ISSN: 2457-0400

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

www.wjahr.com

Impact Factor: 6.711

Volume: 9, Issue: 11

Page N. 55-63

Year: 2025

Original Article

Coden USA: WJAMA3

CLINICAL AND HISTOPATHOLOGICAL PRESENTATION OF IMMUNOGLOBULIN A NEPHROPATHY IN THREE CENTERS AT NORTH OF IRAQ

Yousif Mohammed Hasan[1]*, Dr. Safa Ezzedin Almukhtar (Professor)[2]

[1]M.B.Ch.B, CABM (Int.Med), CABM (Neph.).
[2]FICMS (Med), FICMS (Nephro), MD, FRCP (Edin), FRCP (London).

Article Received: 17 Sept. 2025 **Article Revised:** 07 Oct. 2025 **Article Published:** 01 November 2025

***Corresponding Author: Yousif Mohammed Hasan**

M.B.Ch.B, CABM (Int.Med), CABM (Neph.).

DOI: https://doi.org/10.5281/zenodo.17490016

How to cite this Article: Yousif Mohammed Hasan*, Dr. Safa Ezzedin Almukhtar (2025). Clinical And Histopathological Presentation of Immunoglobulin A Nephropathy In Three Centers At North of Iraq. World Journal of Advance Healthcare Research, 9(11), 55–63.

ABSTRACT

Background: IgA nephropathy (IgAN) is a leading primary glomerulopathy in young and middle-aged adults, but multicenter data from Northern Iraq are scarce. We aimed to describe the biopsy yield and clinical presentation of IgAN across three regional centers to inform earlier detection and standardized care. **Methods:** We performed a retrospective multicenter study of all native kidney biopsies from January 2020 to June 2025 at three centers in Northern Iraq (Erbil, Sulaymaniyah, Duhok). IgAN was defined by compatible light microscopy with dominant or co-dominant mesangial IgA on immunofluorescence; transplant biopsies and cases without immunofluorescence were excluded. Demographics and presentation variables abstracted at diagnosis included age, sex, body mass index (BMI), blood pressure status, edema, urinary findings (microscopic hematuria, recurrent gross hematuria, isolated proteinuria), and renal function category (chronic kidney disease [CKD], acute kidney injury [AKI]). Proportions are reported descriptively; the biopsy yield is presented with a Wilson 95% confidence interval (CI). **Results:** Among 2,119 native kidney biopsies, 127 were IgAN, yielding 6.0% (95% CI, 5.1–7.1%). The cohort included 68 males (53.5%) and 59 females (46.5%), aged 15–56 years. Mean BMI was 26 kg/m² (range 20–33). At presentation, microscopic hematuria with or without proteinuria was most frequent (≈50–60%); recurrent gross hematuria occurred in ≈20% and isolated proteinuria in ≈10%. Hypertension was documented in ~50% and peripheral edema in ~20–30%. CKD was present at diagnosis in ~15%, whereas AKI was uncommon (<5%). Obese patients (BMI ≥30 kg/m²) were observed to have higher rates of hypertension and greater proteinuria at presentation. All diagnoses were confirmed by light microscopy and immunofluorescence. **Conclusion:** Across three centers in Northern Iraq, IgAN accounted for 6% of biopsied native kidney disease and predominantly presented with hematuria and substantial early hemodynamic burden; a notable minority had CKD at diagnosis, while AKI was rare. These findings underscore the need for systematic urinalysis screening in young adults, prompt initiation of renoprotective therapy with tight blood pressure control, and integration of cardiometabolic management, alongside efforts to standardize regional pathways and establish a prospective registry for risk stratification and outcome tracking.

KEYWORDS: The cohort included 68 males (53.5%) and 59 females (46.5%), aged 15–56 years. Mean BMI was 26 kg/m² (range 20–33).

INTRODUCTION

IgA nephropathy (IgAN) is the most common primary glomerulopathy and is a leading cause of chronic kidney disease (CKD) in young and middle-aged adults.[1-3] Regardless of its prevalence in different geographical regions, IgAN epidemiology, clinical phenotypes, and care pathways IgAN are influenced and determined by the local health system, biopsy customs, and existing cardiometabolic risk factors.[4] IgAN is characterized by varied clinical symptoms, which may present as mild

cases of microscopic hematuria or as more serious cases of nephrotic-range proteinuria along with progressive renal dysfunction.[5-7] Some symptoms include chronic microscopic hematuria, recurrent gross hematuria which occurs mostly after mucosal infections, and proteinuria in an otherwise healthy patient with hypertension, which may be a result of glomerular injury and hemodynamic stress.[8] The development of this syndrome is staggered. Some patients may enter complete remission, while others may progress over one to two decades to end-stage kidney disease. The prognosis is contingent upon several factors, including baseline proteinuria, controlled hypertension, preserved renal function, histopathology such as the Oxford MEST-C, and modifiable factors such as lifestyle and obesity.[9-11] The disorder is of a certain complexity and as such, the aetiology and timely medical intervention is essential.

From a mechanistic perspective, IgAN has taken the classical approach of the multi-hit hypothesis.[12] In genetically susceptible populations, an irregular O-glycosylation leads to the formation of a circulating gallactose-deficient IgA1 (Gd-IgA1) (Hit 1) which subsequently results in the production of anti-glycan autoantibodies (Hit 2).[13,14] The formation of immune complexes occurs (Hit 3) and gets stuck in the glomerular mesangial region, which then causes mesangial activation and the release of cytokines, triggering the condensation of the complement system, with particular focus on the alternative and lectin pathways (Hit 4).[15,16]

Downstream effects such as the increase of mesangial proliferation, matrix hyperplasia, and various forms of endocapillary hypercellularity, podocyte stress, and segmental scelerosis are also notable.[17] The clinical manifestation of this form of pathobiology is marked by the presence of hematuria and proteinuria, and the histological representation is captured by the MEST-C variables by Oxford.[18] These Mesangial Hypercellularity (M), Endocapillary Hypercellularity (E), Segmental Sclerosis (S), Interstitial Fibrosis with Tubular Atrophy (T), and Crescents (C) are what comprise the variables. While the current clinical series revolves around the clinical phenotype and having the diagnosis confirmed by LM and IF, MEST-C is something that I believe would augment the risk stratification within the region for the future.

The foundation of diagnosis lies on the kidney biopsy containing either dominantly or co-dominantly deposited mesangial IgA which, along with light microscopy, shows positive IgA immunofluorescence.[19] Diagnosis does not solely rest on the findings of her supportive, but not essential, electron microscopy. In practice, clinicians usually decide about the biopsy based on the severity and persistence of the proteinuria/hematuria along with the patient's renal function, presence of hypertension, or center-specific guidelines, which tend to vary on a global and regional basis.[20] This in turn changes the “biopsy yield” of IgAN estimated from all native kidney biopsies. Therefore, the yield of the biopsy depends not only on the prevalence of the disease, but on the mixture of cases, and the clinical practices and traditions in a particular area. This understanding becomes critical when trying to analyze multicentric data and when health systems are trying to set a benchmark.

Management focuses on the renoprotective strategy and the control of disease activity. The cornerstones include the blockade of the renin-angiotensin-aldosterone system (RAAS) with targeted blood pressure control to minimize intraglomerular hypertension and proteinuria.[21,22] Sodium restriction and weight loss, as well as treatment of cardiometabolic risk factors, complete the pharmacotherapy.[23] In some cases, proteinuria that persists despite optimized supportive care may warrant consideration of immunomodulatory approaches, although the variation in the availability of resources and assessments of risk[24], benefit makes this approach variable. There is an increasing role of SGLT2 inhibitors in patients with proteinuric CKD, including IgAN, but this is dependent on the patient and availability.[25] Against this treatment background, the value of timely diagnosis is underscored: baseline proteinuria, having hypertension that is uncontrolled, and lower eGFR at presentation are tied to worse outcomes. This triad underscores the value of early detection and the need for standardized pathways.

The deployment of nephrology service in the Northern regions of Iraq has expanded in the last decade with increased access to subspecialty care and immunofluorescence diagnostics.[25] The literature is centered on single center studies and small case series in this area.

The current study utilizes a retrospective design across three city areas: Erbil, Sulaymaniyah, and Duhok, from January 2020 to December 2025. Within this time, 2,119 native kidney biopsies were conducted, and 127 of them were identified as having IgAN through light microscopy and immunofluorescence, resulting in a biopsy prevalence of 6.0%. The cohort diagnosed with IgAN was predominantly aged between 15-56 years and exhibited a male bias 53.5% of the time. The most prevalent symptom was microscopic hematuria, which was present either with or without proteinuria. The other common symptoms included recurrent gross hematuria and isolated proteinuria, but to a much lesser extent. At the time of the diagnosis, almost half of the patients were suffering from hypertension, while roughly a quarter were suffering from edema. The mean body mass index (BMI) was noted to be in the overweight range, while obesity was noted to occur in concomitantly with higher rates of hypertension and more severe proteinuria. The prevalence of chronic kidney disease (CKD) at the time of diagnosis was noted to be much higher as compared to acute kidney injury (AKI). The findings were consistent

with the progressive onset of IgAN, while also suggestive of a referral delay for many patients.

There are several ramifications of these observations on health systems planning and clinical pathways in the region. To begin with, simple, systematic urinalysis screening in young adults with hypertension and primary care urinary complaints, in the absence of a more clinically impactful diagnosis, may warrant a presumptive diagnosis of asymptomatic microscopic hematuria. This has strong implications regarding the absence of a urinalysis in these patients. Microscopic hematuria should be presumed as the working diagnosis unless there is stronger evidence towards a more significant diagnosis. This highlights the importance of the assumption of diagnosis in clinical and non-clinical interfaces. More, there is a specialized healthcare gap when there is high burden of hypertension at diagnosis. This indicates the need for a healthcare g ap and for proactive healthcare systems in the form of early, protocolized renoprotection and with RAAS Blockade and, where eligible, SGLT2 inhibitors, with robust blood pressure goals and home bp monitoring, alongside monitoring in the absence of hypertension. In addition, the distal pointer profile with a Mean Weissich-Weibull co-ordinate meridian of 26 kg/m² and a smaller group adhering to clinical obesity allows distinction of such patients with modifiable and non-modifiable risk factors in the disease context. Primary care physicians are likely to greatly benefit if there is a shift in structure where lost renal units are restored as a goal with manageable targets to degree 2 or 3 of sodium losing nephritis. Dominantly of the improvements in sequential nephron syndrome, step 4 of the nephrology care, is likely to have a much clearer goal to change default sodium targets. This is in the framework of the shifting thresholds of reflex protocols. The closing norm: the ~15% of patients with stage 3 chronic kidney disease at the time of presentation captures how many in contrast to severely late accessing specialty line care. This pulls us to better equity in care coverage. The set of patients fulfilling the harmonized criteria, and constrained criteria are set with workflows to smooth in the course with disease bottlenecks in the diagnosis to biopsies.

While analyzing the strengths and weaknesses of the study, the methodology employed, its retrospective nature, and its heavy dependence on the availability of clinical documents bring pros and cons. The study's strengths span all the three centers, all of which used immunofluorescence to confirm the diagnosis, along with the denominator of all biopsies within the period, which furthers the estimates of the biopsy yield. Their weaknesses included incomplete records, absence of some elementary measures of severity, which included proteinuria and the eGFR distributions mapped over time, and the absence of longitudinal outcome data such as eGFR slope or eGFR remission. The centers had available ranges of the eGFR proteinuria and eGFR records as presentation features rather than collected data, and to avoid more common misses, the results were sent with the mid-range estimates along with range displays. These features shape the interpretability of the data. These features shape the interpretability of the data, emphasizing descriptive inference and hypothesis generation rather than causal claims.

CHAPTER TWO
PATIENTS & METHODS

Study design and setting

This study involved the assessment of data at three tertiary nephrology and pathology centers located in the northern region of Iraq at Arbil, Sulaymanaiyah and Duhok from January 1, 2020, to June 2025. All native biopsies taken during that period were analyzed based on a standard method of protocol that was accepted across all sites to ensure conformity in capture and extraction of the data.

Eligibility criteria

The specific participants in the study were those who had their native kidneys biopsied and diagnosed with immunoglobulin A nephropathy. The diagnosis in this case was made based on the dominant or co-dominant mesangial deposition of IgA with the accompanying light microscopy findings. As for the transplant biopsies, specimens that lacked immunofluorescence assessment, and those that were non-diagnostic or had inadequate tissue, along with cases that had different primary diagnoses were excluded in order to maintain the diagnostic specificity.

Diagnostic standards

All centers performed standard microscopy on every sample of the case that was analyzed, as well as immunofluorescent microscopy using the panels of IgA, IgG, IgM, and C3, which were reviewed by certified renal pathologists, so long as the samples did not contain Electron microscopy. The samples lacked additional routine components of transitional workflows. Data that was included in routine procedures, the Oxford MEST-C variables were used as additional, noncentral descriptors for the case in the study.[26]

Data collection and variables

Data abstraction from electronic medical records and standardized paper charts was performed using a harmonized case report form and cross-site training. Variables captured at diagnostic biopsy biopsy included age, sex, body mass index, blood pressure status, presence of edema, urinary findings (microscopic hematuria, recurrent gross hematuria, isolated proteinuria), renal status at presentation (acute kidney injury or chronic kidney disease as recorded by the clinician in charge), and the related confirming diagnostic modalities. While local documentation was abstracted, the prespecified operational definitions along with adjudication by investigators were used to solve ambiguities.

Data management and quality assurance

Datasets from separate centers were merged, then integrated into a single, unified database containing a maintained record of the versions of the database along with a reviewed and documented the data dictionary. Systems automatically checked the data for implausible values, discrepancies in dates, duplicated identifiers, and conflicting elements in logically related fields. An independent reviewer abstracted 10% of random samples from each center, the discrepancies in data being adjusted based on consensus or source document verification. Statistical imputation was not performed; the ignored and unfilled fields containing data were retained as missing, site approach data with ranges from certain specified presentation features being preserved for clear display in figures.

Statistical analysis

The approach of the analysis was solely descriptive and planned in advance. Any categorical variables having exact numerators and denominators were summarized as counts and percentages, and proportions of interest were augmented by two-sided 95% confidence intervals calculated using the Wilson score method without continuity correction. Provided ranges at the site level were visualized as horizontal range bars with midpoint markers to avoid overstating precision. Summary measures were depicted as interval plots and distributed measures were not defined. No hypothesis testing, multivariable modeling, or adjustments for multiple comparisons were undertaken. Ethics review was in accordance with local institutional policies for retrospective analyses of de-identified data, with waiver of informed consent where applicable.

CHAPTER THREE
RESULTS

Study population and biopsy yield (2020–2025)

Across the three participating centers in Northern Iraq (Erbil, Sulaymaniyah, and Duhok), a total of 2,119 native kidney biopsies were performed between 2020 and 2025. IgA nephropathy (IgAN) was diagnosed in 127 cases, corresponding to a biopsy yield of 6.0% (127/2,119; 95% CI, 5.1–7.1%). All IgAN diagnoses were confirmed by light microscopy and immunofluorescence in the local pathology laboratories.

Table 1: Biopsy activity and IgAN yield (2020–2025).

Metric	Value
Total native kidney biopsies	2,119
IgA nephropathy diagnoses	127
IgAN yield among biopsies, % (95% CI)	6.0 (5.1–7.1)

CI based on Wilson method.

Demographic characteristics

The IgAN cohort comprised 68 males and 59 females, yielding a male proportion of 53.5% (68/127; 95% CI, 44.9–62.0%). The age range at diagnosis was 15–56 years. The mean body mass index (BMI) at presentation was 26 kg/m², with a range of 20–33 kg/m².

Table 2: Demographics of patients with IgA nephropathy (n = 127).

Characteristic	Value
Age, range (years)	15–56
Male sex, n (%)	68 (53.5)
Female sex, n (%)	59 (46.5)
Male proportion, % (95% CI)	53.5 (44.9–62.0)
BMI, mean (kg/m²)	26
BMI, range (kg/m²)	20–33

CI based on Wilson method.

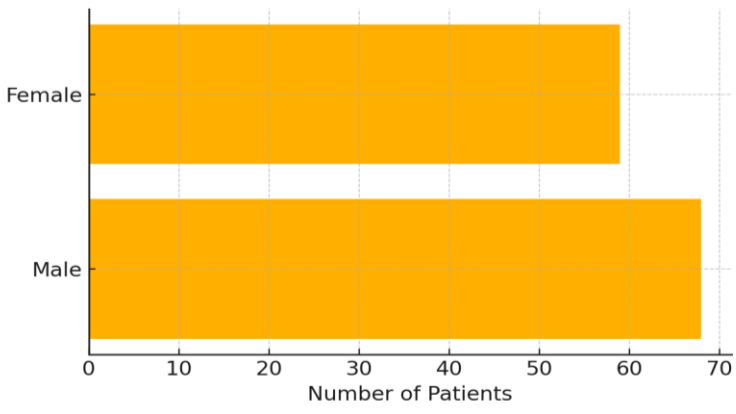

Figure 1: Sex distribution in IgA nephropathy (n = 127).

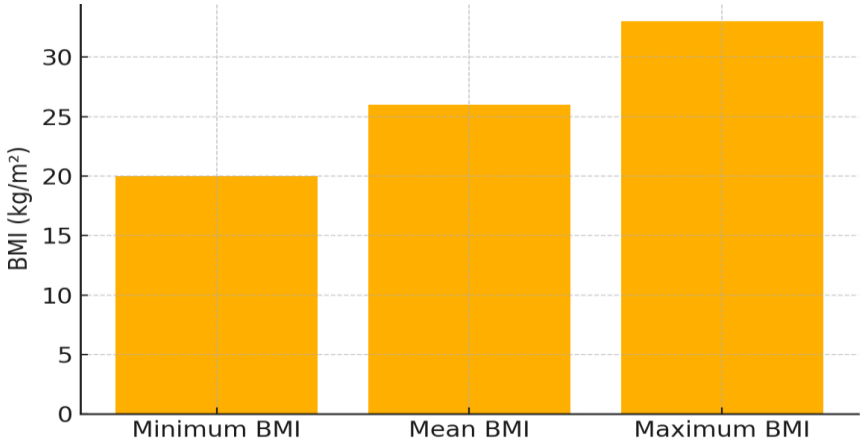

Figure 2: BMI range and mean of patients with IgA nephropathy. This chart presents the minimum, mean, and maximum BMI values among the patients, indicating a moderate BMI range.

Clinical presentation at diagnosis

Microscopic hematuria with or without proteinuria was the predominant mode of presentation, affecting approximately 50–60% of patients. Recurrent gross hematuria occurred in roughly 20% of the cohort. Isolated proteinuria (without hematuria) accounted for about 10% of presentations. Hypertension was documented in approximately half of the patients at the time of diagnosis. Peripheral edema was present in about 20–30% of cases. These figures reflect the distribution observed across the three centers during the study period.

Table 3: Clinical presentation patterns in IgAN (n = 127)

Presentation feature	% of cohort	Approximate n*
Microscopic hematuria ± proteinuria	50–60	~64–76
Recurrent gross hematuria	~20	~25
Isolated proteinuria (no hematuria)	~10	~13
Hypertension at presentation	~50	~64
Peripheral edema	20–30	~25–38

*Approximate counts derived from provided percentage ranges.

Kidney function status at presentation

At diagnosis, chronic kidney disease (CKD) was present in approximately 15% of patients, while acute kidney injury (AKI) was observed in fewer than 5% of cases. These findings suggest that the majority of patients presented without advanced functional impairment, though a meaningful minority had established CKD at baseline.

Table 4: Renal function categories at diagnosis (n = 127).

Renal status	% of cohort	Approximate n*
CKD at presentation	~15	~19
AKI at presentation	<5	~5

*Approximate counts derived from provided percentages.

Anthropometric profile and blood pressure/proteinuria associations

The average BMI at presentation was in the overweight range (mean 26 kg/m²), and the distribution spanned from normal weight to class I obesity (20–33 kg/m²). Patients with obesity (BMI ≥30 kg/m²) were noted to have higher rates of hypertension and proteinuria at presentation across the three centers. While these observations were consistent across sites, they are descriptive; no center-level differences were analyzed here.

Table 5: Anthropometric profile and observed associations.

Variable	Value / Observation
BMI, mean (range), kg/m²	26 (20–33)
Obesity (BMI ≥30 kg/m²)	Present in a subset of patients
Association with hypertension	Higher prevalence among obese patients (descriptive)
Association with proteinuria	Higher burden among obese patients (descriptive)

Diagnostic modality

All diagnoses of IgAN were confirmed by light microscopy in conjunction with immunofluorescence. No cases were classified without immunofluorescence confirmation.

Table 6: Diagnostic confirmation modalities.

Modality	Applied to all cases
Light microscopy	Yes
Immunofluorescence	Yes

Consolidated summary of key proportions

The overall biopsy prevalence of IgAN was 6.0% among 2,119 biopsies. Within the 127-patient IgAN cohort, 53.5% were male, approximately half had hypertension at diagnosis, 50–60% presented with microscopic hematuria (with or without proteinuria), about one-fifth had recurrent gross hematuria, around one-tenth had isolated proteinuria, 20–30% reported edema, 15% had CKD, and fewer than 5% had AKI. The mean BMI was 26 kg/m² (range 20–33 kg/m²), and obesity co-occurred with more frequent hypertension and proteinuria.

Table 7: Key cohort metrics at a glance.

Metric	Value
Biopsy-proven IgAN among all biopsies	6.0% (127/2,119; 95% CI, 5.1–7.1)
Male proportion in IgAN	53.5% (68/127; 95% CI, 44.9–62.0)
Hypertension at presentation	~50%
Microscopic hematuria ± proteinuria	50–60%
Recurrent gross hematuria	~20%
Isolated proteinuria	~10%
Peripheral edema	20–30%
CKD at presentation	~15%
AKI at presentation	<5%

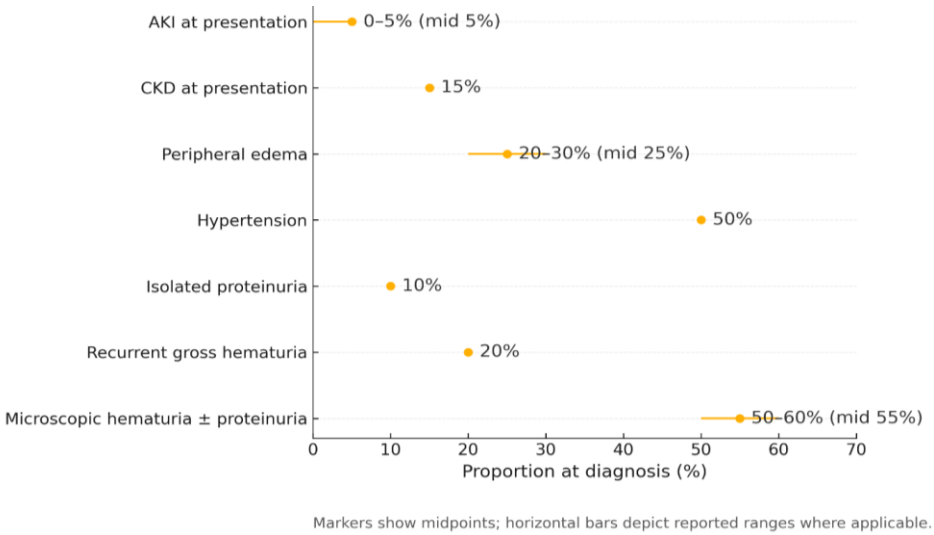

Figure 3: Clinical presentation patterns in IgA nephropathy (n = 127)

CHAPTER FOUR
DISCUSSION

Within the time span of 2020 to 2025, across the three centers located in Erbil, Sulaymaniyah, and Duhok in Northern Iraq, 6.0% of the native kidney biopsies performed IgAN. Out of the 127 verified cases from the biopsy, the population was mostly comprising of patients aged between 15 and 56 years of age, and the ratio of males to females was modest, around 53.5% male predominance. The most common symptom was microscopic hematuria, with 50-60% of patients. Recurrent gross hematuria was present in 1/5 of the population, while isolated proteinuria was present in 10% of the studied population. Around 50% of the population presented with hypertension, while 25% had edema, 15% had CKD, and less than 5% had AKI. The mean BMI was 26 kg/m^2, and some patients had BMI's ranging from 20 to 33 kg/m^2. These patients were found to have co-morbidity with hypertension and proteinuria. The yield of biopsying for IgAN is recorded at 6%, which, given the different IgAN referral patterns and thresholds for biopsy, makes sense on a global scale, and also aligns with the understanding that IgAN is a highly prevalent glomerulopathy in young adults. The clinical

picture corresponds to the classical phenotype of the condition, with the hallmark of microscopic hematuria anchored by episodic macroscopic hematuria in a minority and a range of proteinuria. The lower threshold prevalence of 50% of hypertensive patients at the time of diagnosis is indicative of the hemodynamic burden, which has not been and needs to be addressed in the framework of early preventive renoprotective therapy. The 15% of patients with Stage 1 CKD is indicative of the more advanced stages to which a certain sub-group is referred for biopsy, while the absence of AKI is consistent with the characteristically insidious course, interspersed with relatively innocuous flares rather than a sudden, devastating assault on the kidneys, which is the more common clinical picture for patients with IgAN.

The plausibility of the link between obesity and the conditions of hypertension and proteinuria is rational in biological terms.[27-29] By increasing the internal pressure of the glomeruli, amplifying the glomeruli filtration load, increasing the activity of the RAAS and sympathetic nervous system, and augmenting the excretion of sodium by the nephron tubule, all of which translate to increased albumin excretion and blood pressure, obesity has a major effect. In IgAN, mesangial injury and podocyte stress may, with the addition of hemodynamic strain, become unmasked or accelerated to a clinically evident state.[30] There is circumstantial evidence that the type of data we collected has a different interpretation, these patterns also point to the potential for modification.

There are certain immediate practices that can be identified. Firstly, the systematic institution of RAAS blockade, alongside appropriate SGLT2 inhibitors, and reaching tight blood pressure targets, becomes crucial with hyperention.[31] This is especially important in reducing the level of progression and the amount of proteinuria present. The second conclusion that can be made is that, since the dominant feature of the disorder is microscopic hematuria, primary care physicians are encouraged to start urinalyses in young adults that present with vague symptoms or primary hypertension, especially in areas that have similar epidemiological concerns. Another factor of the obesity signal is the integration of weight loss management into the standard care pathways of IgAN patients. The reduction of albumin in heavier patients, and blood pressure in patients with glomerular disease, is significant particularly with the shedding of modest weight.[32] The last thing to analyze is the presenting subset with established CKD. This represents an earlier opportunity to enhance protocols on the accessibility of referral and biopsy, particularly in regard to the renoprotective approach. This would occur with the assumption that there is no irreversible scarring.

This multicenter study is the first to capture how IgAN presents at the time of biopsy across three cities in Northern Iraq. Disparities in the thresholds for biopsy, the system of referrals, along with the level of local resources allocated to the problem, fundamentally case the difference in yield and stage at diagnosis. Forming a unified criteria for biopsy in cases of sustained hematuria and proteinuria, making immunofluorescence readily accessible, and establishing a region-wide clinical pathway may diminish the variability and time taken to arrive at a diagnosis. The latter, in turn, promotes the establishment of a provincial registry to enable benchmarking such as time taken to biopsy after the first abnormal urinalysis, and the uptake of RAAS/SGLT2 therapies.[33] This will in turn facilitate quality improvement initiatives.

Multiple mechanisms work in concert to drive IgAN: creation of IgA1 with a galactose deficiency, autoantibodies to anti-glycans, immune complexes, and deposition on the mesangial, resulting in activation of the mesangial, engagement of complement (often through alternative/lectin pathways), and subsequent damage to the glomeruli. The clinical phenotype we observe, which is predominantly mesangial, is the dominance of hematuria with varying degrees of proteinuria. The latter condition, along with positively correlating factors such as hypertension and obesity, is plausibly accelerated through glomerular hypertension and tubular-interstitial crosstalk. While we did not consider the intensity of complement staining or the Oxford MEST-C scores, the addition of these histological parameters will enhance mechanistic conclusions if employed in future work.

Some notable strengths pertain to the multicenter scope across three metropolitan areas, the uniform and confirmed diagnoses across centers by light microscopy and immunofluorescence, and the explicit description of proportions and of the exact numerators available. The analysis makes no attempt to claim greater precision than is warranted, and as such, reports the midpoint-with-range method for the variables provided as ranges and confidence intervals for the primary biopsy yield.

The retrospective design poses the risk of information bias and center-level variation in the documentation of heterogeneity. Several core variables were available only as ranges as opposed to patient-level counts, which severely limited the inferential statistics and precluded any adjusted analyses. We lacked detailed metrics of severity such as the quantity of proteinuria in 24 hours, UPCR, eGFR, histologic scoring with the Oxford MEST-C, the use of medications, and the collection of longitudinal datasets which means we lack the ability to estimate the progression rate of the disease or the rate of responsiveness to treatment. Selection bias may arise as a result of differing biopsy thresholds, while survivorship and referral bias may impact the proportion with CKD at baseline. We conservative depicted AKI "<5%," which we feel in our depiction could hide important clinical insight, though we could be wrong.

Capturing data during patient care serves as an important touchpoint for follow-up, and in this case, a prospective

registry on patients' standardized baseline metrics (UPCR/ACR, eGFR, Oxford MEST-C) on therapy initiation, and, subsequently, yearly outcomes (eGFR slope, remission/relapse), could facilitate meaningful risk assessment for the region. Furthermore, conducting region-specific analytics could target actionable differences in practice patterns (time-to-biopsy, antihypertensive intensity, diet/weight-management access). More focused investigations on the cardio-renal protective effect (weight loss, blood pressure reduction, sodium restriction) would help elucidate the effect sizes proposed by these associations. Where possible, mechanistic insights could be obtained by targeted complement profiling (e.g. Gd-IgA1) or clinical biomarker panels.

In three Northern-Iraq centers, IgA nephropathy (IgAN) comprised 6% of biopsached native kidney diseases. IgAN classically presents as a kidney-affected individual with microscopic hematuria, frequent hypertension, and an intermediate burden of proteinuria. This results in a significant number of individuals with IgAN already in CKD at the time of diagnosis. At this stage, the presence of obesity with increased hypertension and proteinuria emerges as an actionable risk factor. This emphasizes the rationale for universal urine screening in young adults with these associations and highlights the potential of early aggressive reno-protective interventions and improved integrated cardiometabolic care. The next step in the region is to build a prospective, multi-center registry with harmonized clinical and histologic data to convert these insights into actionable, precise management for IgAN.

CHAPTER FIVE
CONCLUSION & RECOMMENDATION

This study conducted in 3 centers in Northern Iraq (Erbil, Sulaymaniyah, Duhok) noted that IgA nephropathy renal biopsies was 127 out of 2119 natives in the hospitals from the year 2020 to 2025 which is roughly 6.0%. The biopsies were of individuals aged 15 to 56 years and were noted to have a male bias with some of the specimens showing a 53.5% male demographic. A significant portion of the individuals, nearly 50 to 60% of the individuals strained showed some signs of microscopic hematuria with proteinuria, while a recurrent gross hematuria was noted with the same amount in about roughly 20% of the individuals and some isolated proteinuria in around 10%. Almost one half of the individuals and the same amount were noted to have some signs of edema and hypertension, while around 15% of the individuals were diagnosed with CKD and AKI was noted to be rare to the population sample and was under 5%. The average body mass index of the individuals was noted to be 26 kg/m² with a range of 20 to 33. Also, the individuals diagnosed with obesity coincided with some hypertense and were noted to have heavier proteinuria. Overall, the data demonstrates a hematuria-dominant phenotype with evidence of high hemodynamic stress on the kidney and a significant portion who have considerable CKD have late presentation of the disease, emphasizing the need for more detection and proactive treatment for the patients.

In practice, we recommend a suppression therapy approach for young women with hypertension, non-specific edema, and other vague symptoms, with a uniform regimen that includes the SGLT2 inhibitors where appropriate. These should include routine home BP monitoring with prompt urinalyses and micromorphologically targeted referrals. Care pathways should incorporate cardiometabolic strategies, weight loss, sodium intake, and physical activity, since the association between obesity and elevated BP and proteinuria is well described. Stratified risk assessments should include UPCR/ACR, eGFR, and the Oxford MEST-C score. At the center, biasing the criteria for persistent hematuria/proteinuria, equitable availability of immunofluorescence, and the adoption of a standard data form at the biopsy and first clinic visit reduces heterogeneity and loss to follow-up. Quality indicators such as the interval between the first abnormal urinalysis and biopsy and treatment within 30 days can facilitate improvement, driven by multidisciplinary teams that include BP nursing and dietetic teams.From the viewpoint of research and system infrastructure, a prospective registry across three centers, with uniform baseline, histology, treatment, and outcome records, along with regionally structured risk modeling, will facilitate inter-center practice modifications and support practical studies of lifestyle changes, with mechanisms for complement/biomarker profiling that integrate the clinical phenotype to the mechanism, when possible. In terms of policy, the primary care system will consider the education of practitioners on the importance of simple screenings, such as urinalysis and blood pressure measurements, along with primary care driven referral systems, as well as comprehensive access to diagnostic centers and essential medicines across the three hospitals, which will ultimately result in the decreased diagnostic odyssey and improved prognosis for patients suffering from IgA nephropathy in the Northern regions of Iraq.

REFERENCES

1. Luvizotto MJ, Menezes-Silva L, Woronik V, Monteiro RC, Câmara NOS. Gut-kidney axis in IgA nephropathy: Role on mesangial cell metabolism and inflammation. *Frontiers in Cell and Developmental Biology*, 2022; 10: 993716.
2. Oshima Y, Moriyama T, Itabashi M, Takei T, Nitta K. Characteristics of IgA nephropathy in advanced-age patients. *International urology and nephrology*, 2015; 47(1): 137-145.
3. Wen Q, Rong R, Zhou Q, et al. Clinical, pathological characteristics and outcomes of immunoglobulin A nephropathy patients with different ages. *Nephrology*, 2020; 25(12): 906-912.
4. Wang S, Qin A, Dong L, Tan J, Zhou X, Qin W. stage renal disease in IgA nephropathy patients. *The*

impact of adipose tissue dysfunction on cardiovascular and renal disease, volume II. 2023;
5. Oates A. IgA nephropathy. *Adolescents with Chronic Kidney Disease: From Diagnosis to End-Stage Disease*. Springer, 2018: 107-128.
6. Schena FP, Nistor I. Epidemiology of IgA nephropathy: a global perspective. Elsevier, 2018: 435-442.
7. Tan L, Jin L-H, Wang Y-Q, Chen W, Wen Q. Clinical features, pathological characteristics, and prognosis of patients with IgA nephropathy complicated with nephrotic syndrome. *Scientific Reports*, 2025; 15(1): 1804.
8. Donadio Jr JV, Grande JP. Immunoglobulin A nephropathy: a clinical perspective. *Journal of the American Society of Nephrology*, 1997; 8(8): 1324-1332.
9. Beukhof JR, Kardaun O, Schaafsma W, et al. Toward individual prognosis of IgA nephropathy. *Kidney international*, 1986; 29(2): 549-556.
10. D'Amico G. Natural history of idiopathic IgA nephropathy and factors predictive of disease outcome. Elsevier, 2004: 179-196.
11. Qin Y, Yu Z, Wu H, et al. Prognostic factors affecting long-term outcomes in patients with concurrent IgA nephropathy and membranous nephropathy. *Heliyon*, 2024; 10(1)
12. Suzuki H. Biomarkers for IgA nephropathy on the basis of multi-hit pathogenesis. *Clinical and experimental nephrology*, 2019; 23(1): 26-31.
13. Knoppova B, Reily C, King RG, Julian BA, Novak J, Green TJ. Pathogenesis of IgA nephropathy: current understanding and implications for development of disease-specific treatment. *Journal of clinical medicine*, 2021; 10(19): 4501.
14. Suzuki H, Novak J. IgA glycosylation and immune complex formation in IgAN. Springer, 2021; 669-678.
15. Chang S, Li X-K. The role of immune modulation in pathogenesis of IgA nephropathy. *Frontiers in medicine*, 2020; 7: 92.
16. Hamed M. *The role of the complement system in the pathogenesis of IgA nephropathy*. University of Leicester, 2022.
17. Zhang H, Deng Z, Wang Y. Molecular insight in intrarenal inflammation affecting four main types of cells in nephrons in IgA nephropathy. *Frontiers in Medicine*, 2023; 10: 1128393.
18. Haas M. The Pathology of IgA Nephropathy: How Can It Inform Management? Elsevier, 2025; 151568.
19. Hull KL, Adenwalla SF, Topham P, Graham-Brown MP. Indications and considerations for kidney biopsy: an overview of clinical considerations for the non-specialist. *Clinical Medicine*, 2022; 22(1): 34-40.
20. Moresco RN, Speeckaert MM, Delanghe JR. Diagnosis and monitoring of IgA nephropathy: the role of biomarkers as an alternative to renal biopsy. *Autoimmunity reviews*, 2015; 14(10): 847-853.
21. Kao T-W, Huang C-C. Blood pressure management and renal protection: Revisiting hypertensive nephropathy. *Journal of the Chinese Medical Association*, 2021; 84(10): 911-916.
22. Leoncini G, Viazzi F, De Cosmo S, Russo G, Fioretto P, Pontremoli R. Blood pressure reduction and RAAS inhibition in diabetic kidney disease: therapeutic potentials and limitations. *Journal of Nephrology*, 2020; 33(5): 949-963.
23. Fabbrini E, Klein S. Fundamentals of cardipmetabolic risk factor reduction: achieving and maintaining weight loss with pharmacotherapy or bariatric surgery. *Clinical Cornerstone*, 2008; 9(1): 41-51.
24. Shankar M, Lamech TM. Treatment burden in glomerular diseases: advances and challenges in immunosuppressive therapy. *Frontiers in Nephrology*, 2025; 5: 1545373.
25. Dong Y, Shi S, Liu L, Zhou X, Lv J, Zhang H. Effect of SGLT2 inhibitors on the proteinuria reduction in patients with IgA nephropathy. *Frontiers in Medicine*, 2023; 10: 1242241.
26. Hallford D, Carmichael A, Austin D, Takano K, Raes F, Fuller-Tyszkiewicz M. A study protocol for a randomised trial of adjunct computerised memory specificity training (c-MeST) for major depression in youth: targeting cognitive mechanisms to enhance usual care outcomes in mental health settings. *Trials*, 2020; 21(1): 85.
27. Hall JE, do Carmo JM, da Silva AA, Wang Z, Hall ME. Obesity, kidney dysfunction and hypertension: mechanistic links. *Nature reviews nephrology*, 2019; 15(6): 367-385.
28. Leggio M, Lombardi M, Caldarone E, et al. The relationship between obesity and hypertension: an updated comprehensive overview on vicious twins. *Hypertension research*, 2017; 40(12): 947-963.
29. Hall ME, do Carmo JM, da Silva AA, Juncos LA, Wang Z, Hall JE. Obesity, hypertension, and chronic kidney disease. *International journal of nephrology and renovascular disease*, 2014; 75-88.
30. Thomas HY, Ford Versypt AN. Pathophysiology of mesangial expansion in diabetic nephropathy: mesangial structure, glomerular biomechanics, and biochemical signaling and regulation. *Journal of Biological Engineering*, 2022; 16(1): 19.
31. Redon J, Carmena R. Present and future of drug therapy in hypertension: an overview. *Blood Pressure*, 2024; 33(1): 2320401.
32. Wang TJ, Evans JC, Meigs JB, et al. Low-grade albuminuria and the risks of hypertension and blood pressure progression. *Circulation*, 2005; 111(11): 1370-1376.
33. Riaz MM, Rizvi N, Sabir O, Rafique K, Manzoor S. Page Kidney: Possible complication of renal biopsy. *Pakistan Journal of Kidney Diseases*, 2019; 3(8).