Practice Pattern of Indian Nephrologists Pertaining to The Management of IgA Nephropathy

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Background and Objective of the Survey

Background

IgA Nephropathy, also known as Berger's disease, is the most common form of primary glomerulonephritis worldwide and a significant cause of chronic kidney disease. The condition is characterized by the deposition of immunoglobulin A (IgA) in the glomeruli, leading to progressive kidney damage in many patients. The clinical presentation of IgA Nephropathy can vary widely, from asymptomatic hematuria to a rapid progression towards end-stage renal disease.

In India, the prevalence of IgA Nephropathy appears to be on the rise, reflecting trends observed in other parts of the world. However, management practices can differ substantially due to variations in healthcare systems, availability of resources, and regional differences in disease expression and progression. There is a notable lack of comprehensive data on how Indian nephrologists approach the diagnosis, treatment, and long-term management of IgA Nephropathy. This variability in practice patterns can significantly affect outcomes for patients with this condition.

IgA Nephropathy (IgAN)

IgA Nephropathy (IgAN), also known as Berger's disease, is a kidney disorder that occurs when IgA—a type of antibody—builds up in the kidneys, leading to inflammation that can affect kidney function. It is the most common form of primary glomerulonephritis globally and can progress to chronic kidney disease (CKD) or even end-stage renal disease (ESRD) in some cases.

Pathophysiology

IgA Nephropathy is characterized by the deposition of the IgA antibody in the glomerular mesangium (part of the kidney's filtering system), which triggers a local inflammatory response. This inflammation can cause the glomeruli—the filtering units in the kidney—to become damaged and scarred, impairing the kidneys' ability to filter waste, excess water, and electrolytes from the blood.

Clinical Presentation

Symptoms of IgA Nephropathy can vary widely among individuals:

- Many patients are asymptomatic initially and are diagnosed incidentally through abnormal findings on routine urinalysis, showing blood or protein in the urine.
- Some may present with episodes of visible blood in the urine (gross hematuria), often following an upper respiratory or other infection.

- Other symptoms include proteinuria (excess protein in urine), high blood pressure, and swelling in the hands and feet (edema).

Objective

- The primary objective of this study is to evaluate the practice patterns of nephrologists across India pertaining to the management of IgA Nephropathy.
- This encompasses a range of practices, including diagnostic strategies, choices of therapeutic interventions, and monitoring and follow-up protocols.
- By identifying current practices, the study aims to highlight areas of consensus and divergence among practitioners and to pinpoint gaps in adherence to international guidelines or evidence-based practices.
- This research will provide valuable insights that could inform future guidelines tailored to the specific needs and constraints of the Indian healthcare environment, ultimately aiming to improve patient outcomes across diverse regional settings within the country.

Methodology of the Survey

A survey was conducted to understand the current Opinion on "**Practice pattern of Indian nephrologists pertaining to the management of IgA Nephropathy**" and to understand the market better and offer better services to improve the patient outcome. A total of 80 doctors from India participated in the survey.

Step 1:

A literature search was done on the topic. Below topics were covered in literature search:

- **Clinical Practice Patterns in IgA Nephropathy: A Global Questionnaire-Based Survey**
- **Global Incidence of IgA Nephropathy by Race and Ethnicity: A Systematic Review**

Step 2:

A survey questionnaire was prepared based on the literature search. The survey form was shared through digital medium with 80 doctors across India.

Step 3:

Their responses were analysed and the findings are provided in this survey analysis booklet.

Literature Review

Clinical Practice Patterns in IgA Nephropathy: A Global Questionnaire-Based Survey

Introduction

IgA Nephropathy (IgAN) is recognized as a prevalent primary glomerular disease with a clinical spectrum that ranges from asymptomatic and non-progressive to a rapidly deteriorating condition. This disease carries a substantial risk, with approximately 20% to 40% of patients progressing to end-stage kidney disease within a decade, exhibiting notable ethnic disparities. Particularly in Asian countries, IgAN tends to present more aggressively, influencing management strategies specific to these regions.

Since its inception in 2003, the Kidney Diseases Improving Global Outcomes (KDIGO) Clinical Practice Guidelines have served as a pivotal resource for the management of various glomerular diseases, including IgAN. The 2021 revision of these guidelines primarily focuses on enhancing supportive nephroprotective therapies for patients with IgAN. Notably, some recommendations within the KDIGO guidelines are tailored to specific regions, reflecting the outcomes of localized clinical trials.

Despite the prevalence of prescribed treatments, there remains a scarcity of evidence supporting their efficacy. This gap underscores the necessity of evaluating the practical management of IgAN. To address this, we have initiated a global distribution of an ad hoc questionnaire aimed at capturing diverse nephrological approaches to the various clinical manifestations of IgAN.

Methods

A questionnaire-based survey was developed, focusing on both supportive therapy and immunosuppression use in IgAN in accordance with the KDIGO 2021 Clinical Practice Guidelines for the Management of Glomerular Diseases , one year after publication. It was piloted among 10 nephrologists from different nations with expertise in managing patients with IgAN. The final questionnaire was distributed using mailing lists of various nephrology societies across the world and by scoping the literature for practitioners in nephrology. All participants gave their electronic consent before proceeding with the survey.

The survey questionnaire consisted of two steps. The first step was divided into two parts as follows: (i) demographic data and (ii) practice patterns in IgAN. Considering that the KDIGO guidelines suggest enrolling patients at high risk of disease progression (defined as persistent proteinuria >1g/d despite optimized

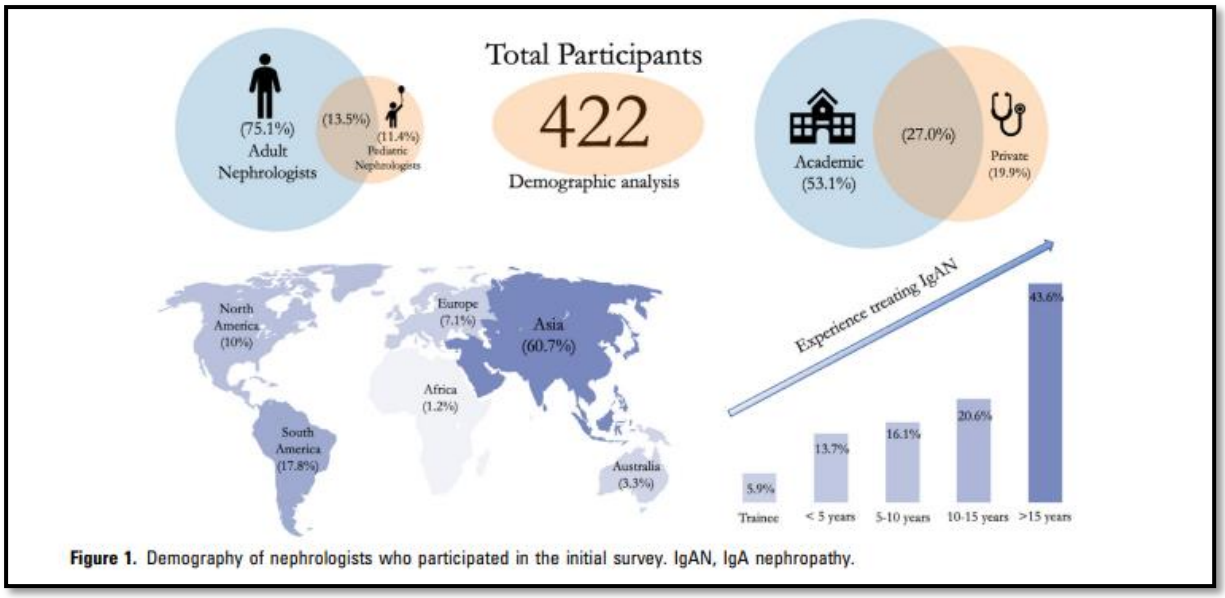

Figure 1. Demography of nephrologists who participated in the initial survey. IgAN, IgA nephropathy.

supportive care for at least three months) in clinical trials, the second step was designed as a short survey to assess the attitude of nephrologists towards randomized clinical trials (RCTs) that evaluate newly developed drugs in IgAN and was circulated among those who had responded to the initial survey. However, some nephrologists who did not participate in the first step of the questionnaire participated in the second step because their colleagues shared the survey. The study was approved by the Institute Ethics Committee, All India Institute of Medical Sciences, New Delhi.

Statistical Analysis

All data were tabulated in Microsoft Excel and analyzed using the statistical software Stata 14.0 (College Station, TX). Descriptive statistics of percentages, medians (interquartile ranges), and means (SD) were reported where appropriate. Standard statistical tests were performed to assess whether regional and demographic parameters influenced responses. A P-value of ≤0.05 was considered significant.

The initial questionnaire was answered by 422 nephrologists across the world, and their demographic details are shown in Figure 1.

Results

Initial Supportive Therapy

Details of the approach to supportive treatment are described in Tables 1 and 2. ACEi/ARB therapy (410/422, 97.2%) for proteinuria reduction and blood pressure control (386/422, 91.5%) are the most common initial supportive treatment strategies used across geographies. The majority of respondents (251/422, 59.5%) target blood pressure of ≤130/80 mm Hg. Dual RAAS blockade with ACEi and ARB is used by only 110 of 422 (26.1%) nephrologists, most commonly in South America

(43/73, 58.9%) and Europe (14/30, 46.7%) (P < 0.001). Overall, about half (224/422, 53.1%) prescribe mineralocorticoid receptor antagonists (MRA) for persistent proteinuria despite maximal doses of ACEi or ARB; this was more common in South America (48/73, 65.8%) and North America (26/42, 61.9%). Only 10 of 422 (2.4%) reported using MRAs in all patients. When the survey was undertaken, spironolactone and eplerenone were the only MRAs available for clinical use in Latin America and India.

SGLT2 inhibitors (205/422, 48.6%) and fish oil (184/422, 43.6%) are the most frequently used non-immunosuppressive therapies beyond RAAS blockade. Fish oil is used primarily in Asia (131/258, 50.8%) and South America (30/73, 41.1%) (P = 0.001).

Initiating Immunosuppression

The initial survey did not allow respondents to choose 'no immunosuppression' or 'recruitment to a clinical trial' as options for patients with persistent proteinuria. Most respondents (390/422, 92.4%) reported waiting at least three months before labeling the disease as unresponsive to supportive therapy and starting immunosuppression (Figure 2). While planning immunosuppression, considerations (Figure 3, Table 4) included proteinuria (371/422, 87.9%), renal function (332/422, 78.7%), and kidney histology (274/422, 64.9%). However, 58 of 422 (13.7%) nephrologists said they do not have access to the MEST-C scores, which was more common in Australia and Africa (Figure 4).

The majority of respondents (260/422, 61.6%) start immunosuppression if there is persistent proteinuria >1 g/d. In newly diagnosed patients with stable eGFR, 166 of 422 (39.3%) will start immunosuppression directly at proteinuria >3.5 g/d, especially in Asia (118/258, 45.7%) and South America (27/73, 37.0%). Many nephrologists (250/422, 59.2%) start immunosuppression immediately after diagnosis for patients with proteinuria >1 g/d if eGFR is <60 ml/min per 1.73 m², 57 of 422 (13.5%) would do so if eGFR <45 ml/min per 1.73 m², and 20 of 422 (4.7%) if eGFR is <30 ml/min per 1.73 m². Many nephrologists reported starting immunosuppression directly in patients with active, proliferative histological signs on biopsy, including E1 (162/422, 38.4%), C1 (108/422, 25.6%), C2 (214/422, 50.7%) lesions, and thrombotic microangiopathy (178/422, 42.2%). This practice is more commonly encountered in Asian countries compared to the rest of the world. A quarter (106/422, 25.1%) of our respondents use immunosuppression in patients diagnosed with secondary IgAN.

Over half (221/422, 52.4%) of the nephrologists, particularly in South America (48/73, 65.8%) and Australia (10/14, 71.4%), would prescribe concomitant cotrimoxazole prophylaxis for infection prevention while using immunosuppression (P = 0.007). Of the nephrologists, 175 of 422 (41.5%) routinely vaccinate patients for influenza virus and Pneumococcus before starting immunosuppression, and 107/422 (25.4%) do so only in high-risk populations.

Type of Immunosuppression

Details of immunosuppression use are depicted in Table 5. Corticosteroids are commonly used as first-line immunosuppression (376/422, 89.1%). Mycophenolate mofetil (208/422, 49.3%) and cyclophosphamide (76/422, 18.0%) are the two most frequently used second-line drugs in resistant patients, particularly in Asia and South America (P = 0.04). Cyclophosphamide (271/422, 64.2%) is most commonly combined with corticosteroids for patients with crescentic (with C2 lesions) IgAN. Asian and South American nephrologists are more likely to use immunosuppression in patients with C1 crescentic lesions, differing from nephrologists in other regions (P = 0.005).

When examining the practice patterns of nephrologists in academic institutes (224), private centers (84), or having a combined academic and private practice (114), we did not observe any significant difference except for less frequent counseling about protein restriction by academic nephrologists compared to others (65/224, 29.0% vs. 41/84, 48.8% vs. 52/114, 45.6%, respectively, P < 0.001) and more widespread use of fish oil by those in private practice compared to those in academic or combined practice (58/84, 69.0% vs. 81/224, 36.2% vs. 45/114, 39.5%, respectively, P < 0.001).

Table 1. Initial supportive treatment

Question	Asia (n = 258)	South America (n = 73)	Europe (n = 30)	North America (n = 42)	Australia (n = 14)	Africa (n = 5)	Total (N = 422)	P-value
Initial supportive treatment strategy								
Salt restriction	195 (75.6%)	61 (83.6%)	23 (76.7%)	25 (59.5%)	7 (50.0%)	2 (40.0%)	313 (74.2%)	0.008
Protein restriction	97 (37.6%)	41 (56.2%)	7 (23.3%)	9 (21.4%)	2 (14.3%)	2 (40.0%)	158 (37.4%)	0.001
Blood pressure control	237 (91.9%)	67 (91.8%)	27 (90.0%)	38 (90.5%)	13 (92.9%)	4 (80.0%)	386 (91.5%)	0.956
Renin-angiotensin-aldosterone system blockade with ACEi/ARB therapy	252 (97.7%)	68 (93.2%)	29 (96.7%)	42 (100.0%)	14 (100.0%)	5 (100.0%)	410 (97.2%)	0.278

ACEi, angiotensin-converting-enzyme inhibitors; ARB, angiotensin receptor blockers

Nephrologists' Attitude to Clinical Trials in IgAN

We received 339 responses to the follow-up survey about clinical trials in IgAN (Table 6). Only 103 of 339 (30.4%) enroll patients in clinical trials, and this practice is less common in Asia (27/157, 17.2%) and South America (35/112, 31.3%) compared to North America, Europe, and Australia (>50%).

Nephrologists in high and upper-middle-income countries were significantly more likely to enroll patients in clinical trials compared to those in LMICs (Figure 5, P < 0.001). Additionally, 81 of 105 (77.1%) nephrologists from high-income countries, 81 of 135 (60%) from upper-middle-income countries, and only 40 of 99 (40.4%) from LMICs were aware of clinical trials with novel drugs being conducted in their respective countries (Figure 6, P < 0.001).

Table 2. Approach to blood pressure control and renin-angiotensin-aldosterone system (RAAS) blockade

Question	Asia (n = 258)	South America (n = 73)	Europe (n = 30)	North America (n = 42)	Australia (n = 14)	Africa (n = 5)	Total (N = 422)	P-value
Target blood pressure?								<0.001
<120/80 mm Hg	76 (29.5%)	41 (56.2%)	15 (50.0%)	21 (50.0%)	4 (28.6%)	0 (0%)	157 (37.2%)	
<130/80 mm Hg	172 (66.7%)	31 (42.5%)	14 (46.7%)	21 (50.0%)	8 (57.1%)	5 (100.0%)	251 (59.5%)	
<140/90 mm Hg	10 (3.9%)	1 (1.4%)	1 (3.33%)	0 (0%)	2 (14.3%)	0 (0%)	14 (3.3%)	
Preference of ACEi vs. ARB in patients prescribed RAAS blockers								<0.001
No preference	94 (36.4%)	30 (41.1%)	12 (40.0%)	17 (40.5%)	7 (50%)	4 (80%)	164 (38.9%)	
ACEi first with ARB used only if intolerant to ACEi	65 (25.2%)	29 (39.7%)	16 (53.3%)	20 (47.6%)	4 (28.6%)	1 (20%)	135 (32.0%)	
ARB first with ACEi used only if intolerant to ARB	99 (38.4%)	14 (19.2%)	2 (6.7%)	5 (11.9%)	3 (21.4%)	0 (0%)	123 (29.1%)	
Feel that ACEi and ARBs have the same effect on proteinuria	181 (70.2%)	48 (65.8%)	19 (63.3%)	33 (78.6%)	12 (85.7%)	5 (100%)	298 (70.6%)	0.26
Usage of dual RAAS blockers	46 (17.8%)	43 (58.9%)	14 (46.7%)	4 (9.5%)	3 (21.4%)	0 (0%)	110 (26.1%)	<0.001
Use of mineralocorticoid receptor antagonists								<0.001
No	128 (49.6%)	18 (24.7%)	17 (56.7%)	16 (38.1%)	7 (50%)	2 (40.0%)	188 (44.5%)	
In all patients	2 (0.8%)	7 (9.6%)	0 (0%)	0 (0%)	1 (7.1%)	0 (0%)	10 (2.4%)	
Persistent proteinuria despite maximal doses of ACEi/ARB	128 (49.6%)	48 (65.8%)	13 (43.3%)	26 (61.9%)	6 (42.9%)	3 (60%)	224 (53.1%)	

ACEi, angiotensin-converting-enzyme inhibitors; ARB, angiotensin receptor blockers. RAAS, renin-angiotensin-aldosterone system.

Table 3. Adjunct non-immunosuppressive therapies

Question	Asia (n = 258)	South America (n = 73)	Europe (n = 30)	North America (n = 42)	Australia (n = 14)	Africa (n = 5)	Total (N = 422)	P-value
Adjunct therapies used for supportive management								
Tonsillectomy	16 (6.2%)	9 (12.3%)	1 (3.3%)	1 (2.4%)	0 (0%)	0 (0%)	27 (6.4%)	0.206
Antiplatelet agents	25 (9.7%)	11 (15.1%)	1 (3.3%)	0 (0%)	0 (0%)	1 (20.0%)	38 (9.0%)	0.054
Fish oil	131 (50.8%)	30 (41.1%)	7 (23.3%)	14 (33.3%)	1 (7.1%)	1 (20.0%)	184 (43.6%)	0.001
Hydroxychloroquine	36 (14%)	12 (16.4%)	2 (6.7%)	5 (11.9%)	1 (7.1%)	0 (0%)	56 (13.3%)	0.674
SGLT2 inhibitors	130 (50.4%)	28 (38.4%)	14 (46.7%)	24 (57.1%)	8 (57.1%)	1 (20.0%)	205 (48.6%)	0.243

SGLT2, sodium-glucose co-transporter-2.

Discussion

IgAN (IgA nephropathy) is a disease characterized by its pathological, genetic, and clinical heterogeneity, which undermines the effectiveness of a universal treatment approach. Treatment strategies are tailored based on factors such as clinical symptoms, histological findings, demographics, geographic location, and ethnic diversities even within the same region.

The 2021 KDIGO guidelines primarily advocate for a nephroprotective strategy which includes stringent blood pressure management, sodium intake reduction, cessation of smoking, and weight management, especially since there were no approved specific therapies for IgAN at the time of the latest publication. The guidelines recommend maximizing RAAS (Renin-Angiotensin-Aldosterone System) blockade for patients with significant proteinuria (exceeding 0.5 g/day), regardless of the presence of hypertension. For high-risk patients with persistent proteinuria greater than 0.75 to 1 g/day despite three months of supportive care, the use of corticosteroids or enrollment in a randomized controlled trial (RCT) is advised. However, the potential adverse effects of corticosteroids, particularly in patients with reduced eGFR (less than 50 ml/min/1.73 m^2), must be carefully weighed against their benefits.

The use of RAAS blockade with ACE inhibitors or ARBs is widely implemented as the initial treatment for IgAN, alongside managing hypertension. Many practitioners also use mineralocorticoid receptor antagonists (MRAs) when proteinuria persists despite maximal tolerated doses of ACEi/ARBs. The application of MRAs, effective in managing hypertension and reducing proteinuria in other kidney diseases, is anticipated to increase with the recent availability of drugs like finerenone.

Additional therapies such as fish oil and SGLT2 inhibitors are often prescribed despite the absence of specific guidelines endorsing their use. Fish oil, favored in Asia and South America, is popular due to its accessibility, affordability, and minimal side effects despite inconsistent evidence of its efficacy. SGLT2 inhibitors have gained attention following trials such as the Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease, which included IgAN patients and suggested benefits in disease progression, despite not being specifically designed for IgAN.

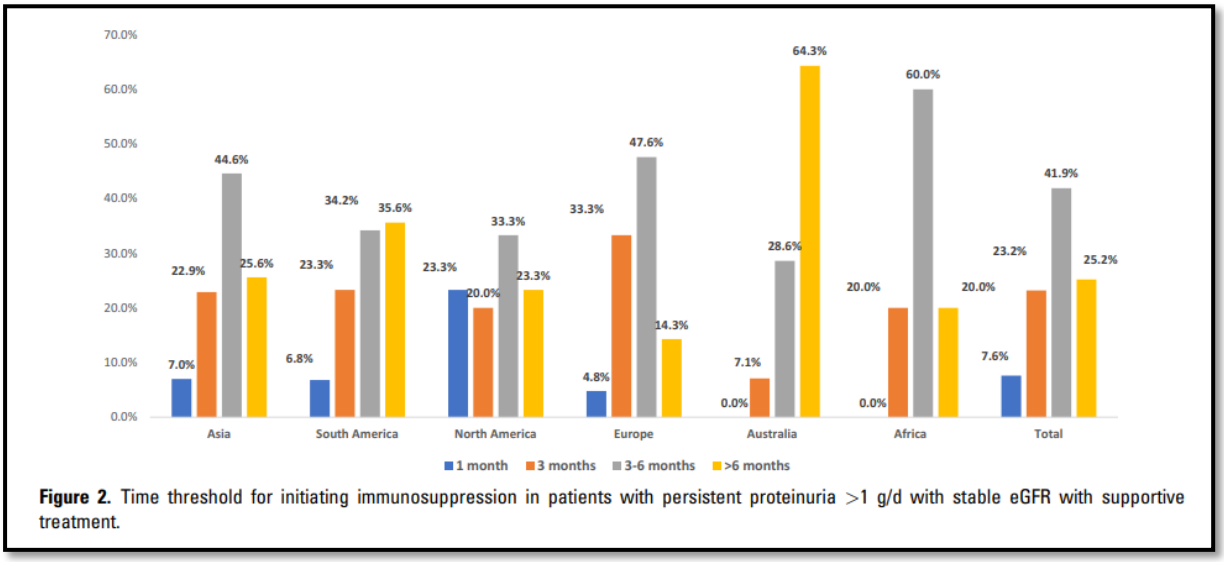

Figure 2. Time threshold for initiating immunosuppression in patients with persistent proteinuria >1 g/d with stable eGFR with supportive treatment.

The employment of immunosuppression in IgAN remains controversial and varies regionally. Most nephrologists adhere to waiting at least three months after initiating supportive care before considering immunosuppression, as per KDIGO guidelines. This is even the case for patients with certain proliferative lesions, where the risks of immediate immunosuppression versus a watch-and-wait approach continue to be debated.

Immunosuppression is also commonly used in advanced disease stages and secondary IgAN, despite recommendations to focus on treating the primary disease in these cases. This highlights a need for improved medical education to prevent unnecessary immunosuppressive treatment and its associated risks.

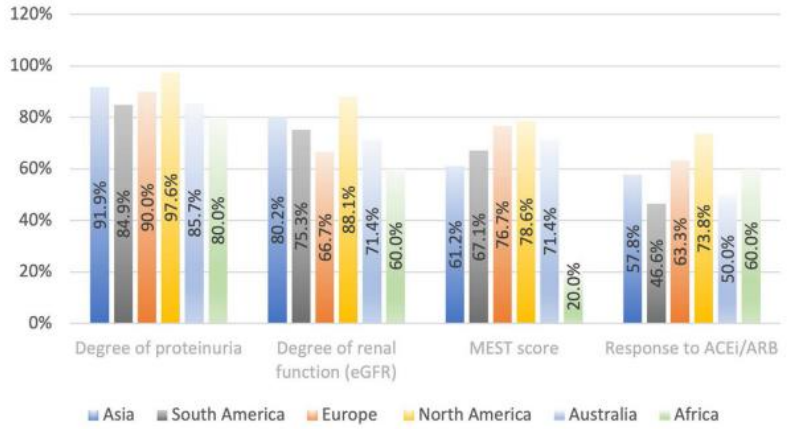

Figure 3. Parameters considered by nephrologists for initiating immunosuppression. ACEi, angiotensin-converting-enzyme inhibitors; ARB, angiotensin receptor blockers; eGFR, estimated glomerular filtration rate.

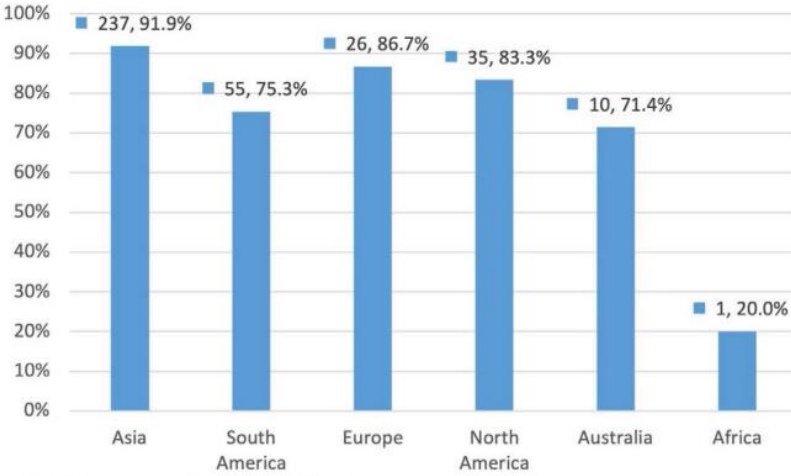

Figure 4. Frequency of MEST-C score reporting in kidney biopsies.

The response from nephrologists globally reveals significant regional variations in the management of IgAN, influenced by local practices, availability of treatment options, and economic constraints. This variation underscores the necessity for guidelines that accommodate diverse healthcare settings and socioeconomic conditions, particularly in low- and middle-income countries where access to care and clinical trials may be limited. The overarching goal should be to harmonize IgAN treatment approaches while considering the practical realities faced by healthcare providers worldwide.

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Global Incidence of IgA Nephropathy by Race and Ethnicity: A Systematic Review

Introduction

IgA nephropathy is diagnosed on the basis of the finding of dominant or codominant IgA deposition in the glomeruli by immunofluorescence microscopy. Failure to biopsy—because of either lack of health care access or rapid progression to ESKD—may result in underdiagnosis. Previous studies have suggested that higher rates of biopsy among those with kidney injury and suspected IgA nephropathy are associated with higher local estimates of IgA nephropathy.1 Race/ethnicity may affect IgA nephropathy incidence estimates both because genetic factors could contribute to true race-based risk for IgA nephropathy and because race may also be associated with access to kidney biopsy. In this review, we sought to estimate the incidence of IgA nephropathy in US populations, place these estimates within an international context, and relate them to race and other demographic characteristics.

IgA nephropathy incidence has been reported to be higher among East Asians than among other groups.2–7 Population-based genome-wide association studies have identified multiple IgA nephropathy susceptibility loci for sporadic IgA nephropathy, but full understanding of the genetics of IgA nephropathy has not been reached.8 International studies have typically stated that the incidence of IgA nephropathy is highest in populations of Asian descent, lower in populations of European descent, and lower still in populations of African descent.9,10 However, Europeans are over-represented in most studies, and research on IgA nephropathy is sparse in African populations where lack of access to biopsy may lead to underreporting of IgA nephropathy.11,12 Meanwhile, relatively little is known regarding the incidence of IgA nephropathy in South Americans or among US Hispanics, who were 18.7% of the US population in 2020.13,14

Most studies of IgA nephropathy incidence have been conducted in racially homogenous countries, making interstudy comparisons perilous. We systematically reviewed the relevant global literature, seeking to understand the roles of race/ethnicity and other factors in IgA nephropathy incidence in the United States and elsewhere.

Methods

Selection of Regions

Initially, we focused on the few studies of the demographic characteristics associated with IgA nephropathy within the United States. For global context, we also examined published IgA nephropathy incidence data from all continents and major world regions: North America, Europe, Asia, South America, Australia, and Africa.

Selection of Studies

Studies were eligible for inclusion if they contained data collected from 1974 to 2021, had abstracts and articles written in English, and reported IgA nephropathy incidence at a population level. L. Segall conducted the initial literature search. A.I. Neugut and D.E. Freedberg screened the abstracts. When there was lack of agreement, complete articles were reviewed, and ties were resolved by consensus. Studies were excluded if they did not directly report IgA nephropathy incidence and did not provide sufficient data to allow it to be calculated (*i.e.*, the annual number of IgA cases or the size of the at-risk population could not be determined). We included reports of regional or population-based IgA nephropathy incidence so that we could compare locations with different demographic makeups. When studies did not directly report IgA nephropathy incidence rates, we calculated them by dividing the number of IgA nephropathy cases reported in the study by the at-risk population. We included all US studies that met the entry criteria and up to two studies each for non-US nations; when we found more than two studies of a non-US nation, we selected the two most recent ones. Relevant studies were identified by searching PubMed, Embase, Google, and Google Scholar using the terms “IgA nephropathy incidence,” “IgAN prevalence,” “IgAN epidemiology,” and “IgAN incidence by race.” We also searched for relevant studies using individual country names to ensure inclusion of countries from all the intended regions.

Results

Studies Identified

Our search terms initially identified 1692 studies, of which 33 seemed to meet criteria for inclusion on the basis of the study abstracts (*i.e.*, these studies seemed to report a population-based incidence for IgA nephropathy). We reviewed these 33 studies in full and excluded ten, keeping five US and 18 international studies for data extraction (Figure 1). The US studies were conducted in Central and Eastern Kentucky; Olmsted County, Minnesota; Shelby County, Tennessee; New Mexico; and Southern California. The international studies that met the criteria

for inclusion were conducted in France, the United Kingdom, Northern Ireland, the Netherlands, Germany, the Czech Republic, Estonia, Japan, Singapore, Australia, Peru, Brazil, and South Africai incidence of IgA Nephropathy in US Studies

In the five US studies, the overall incidence of IgA nephropathy ranged from 0.39 (Tennessee) to 1.4 (Minnesota) per 100,000 population United States. Three studies reported incidence by race. Two reported a higher incidence in individuals self-identified as White compared with Black (Kentucky and Southern California), whereas the study from Tennessee reported a higher incidence in Black patients.16–18 Next, we sought to understand the relationship between race and IgA nephropathy incidence by plotting the overall IgA nephropathy incidence against the proportion of individuals self-identified as White non-Hispanics within the study population. We observed a quasilinear relationship, although with only five data points.

Incidence of IgA Nephropathy Across Various Locations

Southern California

A study within the Kaiser Permanente healthcare system in Southern California, spanning January 2000 to December 2011 and covering over three million individuals, recorded an overall IgA nephropathy incidence of 0.7 per 100,000. The highest incidence rate was observed among Asians (2.75 per 100,000), while the lowest was among Black patients (0.1 per 100,000).

New Mexico

Research in New Mexico, examining over 98% of kidney biopsies between 2000 and 2005 from a population of 1.8 million, reported an incidence of 0.93 per 100,000. The demographic breakdown of the biopsied population included 21% non-Hispanic White, 49% Hispanic, 21% American Indian, and 9% others, including African American and Asian/Pacific Islander. However, race-specific incidence rates were not detailed.

Olmsted County, Minnesota

In Olmsted County, data from the Mayo Clinic for the years 1974-2003, with a background population of three million, showed an IgA nephropathy incidence of 1.4 per 100,000 person-years. The report did not provide incidence by race, noting the county's limited racial and socioeconomic diversity, being 90% White by the study's end.

Central and Eastern Kentucky

From 1975 to 1994, a study in Central and Eastern Kentucky covering one million people reported incidence rates ranging from 0.62 to 1.02 per 100,000. Incidence was 1.07 per 100,000 for White individuals and 1.02 per 100,000 for Black individuals, with no data for other races. The study area was predominantly rural and 92% White.

Shelby County, Tennessee

In Shelby County, Tennessee, from 1975 to 1994, a study within a 200,000 population reported an overall IgA nephropathy incidence of 0.39 per 100,000, with 0.3 per 100,000 among White individuals and 0.57 per 100,000 among Black individuals. Other racial groups were not specified. The local demographic was 47% White and 49% Black.

Context of U.S. Studies Internationally

Internationally, IgA nephropathy incidence varied significantly, from as high as 10.5 per 100,000 in Australia to as low as 0.06 per 100,000 in South Africa. The median incidence internationally was 1.4 per 100,000, comparable to or higher than U.S. rates.

Temporal Trends in the United States

Incidence studies over time in the U.S. (Southern California, Minnesota, and Kentucky) showed regional variability. In Minnesota, incidence rose from 0.7 to 2.1 per 100,000 from 1974 to 2003. In Southern California, it increased from 0.1 to 1.6 per 100,000 from 2000 to 2011. In Kentucky, rates climbed from 0.5 in the late 1970s to 12.4 per 100,000 by the mid-1990s.

Incidence by Sex

Internationally and in the U.S., most studies noted a higher incidence of IgA nephropathy among males compared to females, except in Japan and Brazil where the rates were less skewed by gender.

Review and Future Directions

This systematic review highlights the significant variability in IgA nephropathy incidence both within the U.S. and internationally, with a noted higher incidence among Asians and males. It underscores the need for further studies that are racially and demographically comprehensive to better understand this variability.

Such studies should aim to include diverse populations to capture a broad spectrum of genetic and environmental factors influencing the disease.

SURVEY FORM

1. In your clinical practice, which is the most common form of glomerulonephritis?

A. Immunoglobulin A nephropathy (IgAN)

B. Membranous nephropathy

C. Nephrotic syndrome

D. Minimal change disease (MCD)

E. Focal segmental glomerulosclerosis (FSGS)

F. Lupus nephritis

2. In your clinical practice, how many patients present with IgA Nephropathy per month?

A. <5

B. 5-10

C. 11-20

D. 21-30

E. 31-40

F. 41-50

G. >50

3. In your clinical practice, what % of your CKD patients present with IgA Nephropathy?

A. <5%

B. 5-10%

C. 11-20%

D. 21-30%

E. 31-40%

F. 41-50%

G. > 50%

4. What is the initial support treatment that you offer to patients of IgA nephropathy?

A. Salt restriction

B. Protein restriction

C. Blood pressure control

D. Renin-angiotensin-aldosterone system blockade with ACEi/ARB therapy

5. Currently, what are your preferred first-line immunosuppression options in your patients presenting with IgA Nephropathy?

A. Corticosteroids

B. Mycophenolate mofetil

C. Cyclophosphamide

D. Azathioprine

E. Rituximab

F. Corticosteroid + cyclophosphamide

G. Corticosteroid + mycophenolate

H. Corticosteroid + azathioprine

6. What are the second-line immunosuppression used in patients with steroid resistant IgA nephropathy?

A. Corticosteroids

B. Mycophenolate mofetil

C. Cyclophosphamide

D. Azathioprine

E. M-TOR inhibitor

F. Calcineurin inhibitor

G. Rituximab

7. What is the rate of occurrence of abnormal glycemic control requiring treatment during corticosteroid therapy for IgA nephropathy?

A. ≤10%

B. 10–30%

C. 30–50%

D. ≥50%

8. In your practice, what % of your patients do not respond or remain refractory to the existing immunosuppression medications?

A. 5-10%

B. 11-20%

C. 21-30%

D. 31-40%

E. 41-50%

F. > 50%

9. In your practice, what % of your patients do not tolerate immunosuppression medications?

A. 5-10%

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10. What are the parameters considered by you for initiating immunosuppression?

A. Degree of proteinuria

B. Degree of renal function

C MEST score

D. Response to ACEi/ARBs

11. In which of the following patients do you avoid immunosuppressant?

A. Creatinine>2.5mg/dl

B. GFR<30–50ml/min/1.73m2

C. Extensive tubular interstitial and Advanced glomerulosclerosis in renal biopsy

12. What is the renal survival rate of patients diagnosed with IgA Nephropathy in 10 years?

A. <50%

B. 50-60%

C. 60-70%

D. 70-80%

13. What % of IgA nephropathy patients progress to ESRD over 20 years?

A. <25%

B. 25-50%

C. 51-75%

D. >75%

14. Do you think that there is an unmet need for the definitive treatment of IgA nephropathy?

A. Yes

B. No

15. In what % of your patients with IgA nephropathy, do you use budesonide?

A. 10-30%

B. 31-50%

C. 51-70%

D. 71-90%

E. 91-100%

16. What should be the key features of any drug candidate targeted for IgA Nephropathy?

A. Should reduce proteinuria

B. Should improve GFR

C. Both A & B

SURVEY FINDING

1. In your clinical practice, which is the most common form of glomerulonephritis?

A. Immunoglobulin A nephropathy (IgAN)

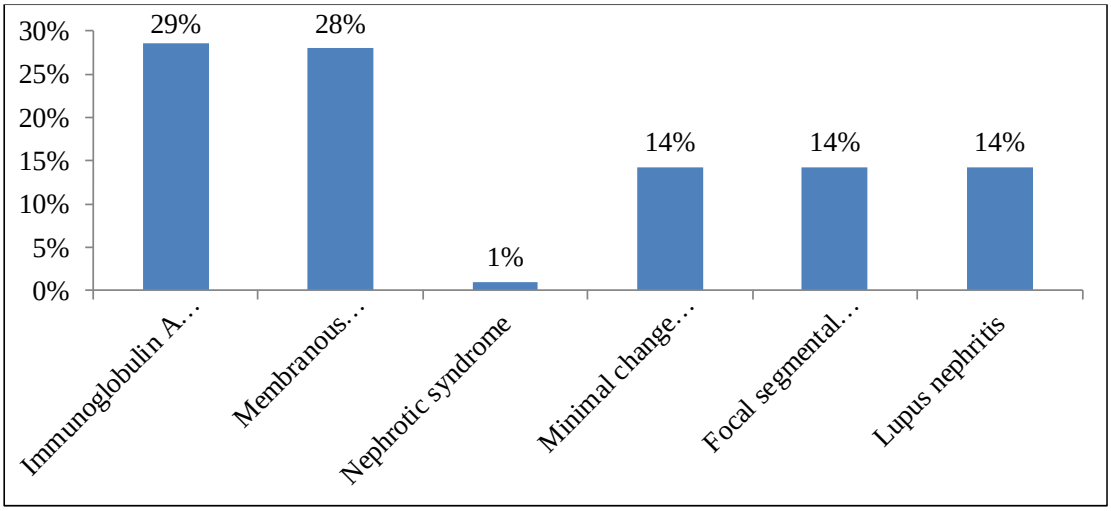
B. Membranous nephropathy

C. Nephrotic syndrome

D. Minimal change disease (MCD)

E. Focal segmental glomerulosclerosis (FSGS)

F. Lupus nephritis



In the clinical practice, the most common form of glomerulonephritis is Immunoglobulin A nephropathy (IgAN). This condition represents a significant proportion of glomerular diseases encountered in clinical settings.

2. In your clinical practice, how many patients present with IgA Nephropathy per month?

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B. 5-10

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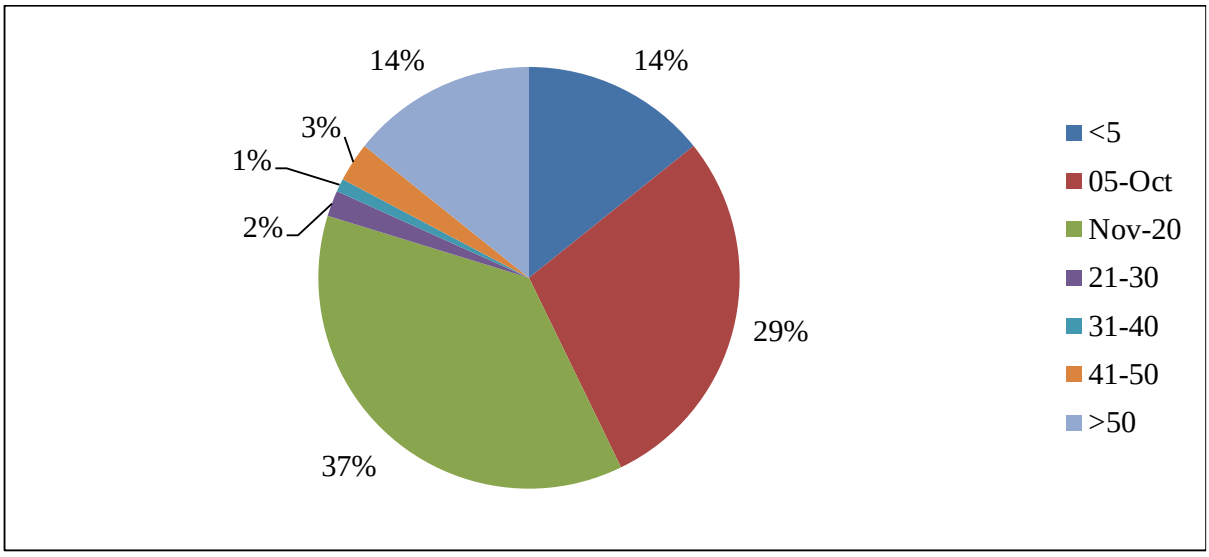

In clinical practice, approximately 11-20 patients present with IgA Nephropathy per month. This condition accounts for a notable portion of the glomerular diseases encountered in my practice.

3. In your clinical practice, what % of your CKD patients present with IgA Nephropathy?

A. <5%

B. 5-10%

C. 11-20%

D. 21-30%

E. 31-40%

F. 41-50%

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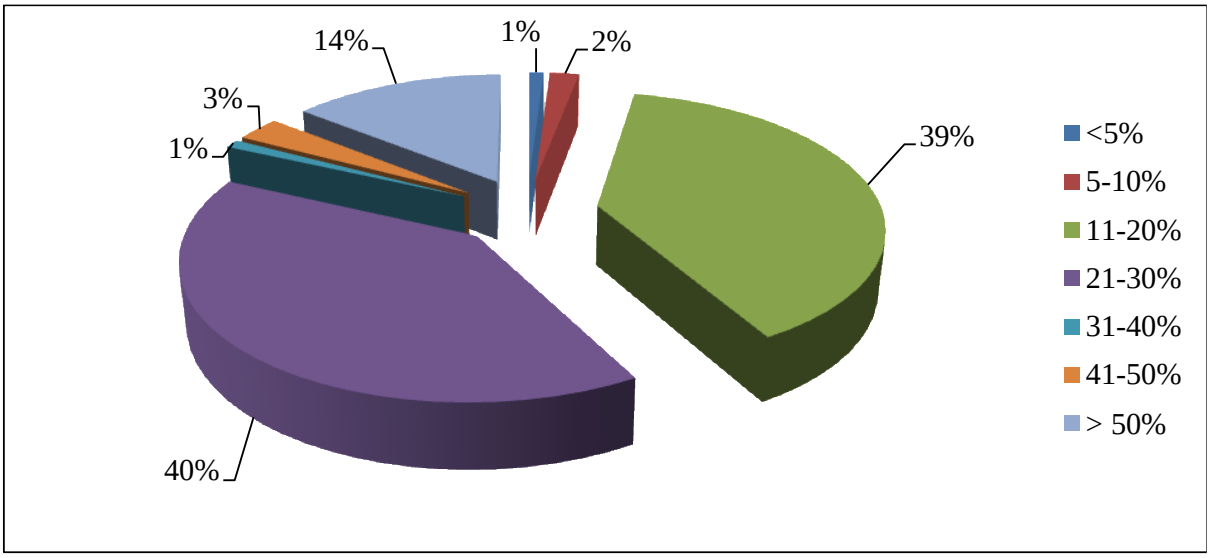


In clinical practice, approximately 21-30% of my CKD patients present with IgA Nephropathy. This indicates that IgA Nephropathy is a significant contributor to the burden of chronic kidney disease among my patients.

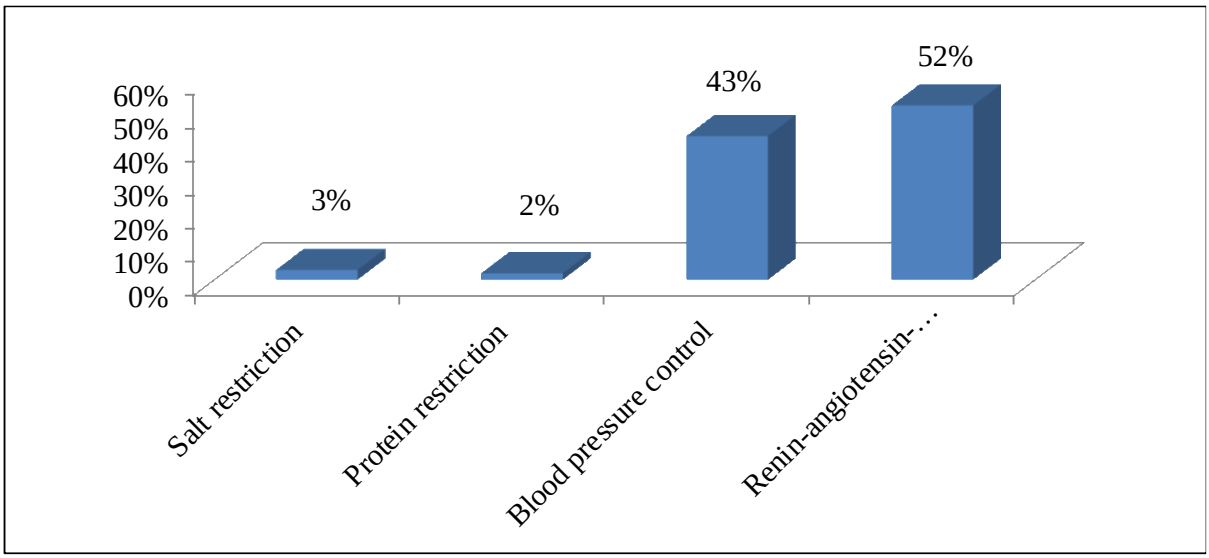
4. What is the initial support treatment that you offer to patients of IgA nephropathy?

A. Salt restriction

B. Protein restriction

C. Blood pressure control

D. Renin-angiotensin-aldosterone system blockade with ACEi/ARB therapy



The initial support treatment that I offer to patients with IgA nephropathy is Renin-angiotensin-aldosterone system blockade with ACEi/ARB therapy. This approach, chosen by 52% of clinicians, aims to manage blood pressure and mitigate renal damage by targeting the renin-angiotensin-aldosterone system.

5. Currently, what are your preferred first-line immunosuppression options in your patients presenting with IgA Nephropathy?

A. Corticosteroids

B. Mycophenolate mofetil

C. Cyclophosphamide

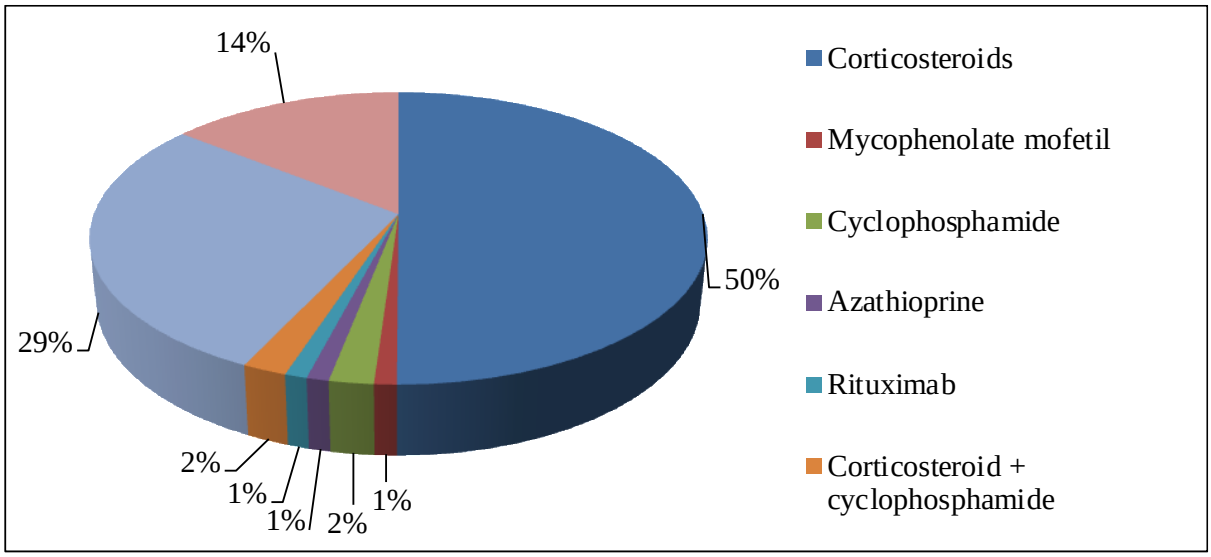
D. Azathioprine

E. Rituximab

F. Corticosteroid + cyclophosphamide

G. Corticosteroid + mycophenolate

H. Corticosteroid + azathioprine



Currently, preferred first-line immunosuppression option in patients presenting with IgA Nephropathy is Corticosteroids, as selected by 50% of clinicians. This choice reflects the commonly utilized approach to managing inflammation and reducing proteinuria in IgA Nephropathy patients.

6. What are the second-line immunosuppression used in patients with steroid resistant IgA nephropathy?

A. Corticosteroids

B. Mycophenolate mofetil

C. Cyclophosphamide

D. Azathioprine

E. M-TOR inhibitor

F. Calcineurin inhibitor

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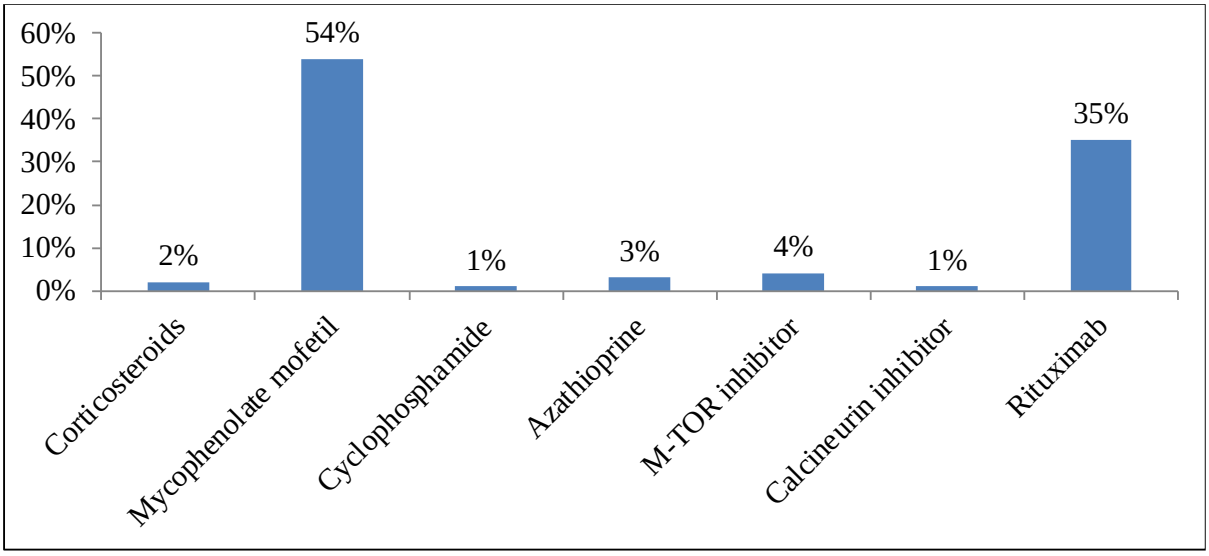


In patients with steroid-resistant IgA nephropathy, the second-line immunosuppression commonly used is Mycophenolate mofetil, selected by 54% of clinicians. This medication is often chosen to target the immune response and mitigate further renal damage in cases where corticosteroids are ineffective.

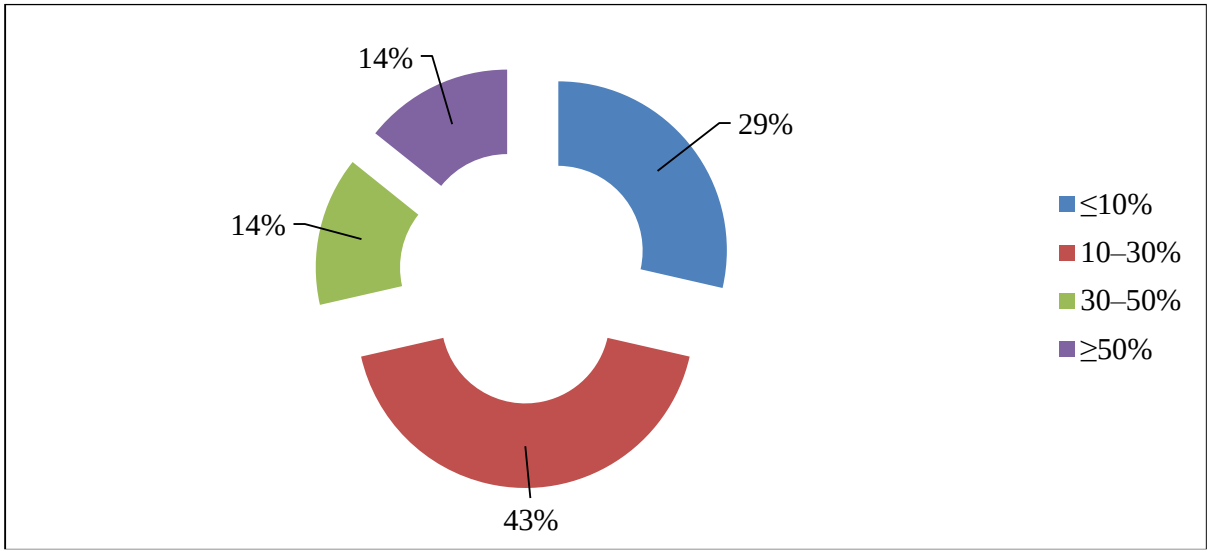
7. What is the rate of occurrence of abnormal glycaemic control requiring treatment during corticosteroid therapy for IgA nephropathy?

A. ≤10%

B. 10–30%

C. 30–50%

D. ≥50%



The rate of occurrence of abnormal glycemic control requiring treatment during corticosteroid therapy for IgA nephropathy is typically in the range of 10–30%. This indicates the importance of monitoring glycemic levels closely during corticosteroid treatment to manage any potential adverse effects.

8. In your practice, what % of your patients do not respond or remain refractory to the existing immunosuppression medications?

A. 5-10%

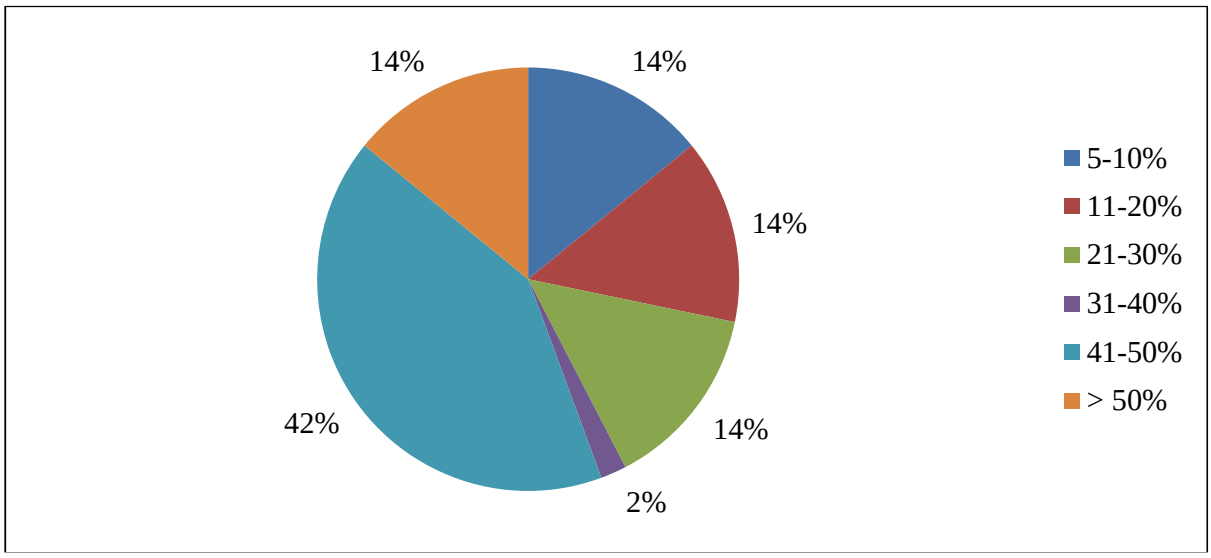
B. 11-20%

C. 21-30%

D. 31-40%

E. 41-50%

F. > 50%



In practice, approximately 41-50% of my patients do not respond or remain refractory to the existing immunosuppression medications. This suggests the need for alternative treatment strategies or adjunct therapies to address the challenges of managing IgA nephropathy in these cases.

9. In your practice, what % of your patients do not tolerate immunosuppression medications?

A. 5-10%

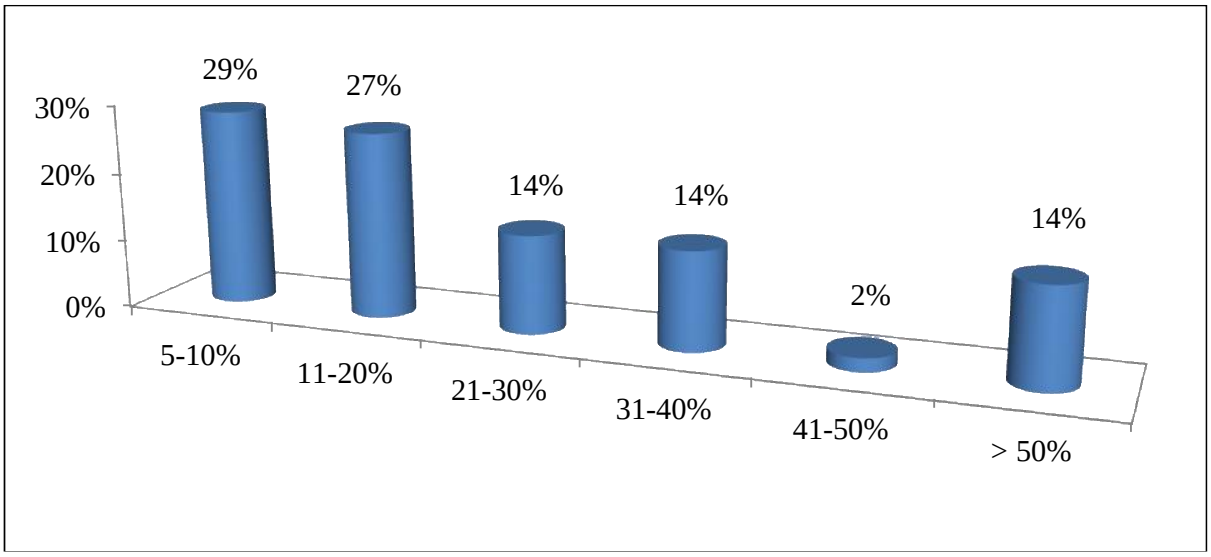
B. 11-20%

C. 21-30%

D. 31-40%

E. 41-50%

F > 50%



In practice, approximately 5-10% of patients do not tolerate immunosuppression medications. This indicates that the majority of patients can tolerate these medications, but a small percentage may experience intolerable side effects or adverse reactions, necessitating alternative treatment approaches.

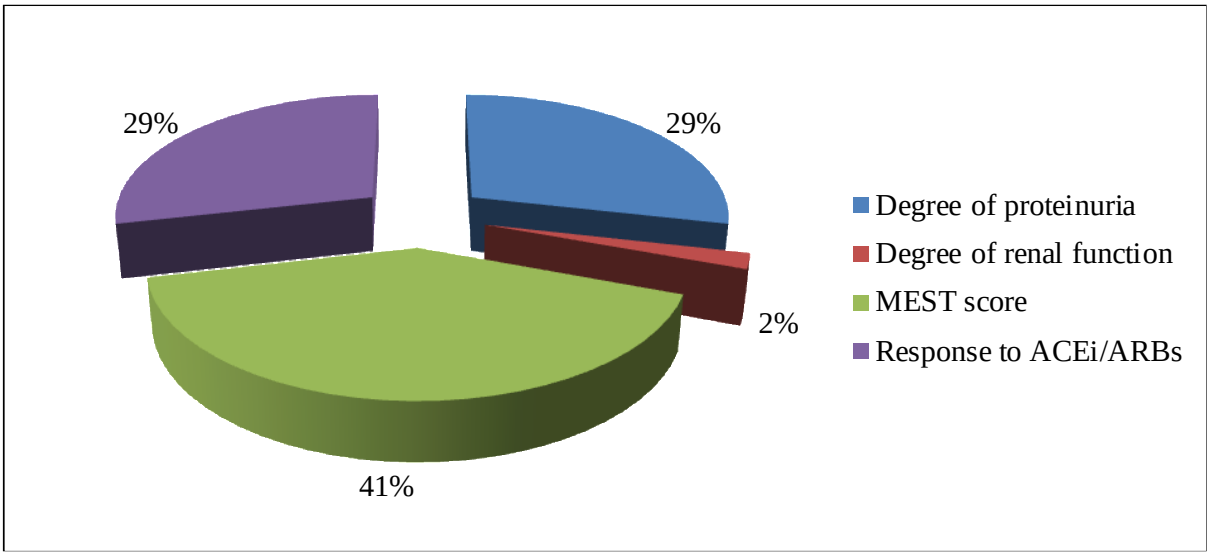
10. What are the parameters considered by you for initiating immunosuppression?

A. Degree of proteinuria

B. Degree of renal function

C MEST score

D. Response to ACEi/ARBs



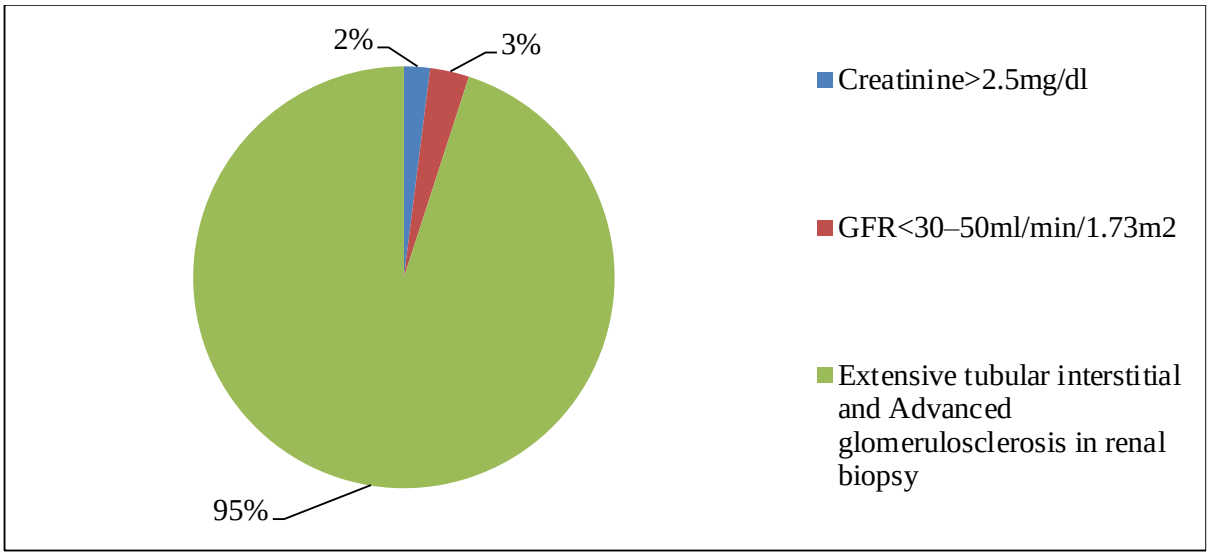
The parameters considered for initiating immunosuppression include the MEST score, which evaluates various histological features of IgA nephropathy, helping to determine the severity and prognosis of the disease.

11. In which of the following patients do you avoid immunosuppressant?

A. Creatinine>2.5mg/dl

B. GFR<30–50ml/min/1.73m2

C. Extensive tubular interstitial and Advanced glomerulosclerosis in renal biopsy



In patients with extensive tubular interstitial involvement and advanced glomerulosclerosis on renal biopsy, doctors typically avoid immunosuppressants.

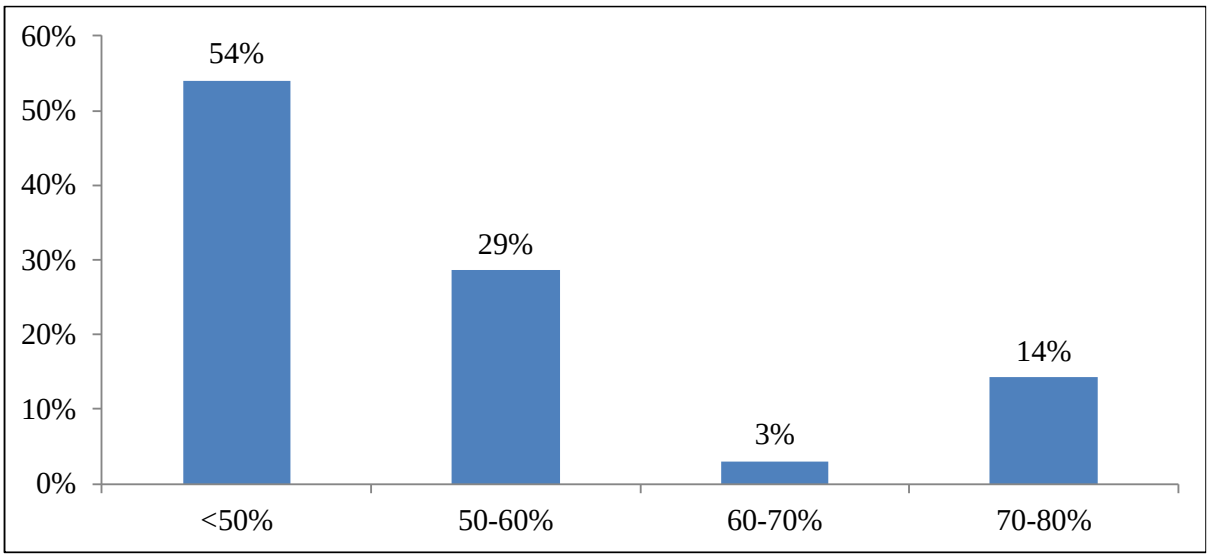
12. What is the renal survival rate of patients diagnosed with IgA Nephropathy in 10 years?

A. <50%

B. 50-60%

C. 60-70%

D. 70-80%



The renal survival rate of patients diagnosed with IgA Nephropathy in 10 years is typically less than 50%. This indicates that a significant proportion of patients may experience progressive renal impairment or require renal replacement therapy within this timeframe.

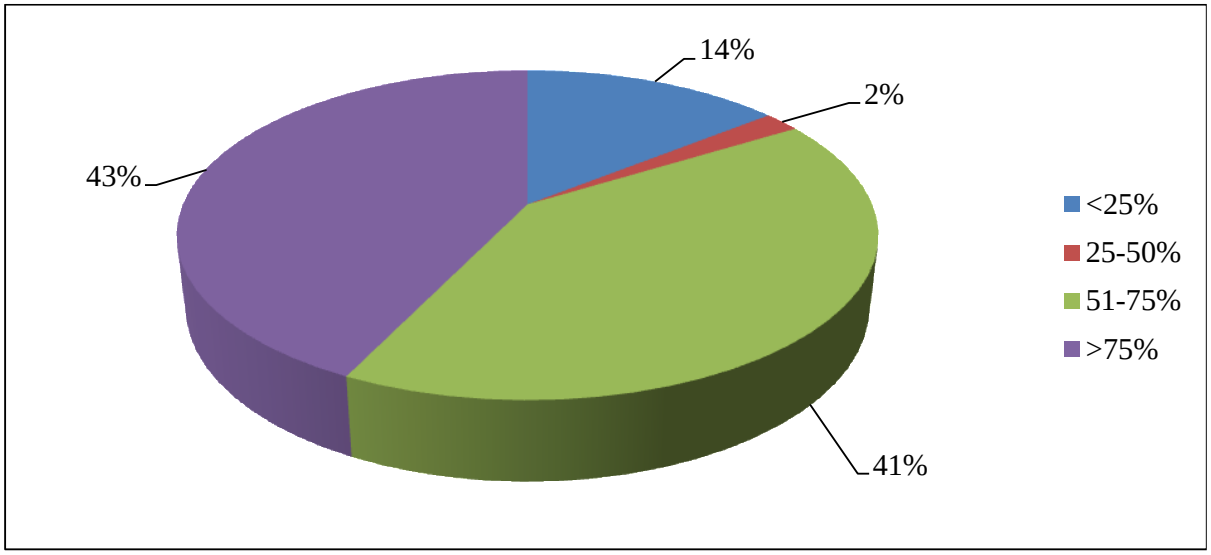
13. What % of IgA nephropathy patients progress to ESRD over 20 years?

A. <25%

B. 25-50%

C. 51-75%

D. >75%

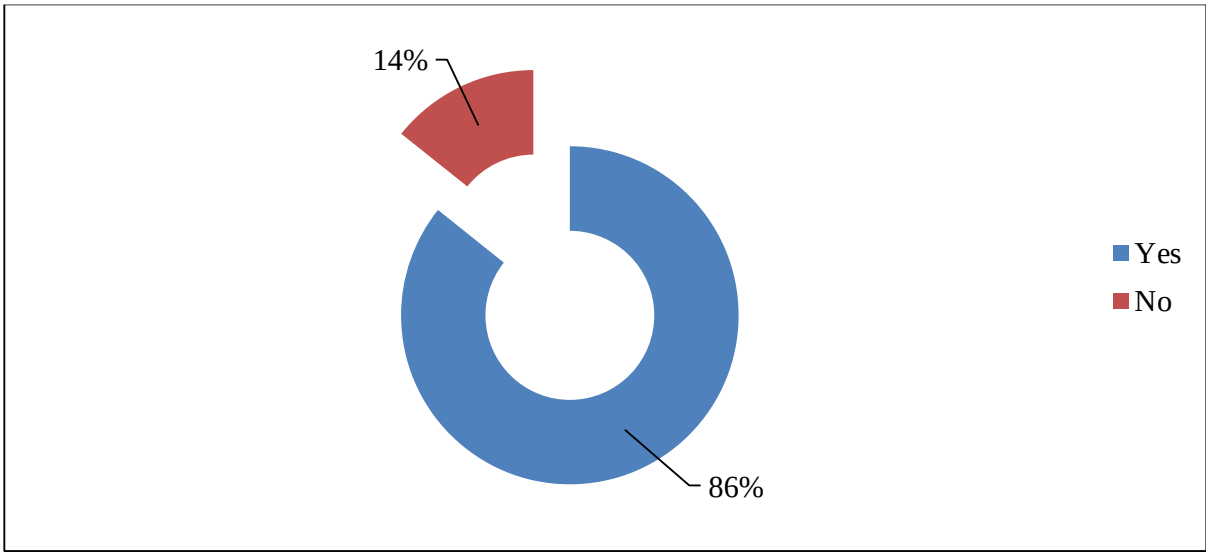


Approximately >75% of IgA nephropathy patients progress to end-stage renal disease (ESRD) over 20 years. This highlights the chronic and progressive nature of the disease, necessitating close monitoring and appropriate management strategies to delay disease progression and preserve renal function.

14. Do you think that there is an unmet need for the definitive treatment of IgA nephropathy?

A. Yes

B. No



There is an unmet need for the definitive treatment of IgA nephropathy, as indicated by 86% of respondents.

15. In what % of your patients with IgA nephropathy, do you use budesonide?

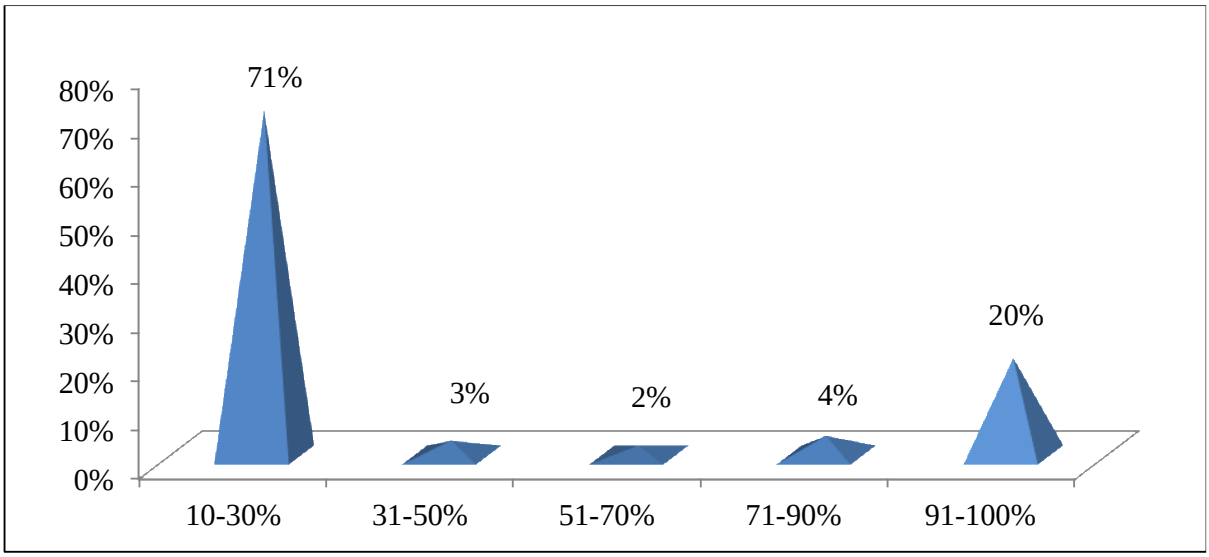
A. 10-30%

B. 31-50%

C. 51-70%

D. 71-90%

E. 91-100%



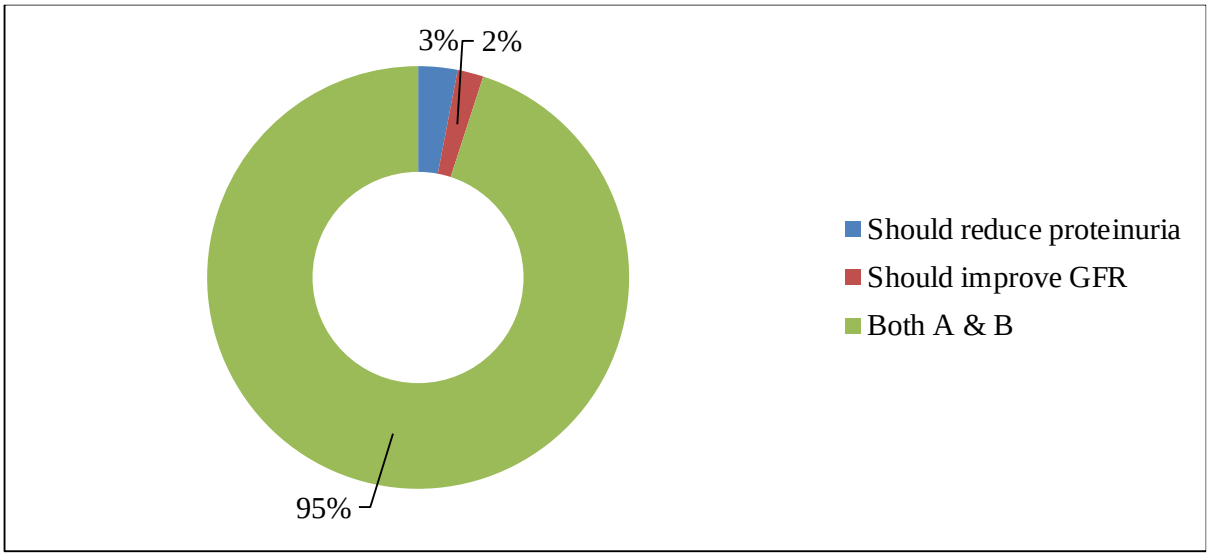
In practice, budesonide is used in approximately 10-30% of my patients with IgA nephropathy. This suggests that while budesonide may be a treatment option for some patients, it is not the primary therapeutic approach for the majority of cases.

16. What should be the key features of any drug candidate targeted for IgA Nephropathy?

A. Should reduce proteinuria

B. Should improve GFR

C. Both A & B



The key features of any drug candidate targeted for IgA Nephropathy should ideally include both reducing proteinuria and improving glomerular filtration rate (GFR)

SUMMARY

1. In the clinical practice, the most common form of glomerulonephritis is Immunoglobulin A nephropathy (IgAN). This condition represents a significant proportion of glomerular diseases encountered in clinical settings.

2. In clinical practice, approximately 11-20 patients present with IgA Nephropathy per month. This condition accounts for a notable portion of the glomerular diseases encountered in my practice.

3. In clinical practice, approximately 21-30% of my CKD patients present with IgA Nephropathy. This indicates that IgA Nephropathy is a significant contributor to the burden of chronic kidney disease among my patients.

4. The initial support treatment that I offer to patients with IgA nephropathy is Renin-angiotensin-aldosterone system blockade with ACEi/ARB therapy. This approach, chosen by 52% of clinicians, aims to manage blood pressure and mitigate renal damage by targeting the renin-angiotensin-aldosterone system.

5. Currently, preferred first-line immunosuppression option in patients presenting with IgA Nephropathy is Corticosteroids, as selected by 50% of clinicians. This choice reflects the commonly utilized approach to managing inflammation and reducing proteinuria in IgA Nephropathy patients.

6. In patients with steroid-resistant IgA nephropathy, the second-line immunosuppression commonly used is Mycophenolate mofetil, selected by 54% of clinicians. This medication is often chosen to target the immune response and mitigate further renal damage in cases where corticosteroids are ineffective.

7. The rate of occurrence of abnormal glycemic control requiring treatment during corticosteroid therapy for IgA nephropathy is typically in the range of 10–30%.

This indicates the importance of monitoring glycemic levels closely during corticosteroid treatment to manage any potential adverse effects.

8. In practice, approximately 41-50% of my patients do not respond or remain refractory to the existing immunosuppression medications. This suggests the need for alternative treatment strategies or adjunct therapies to address the challenges of managing IgA nephropathy in these cases.

9. In practice, approximately 5-10% of patients do not tolerate immunosuppression medications. This indicates that the majority of patients can tolerate these medications, but a small percentage may experience intolerable side effects or adverse reactions, necessitating alternative treatment approaches.

10. The parameters considered for initiating immunosuppression include the MEST score, which evaluates various histological features of IgA nephropathy, helping to determine the severity and prognosis of the disease.

11. The renal survival rate of patients diagnosed with IgA Nephropathy in 10 years is typically less than 50%. This indicates that a significant proportion of patients may experience progressive renal impairment or require renal replacement therapy within this timeframe.

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16. The key features of any drug candidate targeted for IgA Nephropathy should ideally include both reducing proteinuria and improving glomerular filtration rate (GFR)

CONSULTING OPINION

Market Opportunities:

Understanding the practice pattern of Indian nephrologists pertaining to the management of IgA Nephropathy presents significant opportunities for optimizing patient care. By analyzing current practices and identifying areas for improvement, healthcare stakeholders can develop tailored strategies to enhance treatment outcomes and patient satisfaction in the Indian context.

Value for Healthcare Professionals:

Indian nephrologists can derive substantial value from understanding and aligning with evidence-based management practices for IgA Nephropathy. This involves staying updated with international guidelines and adapting treatment strategies to suit local patient demographics, resource availability, and healthcare infrastructure. By providing effective and personalized care, nephrologists can improve patient outcomes and enhance professional satisfaction.

Adverse Effect Management:

Effectively managing adverse effects associated with IgA Nephropathy treatment is crucial for optimizing patient safety and tolerability. Nephrologists must be vigilant in monitoring patients for potential side effects of immunosuppressive therapies, such as infections, metabolic disturbances, and drug toxicities. Establishing robust adverse event management protocols and patient education programs can help mitigate risks and improve treatment adherence.

Effective Management:

Optimizing the management of IgA Nephropathy requires a multifaceted approach that addresses both the underlying disease pathology and associated

comorbidities. Nephrologists should employ evidence-based interventions, including renin-angiotensin-aldosterone system blockade, immunosuppressive therapy, and supportive measures to achieve optimal renal outcomes and mitigate disease progression.

Market Positioning:

Positioning IgA Nephropathy management strategies in the Indian healthcare market necessitates a nuanced understanding of local epidemiology, healthcare practices, and patient preferences. By aligning with emerging trends in nephrology care and leveraging advancements in treatment modalities, nephrologists can position themselves as leaders in delivering high-quality, evidence-based care for patients with IgA Nephropathy.

Personalized Treatment Decisions:

Tailoring treatment decisions based on individual patient characteristics is paramount in optimizing outcomes for IgA Nephropathy management. Nephrologists should consider factors such as disease severity, histological features, comorbidities, and patient preferences when selecting treatment options and monitoring response to therapy. By adopting a personalized approach, nephrologists can enhance treatment adherence and patient satisfaction.

Improving Patient Outcomes:

Ultimately, the goal of optimizing the practice pattern of Indian nephrologists in IgA Nephropathy management is to improve patient outcomes and quality of life. By embracing evidence-based practices, fostering interdisciplinary collaboration, and prioritizing patient-centered care, nephrologists can contribute to better renal outcomes, reduced disease burden, and improved long-term prognosis for patients with IgA Nephropathy in India.

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