflammation and renal clearance; serum/urine assays not interchangeable.	[40,45]

Urinary microRNAs / EVs / proteomics	Molecular, vesicle and peptide signatures across injury pathways.	Potential early multi-pathway signatures; mostly discovery/validation-stage evidence.	Could complement a low-cost Tf-based panel in research settings.	Platform variation, low abundance, overfitting, cost and limited external validation.	[17,47]

Abbreviations: AUC, area under the receiver operating characteristic curve; DKD, diabetic kidney disease; eGFR, estimated glomerular filtration rate; EVs, extracellular vesicles; KIM-1, kidney injury molecule-1; L-FABP, liver-type fatty acid-binding protein; MCP-1, monocyte chemoattractant protein-1; NGAL, neutrophil gelatinase-associated lipocalin; RBP, retinol-binding protein; Tf, transferrin; UACR, urine albumin-to-creatinine ratio.

Diagnostic Performance and Clinical Significance of Urinary Transferrin

Li et al. (2024), in a meta-analysis of six studies, reported promising diagnostic performance for urinary transferrin, with a pooled AUC of 0.92. However, differences in study populations, diagnostic thresholds, and laboratory methods limit the generalizability of these findings. Direct comparisons with other biomarkers in the same patient populations are needed to establish its additional diagnostic value. [18]

Terzić et al. (2026) evaluated urinary transferrin, type IV collagen, and L-FABP in 80 patients with type 2 diabetes and 10 healthy controls. Urinary transferrin differed among patients with normoalbuminuria, microalbuminuria, and healthy controls, while type IV collagen showed the highest reported diagnostic performance, with an AUC of 0.904. Urinary transferrin was also associated with diabetic retinopathy. Although encouraging, these results require confirmation in larger prospective studies. [38]

Biological Basis of Urinary Transferrin in Early DKD

Early diabetes may cause glomerular hyperfiltration, endothelial injury, basement membrane changes, and podocyte dysfunction, increasing urinary protein leakage. Hyperglycemia and oxidative stress may also impair proximal tubular protein reabsorption. Therefore, elevated urinary transferrin may reflect glomerular injury, tubular dysfunction, or both. Combining transferrin with markers of podocyte and tubular injury could improve understanding of these underlying changes. [5,29]

Potential Value in Different DKD Stages

Urinary transferrin may be particularly useful in patients with type 2 diabetes who have normal UACR and preserved eGFR, as it could indicate early renal injury before conventional abnormalities become detectable. In patients with established albuminuria, its additional value depends on whether it predicts renal deterioration independently of UACR. In nonalbuminuric DKD, other tubular or inflammatory biomarkers may provide complementary information. Prospective studies are needed to establish which patient groups benefit most from transferrin testing. [9,35]

Clinical Application and Treatment Monitoring

UACR and eGFR remain the recommended markers for DKD screening, staging, and monitoring. Although urinary transferrin may improve early detection, evidence is insufficient to support its routine use or treatment decisions based on its concentration alone. Current renal protective strategies include blood pressure and glycemic control, renin–angiotensin system inhibition, SGLT2 inhibitors, and mineralocorticoid receptor antagonists in eligible patients. Future studies should examine whether changes in urinary transferrin during treatment predict subsequent renal outcomes independently of UACR. [1,48,49]

Limitations of Current Evidence

The main limitations of urinary transferrin research include small sample sizes, cross-sectional designs, variable diagnostic thresholds, and limited long-term follow-up. Studies comparing advanced DKD with healthy controls may overestimate diagnostic performance. Furthermore, increased urinary transferrin does not necessarily indicate diabetes-specific renal injury, and its ability to predict future kidney function decline remains uncertain. Standardized assays, clinically relevant comparison groups, and independent validation are essential before routine implementation. [18,22,36]

Future Research Directions

Future multicenter studies should include patients with normoalbuminuria, different degrees of albuminuria, and preserved or reduced eGFR. Urinary transferrin should be compared directly with UACR, nephrin, KIM-1, L-FABP, and other promising markers. Clinical characteristics, glycemic control, blood pressure, medication use, and inflammatory status should be considered. Long-term

outcomes should include persistent albuminuria, annual eGFR decline, and progression to kidney failure. These studies should also evaluate diagnostic thresholds, transferrin-to-creatinine ratio, reproducibility, cost-effectiveness, and whether transferrin improves prediction beyond conventional markers. [21,30,45]

Clinical Perspectives

Urinary transferrin is a promising noninvasive biomarker that may help identify early renal injury in patients with diabetes, particularly before albuminuria becomes detectable. Its main potential benefit lies in providing additional information about glomerular and tubular injury. However, current evidence does not establish its superiority over conventional markers or demonstrate improved clinical outcomes from transferrin-guided testing. Larger prospective studies are required to determine its independent diagnostic and prognostic value and its possible role in combined biomarker panels. [18,38]

8. Conclusion

Urinary transferrin is a biologically plausible and quantitatively promising marker of early renal protein-handling abnormalities in diabetes. Evidence from longitudinal observations, diagnostic studies and a 2024 meta-analysis supports further evaluation, particularly in normoalbuminuric phenotypes. Its value appears greatest when interpreted together with established renal indices and complementary podocyte, tubular and inflammatory signals. Before routine adoption, larger prospective studies must establish standardized assays, independent prognostic value and measurable benefit from transferrin-guided clinical decisions.

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