# EPIDEMIOLOGICAL PROFILE CLINICO-PATHOLOGICAL CORRELATION AND TREATMENT RESPONSE IN ADULT PATIENTS WITH IGA NEPHROPATHY

*Dissertation submitted in partial fulfillment of*
*the requirements for the degree of*

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# CERTIFICATE

This is to certify that this Dissertation entitled "**Epidemiological profile, clinico-pathological correlation and treatment response in adult patients with IgA nephropathy**" is the bonafide original work of **Dr.P.SHANKAR**, in partial fulfillment of the requirement for D.M., (Nephrology) examination of the Tamilnadu Dr.M.G.R Medical University will be held in August 2013.


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## DECLARATION

I, Dr.P, SHANKAR, solemnly declare that the dissertation titled "**Epidemiological profile, clinico-pathological correlation and treatment response in adult patients with IgA nephropathy**" is the bonafide work done by me at Department of Nephrology, Madras Medical College under the expert guidance and supervision of Dr.N.GOPALAKRISHNAN D.M, FRCP, Professor of Nephrology, Madras Medical College. The dissertation is submitted to the Tamilnadu Dr.M.G.R Medical University towards partial fulfillment of requirement for the award of D.M. Degree (Branch III) in Nephrology.

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# INTRODUCTION

First described by Jean Berger as a disease entity with diffuse mesangial deposition of IgA deposits. Once thought to have benign entity of self limiting hematuria, now found to have slowly progressive in nature with the propensity to develope chronic kidney disease in 15-20 percent in 15 -20 years.

It presents with constellation of clinical syndrome ranging from asymptomatic urine abnormalities to smoldering rapidly progressive glomerulo nephritis. Diversity of clinical signs and syndrome is a constant feature.

With the advance in genetic, more molecular pathways are unraveled, pathogenesis were defined little better than previous, so this commonest glomerulonephritis is revealing its secrets.

Better understanding of glycation, galactosylation molecular machineries in depth of enzymes and chaperone, better search of happenings of talks of mesangium, podocytes and proximal tubule through cytokines and receptors, better knowledge of mucosa marrow axis and TLR clearly will open new prospective in treatment.

Epidemiological point of view, both increasing awareness such as treatment of for hematuria, prompt referral to the nephrologist, more precise immunoflourescence studies, IgA nephropathy incidence is on increasing trend . Hence proper, long term randomized control trials(RCT) needed in many areas of IgA nephropathy.

# AIM OF THE STUDY

1. To study the epidemiological profile of IgA nephropathy in adult patients.

2. To study the clinicopathological correlation of IgA nephropathy.

3. To evaluate the response to treatment, predictors of response and Risk factors in the progression to CKD in these patients.

# REVIEW OF LITERATURE

The first description of IgA nephropathy dated back in 1968 by Jean Berger[1]. Levy coined the term Berger's diseasein1973.Now it is the most frequent type of glomerulonephritis. Once thought to be benign recurrent hematuria, now an important cause for end stage renal disease. It is thought to IgA nephropathy be a constellation of clinical entity due to various injurious mechanism.

**Definition of IgA nephropathy**:

It is a pathological diagnosis needs light microscopy and immunoflourescence study of renal biopsy. Study of IgA nephropathy is defined as dominant or codominant staining with IgA of at least 1 + in the mesangial area[2].

**Epidemiology:**

IgA nephropathy is recognized as the most common form of primary glomerulonephritis in the world[3]. Incidence and prevalence of IgA nephropathy in general population shows a considerable variation among geographical regions. The reported incidence in three regions in France and one each in the Netherlands, Germany and Italy varied from 15 to 40 new cases per million populations per year[4-8]. Japan and Korea had highest recorded incidence . 48 percent of Japanese children initially identified through urinary screening program who subsequently

underwent a renal biopsy had IgA nephropathy. Fifty percentages of new cases of glomerulonephritis in Japan attributed to IgA nephropathy[9].

Available evidence suggests an increasing incidence in India. Indian studies showed 8.6% of renal biopsies (Vellore)[10], 14% of renal biopsies from Kerala[11], 16% of renal biopsies from western India[12]. Primary IgA nephropathy occurs at any age, most commonly with clinical onset in the second and third decades of life Male to female ratio around 1.5 to 1.85:1.

**Genetics:**

IgA Nephropathy mostly seen in Asian cohorts, rare among American and African blacks, highly prevalent in Zuni Manitoba Native Americans and Australian Aborigine, obviates search for genetic association.[13-18] Search for susceptible loci, modifier gene, environmental trigger was started[19]. Many genome wide studies points towards locus like IGAN1 on chromosome 6q22[20], 17 q12[21], and 2q36[22]. Micro RNA mirco148 b were upregulated[23]. Family history of IgA nephropathy was noted in 4-10% in UK[24]. So IgAN thought to be associated with polygenic genes includes both major histocompatability genes and non compatability genes. The gene mutation associated with beta 1,3 galactosyl transferase enzyme and cosmc were inconclusive[25-29]

**Lanthanic IgA deposits**

IgA deposits in mesangium is common in normal healthy individuals. (around 1 in 400) but only a few show clinical signs and picture of IgA. So, there lies an second hit mechanism either genetics or environmental.

**Pathogenesis:**

Basic structure of IgA:

IgA first appears in life in eleventh week after birth. IgA exists in two form.1.Serum IgA, 2.Mucosal (secretory) IgA. Serum IgA mostly present in monomeric (mostly IgA1) form with molecular weight 160000, produced from bone marrow. Mucosal IgA present with polymeric form joined by J chain, secreted from the mucosal surface. IgA1 accounts for 90% of serum IgA, produced in bone marrow, lymph nodes, plasma cells and spleen. IgA2 comprises 60% in mucosal areas. J chain produced from the same plasma cells that produce the dimeric IgA. This dimeric IgA-J chain complex get internalized from the basal layer of mucosa through IgA/RR dimer complex. This dimeric IgA extruded through the mucosal apical surface along with J chain and a extracellular part of RR IgA poly known as secretory component (SC).

IgA consists of two sub classes-IgA1, IgA2.

| | | |
|---|---|---|
| IgA1 | 10 O- glycosylation sites | 2 N - glycosylation sites |
| IgA2 | No O- glycosylation sites | 2-3 additional N - glycosylation sites |

**Glycosylation &galactosylation**

IgA1 contains 17 amino acid(AA) hinge region rich in serine, threonine and proline[31]. Three proline in the hinge region forms the universal joints and forms right angle bends.IgA2 devoid of 13 AA in the hinge region , resistive to proteolysis by bacteria, hence naturally present in mucosa. These hinge regions by addition of O- glycan chains thus undergoes post translation modifications. Glycosylation in hinge region (AA 223-240) takes place by addition of N acetyl galactosamine (GalNAC).Galactose get incorporated to the Serine or Threonine/GalNAC complex by C1GalT1(core1β 1,3 galactosyltransferase enzyme.) These Galactose residue sialylated by α 2,3 sialyltransferase enzyme. Addition of sialic acid directly to GalNAC by α2,6 sialyltransferase enzyme[32]. The beta 1, 3 galactosyl transferase enzyme stabilized by Cosmc (core 1 beta 1,3 galactosyltransferase molecular chaperone) which ensure proper folding.[33] Addition of sialic acid prevents the incorporation of galactose. So pathogenesis mainly resides in under galactosylation or over sialysation. The immortalized B-cells of patients with IgA nephropathy produce galactosylation deficient IgA[34] .

Normally IgD produced earlier in life were heavily glycosylated and less sialylated than IgA. Serum IgA was heavily glycosylated and sialylated. Mucosal IgA was poorly galactosylated. So there is down regulation of galactosylation and up regulation of sialyltransferase when there is class switch. In IgA Nephropathy IgD galactosylation pattern is not affected implies pathogenesis doesn't affect the entire B cell lineage[35]

**Two hit model** :

***Under galactosylation:***

Pathogenesis includes two hit model. First one is the presence of under galactosylated IgA1 O glycoforms in circulation and second one is the formation of IgG antibodies to it. Under galactosylation either by defective core1 β 1,3 galactosyltransferase enzyme,its chaperone cosmc or over sialysation by α2,6 sialyltransferase enzyme may elucidate pathogenesis, but genetic studies for mutation are inconclusive.

Ultimatum was the mesangial IgA deposition.Only 15% of deposits colocalise with secretory compononent (SC), others were not. So it is of polymeric IgA1 with undergalactosylation. Van Es et al suggested impaired mucosal bone marrow axis produce nephritogenic IgA. Due to mucosal infection there is a class

switch mediated by Toll like receptor (TLR 4,9)[36],IgA+ antibody secreting cells(ASC),which homes in systemic sites, produce normal mucosal type IgA 1

***IgG antibodies:***

These poorly galactosylated IgA1 invokes IgG antibodies react with neoepitopes. Cross reacting antibody produced molecular mimicry also reacts with it. Polymeric IgA also interacts with FCαR1 (CD 89) receptors on myeloid cells breaks to form larger sCD89 isoform (50-70 KDa), results in circulatory immune complexes[37-39]. These immune complexes (IC) reaches a molecular weight of 800-900 kDa . Normal serum IgA had short half life of 6 days as it is cleared through asialoglycan receptors in liver. As the fenestrae in liver to enter space of disse is around 200 A where as in glomerular capillary around 500-1000 A ,these IC got deposited in mesangium than cleared by liver[40].

***Mesangial and podocyte injury:***

This immune complexes recognized by transferring receptor (CD71), produce proinflammatory and profibrotic cytokines (IL-6,TGF β). Secretory component of IgA, with a high sialic acid content and its anionic property stimulates mesangial cells resulting in activation of the p42/p44 mitogen activated protein kinase, activator protein-1, and NF-B signal transduction pathways along with up-regulation of IL-6, transforming growth factor-β (TGF-β), tumor necrosis

factor (TNF-α), monocyte chemo attractant protein1 (MCP-1), IL-8, and macrophage migration inhibitory Factor[41-43].

By binding of IgA and immune complexes to the podocyte not through transferrin receptors but through an unidentified receptors , by loss of nephrin and by mesangium podocyte talk produces glomerulo sclerosis by damaging podocyte.

Extracellular matrix production increased. Filtered cytokine incites proximal tubular cell activation and through glomerular tubular cross talk mediated through angiotensin II, IL6, TNFα. TGFβ mainly through PPAR-γ promotes tubule interstitial scarring. IgG antibody to underglycosylated IgA1 are specific for IgA nephropathy and correlates with clinical disease.

Thus pathogenesis summarized in 3 steps. IgA deposit in the Mesangium; II) generation of the mesangial lesion mediated by the interaction of the IgA1 complexes with specific receptors or through the activation of the complement, and III) progression of the mesangial IgA lesion towards chronic renal failure.

Pathogenesis of mucosa marrow axis in IgAN is simplified as

1. Class switch production of IgA+ antibody secreting cell(ASC)
2. Mistraffiking to bone marrow

3. Monomeric to polymeric IgA

4. Retaining of poorly galactosylated form

5. Formation of IgG antibody.

6. Binding to CD89 in myeloid and its shedding

7. IgG+ CD89+poorly galactosylated form deposition in Mesangium

**Complement in IgAN:**

In 80% cases IgA was co deposited with C3, membrane attack complex. In IgA nephropathy, immune complexes activate classical pathway where as polymeric IgA activates lectin pathway through recognisation molecules like mannose binding lectin, ficolin. Lectin pathway activation had an unfavorable progression.Glomerular C3c deposits parallel with disease severity.[44-45]

**Animal models:[46]**

1. Murine antidinitrophenole and dinitro phenole conjugated bovine serum model

2. Animal immunized with bacterial derived polysaccharide or chemically modified dextran.

- Both the model confirmed IgA-IC IN mesangial deposition.

3. Uteroglobulin deficient mouse model;-shows Fibronectin collagen co deposition

4. Spantanous IgAN prone mouse(ddY) mouse

5. Autoimmune prone mouse (NZW×C 57BL/6):- presents with IgA hyperglobulinemia

6. Mice lacking β 1,4 galactosyl transferase

**Clinical features**

**Pattern of clinical presentation:**

**Common:**

1. Synpharyngitic macroscopic hematuria
2. Microscopic hematuria
3. Hypertension
4. Chronic Kidney Disease
5. Henoch schonlein Purpura

**Uncommon:**

1. Malignant Hypertension
2. Acute renal failure
3 Acute Nephritic Syndrome
4. Nephrotic syndrome

**Macroscopic Hematuria:**

Most often present as painless hematuria, in noted around 40% patients. Macroscopic hematuria mostly presented in children and young adults, rare after 40 years. It is usually seen 1 to 2 days after the sore throat. It is usually recurrent one after each infection. Macroscopic hematuria may present with loin pain. Macroscopic hematuria resolves spontaneously in majority of the patients.

**Asymptomatic Hematuria:**

Around 30 to 40 % of patient presented with asymptomatic hematuria, associated with or without proteinuria. It shows an iceberg effect in its prevalence. Mostly detected in population screening.

**Proteinuria and Nephrotic syndrome:**

Proteinuria in the absence of hematuria is an uncommon presentation. Nephrotic syndrome is uncommon and seen around 5 percent of patients with IgA nephropathy. It may be a manifestation of early disease or advanced stage of disease. Though a threshold of 1g/day of proteinuria had a risk of progression but seems to be a continuum.

**Acute renal Failure:**

Acute kidney injury (AKI) was seen around 5 percent of patients. AKI occurs mainly during the episodes of macroscopic hematuria. Renal biopsy in these patients reveals mesangial proliferation and crescents in small proportion of glomeruli (25%). Mechanism for causing AKI in these patients may be attributed to tubular obstruction by red cell casts. But most common histological lesion is acute tubular necrosis which is probably induced by the iron released from the lysed red blood cell in the tubule,toxic free oxygen radical generated via the Haber –Weiss-Fenton reaction.Crescentric nephropathy(crescent affecting >50% of glomeruli)may be an another factor.

**Hypertension and Malignant hypertension:**

Some proportion of patients with IgA nephropathy is detected to have newly diagnosed hypertension. In young adults it is one of the major causes of hypertension. Malignant Hypertension is the most dramatic presentation in IgA nephropathy. Some studies documented up to 5% of accelerated hypertension.

**Rapidly progressive renal failure:**

It is a manifestation of acute necrotizing glomerulonephritis which warrant immunosuppressive therapy. Mostly mimics pauci immune crescentric glomerulonephritis, sometime associated with IgA ANCA[47].

**Chronic Renal Failure;**

Approximately 10 to 20 percent of patients with IgA nephropathy had chronic established renal failure at presentation. Mostly tend to be older and with long standing disease.

**Natural history;**

Most studies now addressing natural history of IgA[48] .A study from France documented 7 year renal survival of 82%[49]. Twenty five percent end up ESRD in 20 years and another 20% had progressive impairement .According to Canadian study but those who achieved urine protein <0.2 g had least risk and also better renal survival with urine protein<1g/day.[50] But in 7 year follow up study of patient with isolated microscopic hematuria, 44% reached renal impairement[51].

**Histopatological classification:**

There are various classification of IgAN nephropathy. They are

1. Lee classification[52]
2. Hass classification[53]
3. Churg and sobin classification[56]
4. New oxford MEST scoring system[57]

As older classification divided as two system, 1.Lumped system 2.split system lumped system named for its simplicity, applicability in larger studies hence it plays a role in diagnosis and grading. E.g. Lee et al.

Split system looks into the detailed aspects of glomeruli, interstitium, vessels and had global score. Hence it is useful in assessing progression of disease.Eg. Kobayashi et al[54] Waldo et al[55] .

**1. Lee classification**:

***Grade1:***

Glomeruli : normal with or without hypercellularity

Tubulointerstitium (TI) ; normal

***Grade2:***

Glomeruli : <50% of glomeruli show localized mesangial proliferation with sclerosis

Tubulointerstitium (TI) ; normal

***Grade 3:***

Glomeruli ; diffuse mesangial proliferation, occasional crescents

Tubulointerstitium (TI) ; focal interstitial edema, rare tubular atrophy

***Grade4:***

Glomeruli ; marked diffuse mesangial proliferation and sclerosis

Crescents<45% of glomeruli

Tubulointerstitium (TI) ; tubular atrophy and interstitial inflammation

Mark Hass et al modified Lee et al and added D'Amico et al[48] and introduced his classification

**2 .Mark Hass classification**

***Subclass I:***

Minimal histological lesion

Glomeruli ; minimal increase in cellularity

No segmental sclerosis or crescents

***Subclass II:***

Focal segmental glomerulosclerosis like

Glomeruli : focal segmental sclerosis with slight mesangial

cellularity ,no crescents

***Subclass III:***

Focal proliferative GN

Glomeruli ; 50% hyper cellular which is either mesangial or Endocapillary

***Subclass IV;***

Diffuse proliferative GN

Glomeruli : >50% hyper cellular which are either segmental or global .Crescents may be present

***Subclass v:***

Advanced chronic GN

Glomeruli : 40% of glomeruli are globally sclerotic with 40% tubular atrophy.

There is statistically significant between Hass subclass and renal survival. I, II had greatest survival > Ill> IV, V.

***3. Chrug and sobin classification[56]***

Grade I : ClassA; normal glomeruli

Class B: slight mesangial hypercellularity

Class C: Slight mesangial matrix expansion

Grade II :

Class A : <25% glomeruli with moderate focal segmental proliferation. occasional tubular infiltrates.

Class B : upto 50% glomerulo with focal and segmental proliferation. cellular crescents <25% of glomeruli. Tubular atrophy( TA) and interstitial infiltrate up to 50%

Class C ; >50% of glomeruli with segmental proliferation and sclerosis. Crescents up to 50%.TA and interstitial changes in 50% cortical area.

Grade III :

Class A ; sclerosis <25% of glomeruli, fibrous crescents in <25%, Tubular fibrosis in <25% of cortical area.

Class B ; sclerosis up to 50% of glomeruli, fibrous crescent in 50%, tubular fibrosis and interstitial infiltrate upto 50% of cortical area.

Class C ; sclerosis>50% of glomeruli, fibrous crescents in >50% of Glomeruli. Tubular atrophy and interstitial infiltrate >50% of the Cortical area.

**New oxford MEST scoring**

Daniel C. Cattran, Rosanna Coppo, H. Terence Cook, Ian S.D. Roberts, John Feehally introduce this scoring system by analyzing the biopsies of 265 adults and children with IgA nephropathy[57]

Four variables were analysed (1) the mesangial hypercellularity, (2) segmental glomerulosclerosis, (3) Endocapillary hypercellularity, and (4) tubular atrophy/interstitial fibrosis. This scoring system was validated in a north American study[58].

| Variable | Definition | Score |
|---|---|---|
| Mesangial hypercellularity | <4 mesangial cells/mesangial area=0<br>4-5 mesangial cells/mesangial area=1<br>6-7 mesangial area/mesangial area=2<br>>8mesangial area/mesangial area=3 | M<0.5<br>M>0.5 |
| Endocapillary hypercellularity | Due to increased number of cells in lumina to cause narrowing | E0 –absent<br>E1-absent |
| Segmental sclerosis | Any amount of tuft involving sclerosis | S0-absent<br>S1-present |
| Tubular atrophy/interstitial fibrosis. | % of cortical area involved | 0 -25%-T1<br>25-50-T2<br>>50-T3 |

Advantages of this scoring lies in the high inter observer reproducibility. Its weakness lies in the non includes of crescents or necrotizing lesions

**Treatment strategies;**

Patients were treated according to clinical syndrome. Patient presenting with asymptomatic hematuria and proteinuria <500 mg/dl were given only supportive care. Those with 500mg to 1 g/day were suggested ACEI. Patients with >1g/day ACEI drug is titrated to blood pressure of <125/75 mm of Hg with aim of reduction of urine protein of <1g/day. If it is not achieved and GFR is above 50ml/min then steroids are added. (Dosage: 1mg/kg/day×2 months, tapering of 0.2 mg/kg over 4 months). Those with nephrotic syndrome were treated as per MCD protocol. Those with crescents were treated as per vasculitis protocol (regimen; Pulse steroid 7-15 mg/kg×3days followed with oral steroid 1mg/kg/day×4 weeks tapered to 20 mg/day in 2 months and iv cyclophosphamide 15 mg/kg/day every 2 week ×3 doses ,then every 3 weekly.).

In patient present with RPGN, combination of steroid and cyclophosphamide as per vasculitis protocol and followed with maintenance therapy with azathioprine/MMF if there is response.

It is better to renal biopsy if there is no improvement after 5 days in acute kidney injury to rule out crescent as a cause which needs immunosuppressant drugs where as ATN needs only supportive therapy.

**Treatment strategy in IgA nephropathy**

| Presentation | Treatment |
|---|---|
| Hematuria &proteinuria<500mg/dl | Supportive treatment |
| Urine protein(500 -1000mg/day) | ACEI/ARB |
| Urine protein>1000 mg | ACEI/ARB, target BP 125/75 mmHg |
| Optimal ACEI but urine protein>1000mg/day<br>And GFR>50 ml/min | Steroids(1mg/kg/day×2 months and tapered to 0.2mg/kg/day over 4 months) |
| AKI with gross hematuria | Renal biopsy if no improvement by day5<br>ATN-supportive care<br>Crescents-treat as below |
| IgA with crescents | Treat as ANCA vasculitis |
| IgA with MCD | Steroids as MCD protocol |
| IgA with s.creatinine >2.5 mg/dl | CKD supportive care |

**Role of ACEI/ARB**

Praga et al showed renal survival even in patients with high degree of proteinuria[59]. Horita et al showed significant reduction in proteinuria even in

patients with crescents.[60]HKVIN trial in china and IgACE were underpowered enough to comment on role of ACEI.

**Role of fish oil;**

By reducing eicosanoid, curtailing cytokines, fish oil had anti inflammatory action. Donadio et al showed in patients with nephrotic range of proteinuria, high dose fish oil(12g) significantly reduce proteinuria and had long term renal survival in their 6 years follow up. They also showed better outcome with low dose (4g)[61].Appel et al documented improvement in low dose treatment also[62] .Ferraro showed reduction of proteinuria, but RCT was definitely lacking. Considering cardiovascular beneficiaries and low risk profile it may be an option.

**Role of steroids**

In non proliferative IgA N Pozzi et al showed renal survival. In their study of 86 patients, after 6 months of therapy, patients with <1 g proteinuria had better renal survival[63]. Katafuchi et al in 90 patients of steroid for 2 year,long term study fails to have better renal survival[64].Lai et al documented the benefits of short course of steroid in proliferative IgAN with improvement in GFR.

**Combination of steroid and cyclophosphamide**

Bellardie et al and Roccatello et al, both the studies showed better renal survival in patient treated with combination drugs compared to control. Bellardie et al showed 5 year survival of 72%[65]. Roccatello et al showed 5 year survival of 91% even with crescents treated with steroid and cyclophosphamide[66]. No RCT available.

**Role of MMF**

RCT findings are variable. A Belgian study and North American study showed no renal survival and reduction of proteinuria but a Chinese study showed significant reduction of proteinuria[67-68]

**Role of tonsillectomy:**

Studies from Japan[69-70] showed better renal survival but European study gave negative result[71-72]. Argument for better survival includes that tonsil by homing of mucosal type of B cell, produces poorly galactosylated antibody and recurrent tonsillitis provokes hematuria.

Other studies showed that it is not tonsillectomy but combined steroid therapy had beneficiaries. Recent study showed that tonsillectomy had survival advantages over steroid. But still now there were no proper RCT.

**Newer drugs and hopes**

1. Locally acting budesonide-acting at ileocecal region

2. TLR agonists

3. Small molecule inhibitors-of nucleic acid sensing TLR

4. Hydroxychloroquinine; inhibition of antigen processing and presentation by

    i) Inhibitor of TLR9

    ii) Alkalinization of proteosome.

# MATERIALS AND METHODS

**Study design**: Prospective observational study

**Study period**: November 2011-February 2013

**Study centre**: Department of nephrology, Madras medical college, Chennai

**INCLUSION CRITERIA:**

All patients who have biopsy proven IgA nephropathy under the care of department of nephrology, has been included in the study.

**EXCLUSION CRITERIA:**

1. Liver disease
2. Skin disease like psoriasis
3. Malignancy
4. Human immune deficiency virus
5. Leprosy
6. Systemic lupus erythromatosus, rheumatoid arthritis and other Reactive arthritis
7. Diabetic nephropathy

Patients who got admitted under care of our department of nephrology were taken of detailed clinical history. Clinical history include, edema, difficulty of breathing, head ache, blurring of vision, reduction of urine output, hematuria, loin pain, fever, and other relevant history are taken. History regarding systemic illness, regarding comorbitidies, drug history, and personal history, dietary habits was taken. History of cigarette smoking and alcohol intake were probed. Detailed clinical examination including blood pressure examination in all 4 limbs and complete systemic examination were done. Those with blood pressure >140/90 were diagnosed to had hypertension.

Patients were subjected to routine urinary examination includes urine for protein, deposits like red blood cell, white blood cell. Urine was analyzed also red blood cell cast, white blood cell cast. Urine protein/creatinine ratio was done . Patients underwent routine hematological investigation like blood hemoglobulin, total count, differential count, peripheral smear study. Blood investigation include blood urea, serum creatinine, serum electrolyte, lipid profiles were taken. Liver function test including serum bilirubin were taken. GFR estimated by Cockcroft gualt equation (ml/min) .Urine for culture and sensitivity and blood for culture and sensitivity was done. Ultra sonogram of abdomen, ultra sonogram kidney and

urinary tract which includes size of kidney, cortical echogenesity, and whether cortical medullary differentiation present or not. Chest x ray PA view and electrocardiography were done in appropriate patients.

Renal biopsies were done where there is an appropriate indication. Indication for renal biopsy includes unexplained renal failure, those presented with nephrotic syndrome, those with nephritic syndrome, on subnephrotic proteinuria those had an sudden rise in serum creatinine. Bleeding time(BT) ,clotting time(CT),prothrombin time(PT),activated partial thromboplastin time(APTT) were done. Those who presented with contracted kidney were not biopsied. Kidney and urinary tract were also looked for dilated systems. Blood pressure was recorded. Sterility of urine culture was ensured. Patients were explained in detail about the renal biopsy procedure and informed and written consent were obtained.

Renal biopsy was done in prone position. Ultra sound was to locate the lower pole of kidney and skin marking was done. Under strict aseptic precaution, local anesthetic (2% lignocaine) was infiltrated in renal angle area. Under ultra sound guidance, using 16 G biopsy needle, renal biopsy was done with the patient in deep inspiration. After conforming renal tissues, patients were advised bed rest and collection of urine sample. Patient informed to report any increase in abdominal pain.

Renal biopsy tissues sent for histopatological examination. These were done by light microscopy and immunoflourescence study. Glomeruli, tubule, interstitium and vessel were examined with hematoxylin and eosin, periodic acid Schiff and trichrome. MEST scoring was done. Immunoflourescence studies for IgA.IgM, IgG, C3, C1q were done. Intensity graded from 0 to 4. Those with 2 + and more of dominant or codominant deposit of IgA, diagnosis of IgA nephropathy was made.

After excluding those who met exclusion criteria diagnosis of primary IgA nephropathy were made. Patients were treated according to clinical syndrome. Patient presententing with asymptomatic hematuria and proteinuria <500 mg/dl were given only supportive care. Those with 500mg to 1 g/day were suggested ACEI. Patients with >1g/day ACEI drug is titrated to blood pressure of <125/75 mm of Hg with aim of reduction of urine protein of <1g/day. If it is not achieved and GFR is above 50ml/min then steroids are added. (Dosage: 1mg/kg/day×2 months, tapering of 0.2 mg/kg over 4 months). Those with nephrotic syndrome were treated as per MCD protocol. Those with crescents were treated as per vasculitis protocol (regimen; Pulse steroid 7-15 mg/kg×3days followed with oral steroid 1mg/kg/day×4 weeks tapered to 20 mg/day in 2 months and iv cyclophosphamide 15 mg/kg/day every 2 week ×3 doses ,then every 3 weekly.).Sterility of urine and blood and chest X ray be must to start

immunosuppression. Response to treatment was assessed with improvement of renal function and remission of proteinuria (complete remission as urine protein<300 mg/day, partial remission as urine protein 300-3000mg/day and nil response of >3000mg/day).

Patients presented with acute kidney injury, if there were no renal improvement biopsy attempted at 5$^{th}$ day to exclude crescents or acute tubular necrosis.

Patients were divided into two cohorts, those had renal failure at presentation (GFR<60ml/min) and those had no renal failure at presentation (>60ml/min). Various factors including clinical and biopsy study were analyzed.

Patients were on regular follow up. Those who progressed to chronic kidney disease [CKD (GFR<60 ml/min)], end stage renal disease [ESRD(GFR<15 ml/min)] were analyzed with various clinicopathological factors. These patients were compared with the patients who never reach CKD and ESRD respectively.

# RESULTS

A total of 92 patients with biopsy proven IgA Nephropathy were included in the study. Of which 5 patients who present with end stage renal disease at presentation were excluded. Eighty seven patients are finalized into this study. Sixty eight (67.8%) patients were male. The follow up period ranged from 6-28 months. The mean age at presentation was 27.3years. Majority of patients (35) presented in 10-19 years age groups (40.2%),followed by twenty five patients in 20-29years age groups (28.8%). Five patients were in 30-39 years age groups (5.7%). Fourteen were in 40-49 age groups (16.1%). Seven were in 50-59 age groups (8%) and one was in 60 years. Patients were stratified according to age groups as given in table 1.

**TABLE:1**

| Table1 | |
|---|---|
| Total number of patient | 87 |
| Male | 59(67.8%) |
| Female | 28(32.2%) |
| Mean age | 27.3 years |
| 10-19 years | 35(40.2%) |
| 20-29 years | 25(28.8%) |
| 30-39 years | 5(5.7%) |
| 40-49 years | 14 (16.1%) |
| 50-59 years | 7 (8%) |
| 60 years | 1(1.1%) |

Clinical presentation of patients were classified as in table 2.Macrohematuria was noted in 36(40%) patients. Hypertension prevailed in 40 (54%) patients. Edema was present in 66(76%) patients. Oliguria was seen in 59 (67%). Seven (8%) presented with hypertensive encephalopathy. Nineteen (21.8%) had hypertensive retinopathy.

**TABLE: 2; Clinical presentation**

| Clinical presentation | Number of patients | Percentage (%) |
|---|---|---|
| Macrohematuria | 36 | 40 |
| Edema | 66 | 76 |
| Oliguria | 59 | 67 |
| Hypertension | 40 | 54 |
| Hypertensive encephalopathy | 7 | 8 |
| Hypertensive retinopathy | 19 | 21.8 |

Depending upon clinical syndrome patients were categorized as in table 3. Twenty patients had Nephrotic syndrome (22.9%).Nephritic syndrome was noted in 11 patients (12.6%). Twelve presented with rapidly progressive renal failure

(13%). Six presented with acute kidney injury (6%). Those who presented with end stage renal failure at presentation were excluded from the study.

**TABLE: 3;Clinical syndrome**

| Syndrome | Number of patients | Percentage (%) |
|---|---|---|
| Nephrotic syndrome | 20 | 22.9 |
| Nephritic syndrome | 11 | 12.6 |
| Rapidly progressive glomerulonephritis | 12 | 13 |
| Acute kidney injury | 6 | 6 |
| Chronic kidney disease | 5 | 5.4(excluded) |

Renal biopsy findings were tabulated as follows in table no 4 .Scoring was based on Oxford MEST. Mesangial score (M0&M1) was seen in 28 and 59 patients respectively. Endocapillary cellularity (E1) was noted in 44 patients. Sclerosis score (S0 &S1) observed in 45and 43 patients respectively. Tubular atrophy and interstitial fibrosis score of T1 and T2 was noted in32 and 40 patients respectively. Crescents were noted in 16 patients. Vessel wall thickening was present in 24 patients.

**TABLE: 4: Biopsy findings**

| Biopsy findings | Number (Percentage (%) |
|---|---|
| M0 | 28(32.1%) |
| M1 | 59(67.9%) |
| E0 | 43(49.4%) |
| E1 | 44(51.6%) |
| S0 | 45(51.7) |
| S1 | 43(49.3%) |
| T0 | 15(17.2%) |
| T1 | 32(36.7%) |
| T2 | 40(46%) |
| Crescents | 16(18.4%) |
| Vascular thickening | 24(27.6%) |

Renal biopsy tissues were also studied with immunoflourescence staining for IgA, IgM, IgG, C3and C1q showed IgA+C3 in 42 patients(48.2%), IgA+C3+IgM in 30 patients(34.4%), IgA+C3+IgM+IgG in 14 patients (16.1%),%)and IgA+C3+IgM+C1q in 7 patients (8%).Results were given in table 5.

**TABLE 5: Immunoflourescence (IF) finding**

| IF finding | Number & Percentage |
|---|---|
| IgA + C3 | 42(48.2%) |
| IgA+C3+IgM | 30(34.4%) |
| IgA+C3+IgM+IgG | 14(16.1%) |
| IgA+C3+IgM+C1q | 7(8%) |

Clinicopathological variable with renal failure at presentation

Among the 87 patients 59 (67.9%) were presented with renal failure at presentation. Mean age in who presented with renal failure at presentation was 27.9 years. Male dominated as 42 (59%). Male: female 2.4:1. Hypertension was noted in 35 (59%) patients. Macrohematuria occurred in 21 (35.6%).Nephrotic range of proteinuria was present in 27 patients (47.8%).

Renal biopsy showed mesangial hypercellularity(M1) in 49(83%) ,mesangial score(M1) >0.5 was noted in 34(83%) ,endothelial proliferation(E1) was seen in 33(56%), segmental score ( S1) noted in 49%,tubular atrophy /interstitial fibrosis score T1 and T2 was noted in 28(46%) and 29(51%) patients respectively. Crescents were noted in 12 (20.2%).Vessel wall thickening was noted in 22 patients. Various factors which were studied between those who presented with renal failure at presentation (GFR <60ml/min) and those without renal failure at presentation were tabulated in table 6.

**Table 6 :**

| Variables | No renal failure at presentation N =28 patients | Renal failure at presentation N =59 patients | P value |
|---|---|---|---|
| Mean age | 25.5 years | 27.9 years | Not significant |
| Sex (M% :F % ) | 61:39 | 71:29 | P=0.33 |
| Hypertension | 43% | 59% | P=0.1 |
| Macrohematuria | 54% | 35% | P=0.1727 |
| PCR>3g | 39% | 46% | P=0.647 |
| M0 | 36% | 17% | **P=0.001** |
| M1 | 64% | 83% | |
| E0 | 64 | 44% | P =0.108 |
| E1 | 36 | 56% | |
| S0 | 57% | 51% | P =0.358 |
| S1 | 43% | 49% | |
| T0 | 46.4% | 3% | **P=0.0019** |
| T1 | 14.3% | 46% | |
| T2 | 39.3% | 51% | |
| Crescents | 14.2% | 20.3% | P=0.568 |
| Vascular thickening | 39.2% | 22% | P=0.835 |

Twenty five patients (28.74%) progressed to chronic kidney disease (GFR<60 ml/min) on follow up period. Mean age was 32.6. Male: female was 64:36. Macrohematuria was presented in 7 patients (28 %).Hypertension persisted

in 17 patients (68%). Response to proteinuria was assessed by those achieved complete remission (proteinuria<300mg/day), partial remission(proteinuria 300-3000mg/day) and nil remission(proteinuria>3000mg/day). Ten patients (40%) never attained remission. One attained complete remission. Fourteen patients (56%) attained partial remission. Mesangial hypercellularity was noted in 18 patients (72%). Fifteen presented with endothelial hypercellularity (60%). Segmental sclerosis was observed in 17 patients (68%). Twelve patients (48%) showed tubular atrophy and interstitial fibrosis. Crescents were noted in patients (28%). Twenty one patients had GFR<60 ml/min since from presentation.

Sixty two patients (71.6%) had normal renal function at the end of follow up period. Mean age was 28. Macrohematuria was present in 29 (47%).Thirty patients had hypertension (48.3%). Twenty eight patients had complete remission (45%). Another twenty four attained partial remission (38.7%). Six never attained remission. Cresents were noted in 9 patients (14.5%). Thirty eight patient had GFR <60 ml/min at their presentation itself.

Variables analyzed in those who progressed to CKD were tabulated in table 7

**TABLE 7**

| Variables | Progressed to CKD N =25 | Normal renal function at the end of follow up N=62 | P Value |
|---|---|---|---|
| Mean age | 32.6 | 28 | No significance |
| Sex (M% :F % ) | 64;36 | 60:40 | 0.62 |
| Hypertension | 68% | 43% | 0.98 |
| Macrohematuria | 68% | 48.3% | |
| Response to proteinuria CR | 4% | 45% | 0.0001 |
| Partial response | 56% | 38.7% | |
| No response | 40% | 9.7% | |
| M1 | 72% | 66% | 0.8 |
| E1 | 60% | 46.8% | 0.344 |
| S1 | 68% | 40%% | 0.031 |
| T0 | 4% | 32.3% | 0.07 |
| T1 | 46% | 43.5% | |
| T2 | 46% | 25.8% | |
| crescents | 28% | 14.5% | 0.2192 |
| GFR<60 ml/min at present | 84% | 61.2% | 0.04 |
| Vessel wall thickening | 36% | 24% | 0.29 |

**Clinicopathological variables in those reach ESRD**

Of the total 87 patients 15(17.24%) needed dialytic support due to end stage renal disease. Mean age was 29.4 years. Hematuria was noted in 40%.hypertension in 32% .Those who presented with Nephrotic syndrome was 52% and nephritic syndrome was 28%.crescents was noted in 24%. Variables analyzed in those needed dialytic support are tabulated below in table 8

**Table 8**

| Variables | Patient progressed to ESRD (N=15) |
|---|---|
| Mean age | 29.4 |
| Hematuria (%) | 40 |
| Hypertension (%) | 32 |
| Nephrotic syndrome (%) | 52 |
| Nephritic syndrome (%) | 28 |
| Crescents(%) | 24 |

**Treatment response with Nephrotic syndrome**

Of the 20 patients presented with nephrotic syndrome, all were started with ACEI titrated to reduce the BP target of 125/75 mm Hg, Eighteen were started with steroids.

Eleven (55%) had partial remission. Three (20%) had complete remission. Six (30%) never attained remission. Three patients who attained complete remission retained their renal function. Of the seventeen who had partial and nil remission 7 patients progressed to chronic kidney disease.

**TABLE 9**

<table>
<tr><th>Response to proteinuria</th><th>Progressed to chronic kidney disease</th><th>Stable renal function</th><th rowspan="4">P =0.5</th></tr>
<tr><td>Complete remission n=3</td><td>Nil</td><td>3</td></tr>
<tr><td>Partial remission n=11</td><td rowspan="2">7</td><td rowspan="2">10</td></tr>
<tr><td>Nil remission n=6</td></tr>
</table>

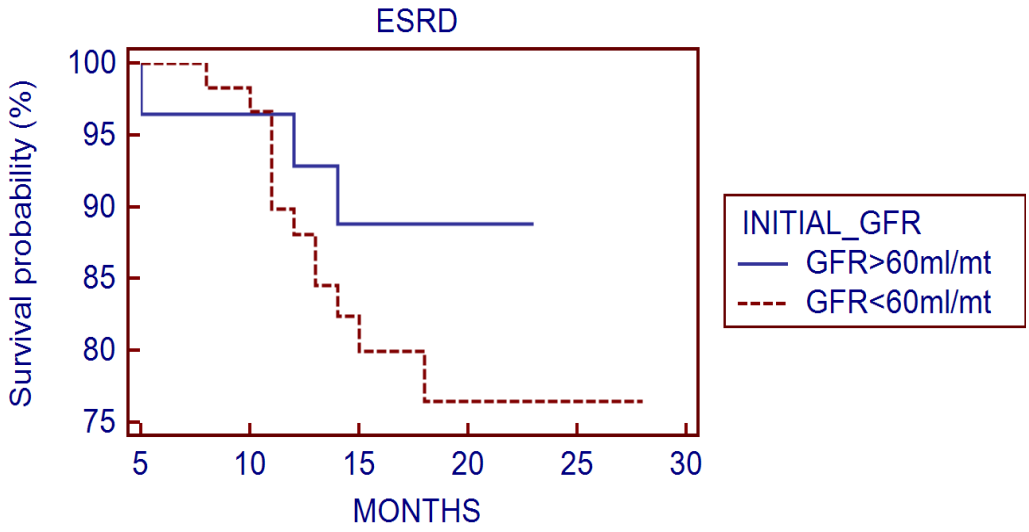
**Treatment response in RPGN and in AKI**

Of the twelve patients presented with rapidly proliferative glomerulonephritis, nine patients presented with nephrotic range of proteinuria with nephritic sediment. Steroid was given in 11 patients and cyclophosphamide with steroid was given in 7 patients as per vasculitis protocol .Six patients progressed to chronic kidney disease. Other six were not.

Acute kidney injury was noted in six patients. Four had acute tubular necrosis. One had crescent and another with no discernible findings

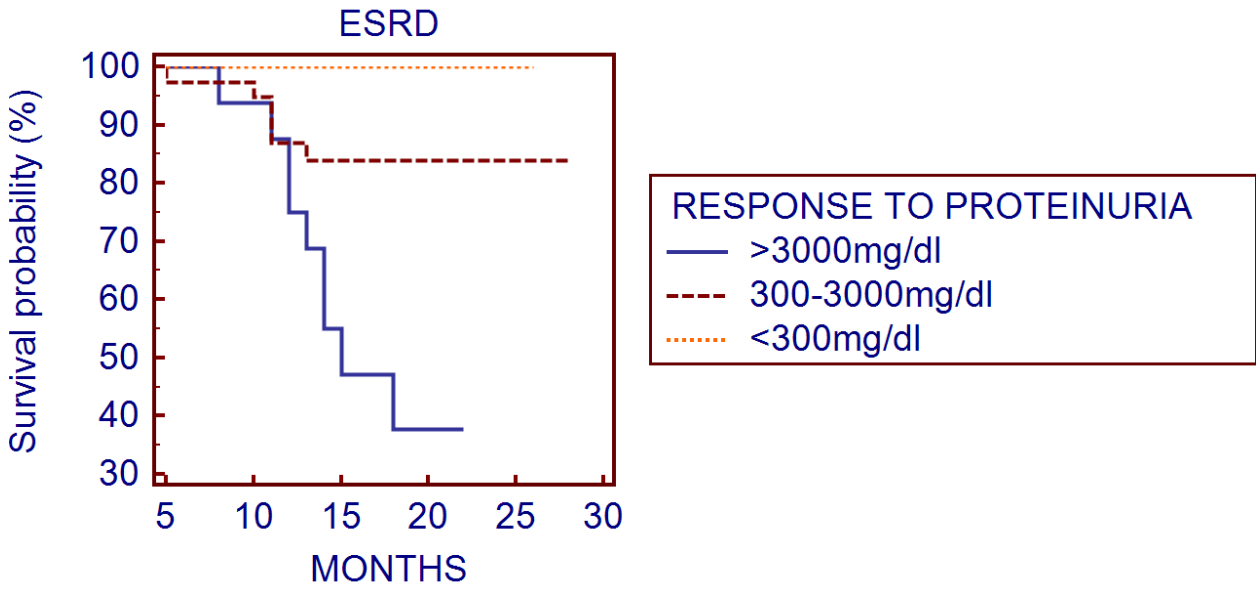
**Survival probability in response to GFR at presentation**

Survival probability curve by Kaplan Meyer curve shows that those who had renal failure at presentation had progressed to end stage renal disease than those who had not renal failure.



**Survival probability in response to proteinuria;**

This Kaplan Mayer curve shows that those who attained no remission went to end stage renal disease more probable than who attained partial or complete response.



# DISCUSSION

Of the 87 biopsy proven IgA Nephropathy, 68 patients were male. Male: Female ratio in our study was 2.1:1 which was comparable to Chaco et al[10], with M: F ratio 1.85:1. Mean age at presentation in our study was 27.3 years compared to Neha mittal et al, had mean age of 29.9 years[73], and Muthukumar et al[74] showed mean age of 25.7 years but a decade younger than that quoted in western world. On age wise distribution 35 patients (40.2%) were in 10-19 years , in age group 20-25 years 25(28.8%),in 30-39 age groups 5(5.7%),in 40-49 years 14(16.1%),in 50-59 years 7(8%) and in 60 years there was one patient.

**Clinical symptoms**

Thirty six (40%) patients presented with macrohematuria in our study. Chandrika et al, documented 49.3% had macrohematuria. Macrohematuria was presented in 25% of patients with primary IgA Nephropathy from university hospital St.Eetinne. Hypertension was noted in 40 patients (54%), which was comparable to Chaco et al,(58%). Seven patients (8%) had Hypertensive encephalopathy. Nineteen patients (12.8%) had hypertensive retinopathy.

Muthukumar et al, documented 21.4% had malignant hypertension. In our study macrohematuria was noted in 20 (40%), Hematuria (macro and micro) thus observed in 56 (64%) patients. Chako et al showed 69% had hematuria.

## Clinical syndrome

Nephrotic syndrome documented around 3% in western studies. Chako et al documented 55% had Nephrotic syndrome. Chandrika[11] et al, documented 36.7%.Muthukumar [74]et al, documented 25.5% had nephrotic syndrome. Neha mittal et al[73] study showed 23.1% had Nephrotic syndrome. In our study 22.9% had nephrotic syndrome. Rapidly progressive glomerulonephritis (RPGN) was noted in 13% patients. Muthukumar et al documented 21% had RPGN.Acute kidney injury was present in 6% patients compared to Muthukumar et al (4.1%). Mean serum creatinine was 2.03 mg/dl in our study compared to Chako[10] et al, with 2.3 mg/dl. Comparison of clinical presentation and syndrome with other studies are tabulated below.

**Table 8**

| | **Chandrika et al** | **Chako et al** | **Neha mittal et al** | **Muthukumar et al** | **Present study** |
|---|---|---|---|---|---|
| Mean age years | 30 | 32 | 29.9 | 25.7 | 27.3 |
| M ;F | 1.5;1 | 1.85:1 | 3;1 | 2:1 | 2.1:1 |
| Mean serum creatinine | 2.2 | 2.3 | 3.1 | - | 2.03 |
| Hematuria (%) | 49.3 | 69 | 78.8 | 54.9 | 64 |
| Hypertension (%) | 49 | 69 | 81 | 30 | 54 |
| Nephrotic syndrome(%) | 36.7 | 55 | 23.1 | 25.5 | 22.9 |
| RPGN(%) | - | - | - | 21.4 | 13 |
| AKI(%) | 11 | - | - | 4.1 | 6 |

**Biopsy findings**

Renal biopsy results of the 87 patients revealed mesangial hypercellularity (M score >0.5) in 67.9%. Endocapillary proliferation was noted in 51.6%. Sclerosis score (S1) was noted in 49.3%.Tubular atrophy/interstitial fibrosis score (T1&T2) was36.7%&46% respectively in our study. Arterial score was around 24%.

Daniel C.Cattran showed mesangial score >0.5 as 66%, Endocapillary proliferation in 42%, sclerosis score (S1) in 76%, tubular atrophy/interstitial fibrosis score(T1&T2) 88% and crescents 42%.arterial score present around 40%[57].

Neha mittal et al, showed mesangial hypercellularity (M score >0.5) in 68.18%, endocapillary hypercellularity in 24.4%, sclerosis score (S1) in 48.6%,T1 score in 30.3% and T2 in 43.93%. Crescents were present in 56%.In our study crescents were noted in 18.4%, which was to Chandrika et al (12.3%).[73]

Hamid Naseri et al, showed M1 score in 90.2%, Endocapillary proliferation in (E1) 32%, sclerosis score (S1) in 62%, tubular atrophy/interstitial fibrosis score in (T1&T2) 30% and 50% respectively[75]

**MEST scoring in various studies**

| | Cattran et al | Neha mittal | Hamid Naseri | Our study |
|---|---|---|---|---|
| Mesangial score >0.5 | 66% | 68.18% | 90.2% | 67.9% |
| Endocapillary score (E1) | 42% | 24.4% | 32% | 51.6% |
| Sclerosis score (S1) | 76% | 48.6% | 62% | 49.3% |
| Tubular atrophy/interstitial fibrosis score in (T1&T2) | 88% | 73.96% | 80% | 82.7% |

**Immunoflourescence study**

Immunoflourescence study of renal biopsy tissue in our study showed IgA+C3 present in 42 patients(48.2%), IgA+C3+IgM in 30 patients(34.4%), IgA+C3+IgM+IgG in 14 patients (16.1%),%)and IgA+C3+IgM+C1q in 7 patients (8%).Chandrika et al showed IgA+C3 present in 105 patients(46.25%), IgA+C3+IgM in 80 patients(35.24%), IgA+C3+IgM+IgG in 20patients (8.82%), and IgA+C3+IgM+C1q in 5 patients (2.20%)[11].In their study full house pattern was noted in 4 patients (1.76%),but not in our study.

**Clinical presentation of renal failure at presentation(diagnosis)**

In our study renal failure at presentation (GFR <60 ml/min) was noted in 59.4 patients (67.9%).Muthukumar et al showed 61% had renal failure at diagnosis.

The mean age was 27.9 years in who presented with renal failure at diagnosis. Seventy one (81.6%) patients were male, which was comparable to Muthukumar et al,(70%.)

Hypertension was noted in 35 (59%) patients in our study who presented with renal failure at presentation. Macrohematuria was noted in 21(35.6%), nephrotic range of proteinuria was present in 27(46%).

**Biopsy finding in renal failure at presentation**

Of the 59 patients who presented with renal failure at presentation, 83% had mesangial score (M>0.5),44% had endocapillary proliferation,49% had sclerosis score (S1 ).Tubular atrophy/interstitial fibrosis score(T1&T2) was noted in 47% and 51% respectively. Crescents were noted in 27% of the above cohort. Muthukumar et al showed hypertension in 28.3%, proteinuria >3g/day in 41.7%, interstitial fibrosis in 90%, Crescents in 16.7%.

**Statistical analysis;**

Statistical analysis was done by bivariate analysis using chi-square for fisher's exact test, multivariate analysis done by multiple regressions. Male sex, mean age both had no significant correlation in those with renal failure at presentation. Hypertension, Macrohematuria, proteinuria >3g/day were had no significant correlation in this cohort. Mesangial hypercellularity (M score >0.5), segmental score (S1), tubular atrophy/interstitial fibrosis score (T1&T2),were significantly associated with renal failure at presentation.

Daniel C.Cattran et al showed there was significant correlation between for mesangial hypercellularity score (M1),endocapillary proliferation score, tubular atrophy/interstitial fibrosis score (T1&T2) with reduction in glomerular filtration rate .They also showed that there is a significant correlation between mesangial hypercellularity score (M1),endocapillary proliferation score, tubular atrophy/interstitial fibrosis score (T1&T2) with blood pressure.

In our study by multiple regression analysis there is a significant correlation between mesangial hypercellularity score (M1), endocapillary proliferation score, segmental sclerosis, tubular atrophy/interstitial fibrosis score (T1&T2) with blood pressure ( P=0.029) .Crescents had no significant statistical association. There is no

statistical association between vessel wall thickening and those with renal failure at presentation.

Muthukumar et al showed that there were no significant correlation between male, hypertension, macrohematuria, proteinuria >3g/day in those who presented with renal failure at presentation. They showed interstitial fibrosis and vessel wall thickening were associated with renal failure at presentation. By multivariate analysis they showed only interstitial fibrosis was associated with renal failure at presentation, but not vessel wall thickening.

Variables analyzed for those presented with renal failure at diagnosis are tabulated below in table 9

**TABLE 9:**

| Variables | Muthukumar et al | Our study |
|---|---|---|
| Mean age(years) | 25.7 | 27.9 |
| Sex (M:F) | 2:1 | 2.1:1 |
| Hypertension(%) | 28.3 | 59 |
| Hematuria(%) | 21.7 | 35 |
| Proteinuria >3g/day | 41.7 | 46 |
| Interstitial fibrosis(%) | 90 | 51 |
| Vessel wall thickening(%) | 56 | 22 |
| Crescents(%) | 16.7 | 27 |

**Treatment response in nephrotic syndrome;**

In our study 20% presented with nephrotic syndrome, all of them are started with ACE inhibitors and BP was titrated to 120/75 mmHg. Steroid was started in 16 of them, three (15%) patients attained complete remission, 11(55%) patients had partial remission, and six (30%) patients had no remission. Of the 3 patients who attained complete remission none progressed to renal failure. Seventeen patients with partial and nil remission, 7 of them progressed to renal failure, 10 were not, but statistically not significant (P=0.54). Reich et al, showed those who had sustained proteinuria >3g/day had 25 fold faster decline in renal function.

By multivariate analysis those with nephrotic syndrome who progressed to renal failure there was significant correlation between mesangial hypercellularity score (M1),endocapillary proliferation score(E1),segmental sclerosis(S1), tubular atrophy/interstitial fibrosis score (T1&T2) (P=0.001).By univariate analysis endocapillary proliferation score(E1),segmental sclerosis(S1) had correlation (P=0.04) .

**Treatment response in RPGN**

Twelve (13%) patients presented with RPGN of whom 9 presented with nephrotic range of proteinuria with nephritic sediment. Steroid was given in 11 patients and cyclophosphamide with steroid was given in 7 patients as per

vasculitis protocol . Half of them progressed to chronic kidney disease, half were not.

**Treatment of Acute kidney injury**

Acute kidney injury (AKI) was noted in six patients. Four had acute tubular necrosis. One had crescent and another with no discernible findings. Two need dialytic support, one need immunosuppressive therapy with cyclophosphamide.

**Clinical variables in progression of CKD cohort**

In our study during follow up period twenty five patients (28.74%) progressed to chronic kidney disease. Mean age was 32.6years. Twenty eight percentages of them had macrohematuria. Hypertension persisted in 17 (68%) patients. There is no statistical significance noted for hypertension and macrohematuria. Those progressed to CKD 10 patients had proteinuria >3g/day (nil remission), 14 patients had proteinuria in the range of 0.3-3g/day (partial remission), 1 patient had urinary protein of <0.3g/day. There was statistical significance noted for who had no response to reduction in proteinuria with that progressed to CKD.

**Analysis of biopsy findings in progressor of CKD**

There was no statistical significance noted for mesangial score (M1) in 72% and Endocapillary proliferation 60% of patients in those who progressed to chronic kidney disease. Segmental score (S1) was noted in 68% who progressed to chronic kidney disease, which was statistically significant. Tubular atrophy/interstitial fibrosis score (T1&T2) was noted in 46% of each who had progressed to chronic kidney disease, which was not statistically significant. Twenty eight percentages had crescents which was not statistically significant. There is no statistical association between vascular wall thickening and chronic kidney disease progression.

**Clinicopathological variable in patients not progressed to CKD**

Sixty two patients (71.6%) had normal renal function at the end of follow up period. Mean age was 28. Macrohematuria was present in 29 (47%).Thirty patients had hypertension (48.3%).Twenty eight patients had complete remission(45%),another twenty four attained partial remission(38.7%).Six never attained remission. Crescents were noted in 9 patients (14.5%). Thirty eight patient had GFR <60 ml/min at their presentation itself.

**Clinicopathological variable in those who reach ESRD**

Of the total 87 patients 15(17.24%) needed dialytic support due to end stage renal disease. Mean age was 29.4 years. Six patient (40%) associated with hematuria. 8 patient had sustained hypertension ( 32% ).Those who presented with nephrotic syndrome was 52% and nephritic syndrome was 28%.crescents were noted in 24%.By multiple regression analysis there is a significant association between hypertension, mesangial hypercellularity score (M1), endocapillary proliferation score(E1),segmental sclerosis(S1), tubular atrophy/interstitial fibrosis score (T1&T2), presence of nephrotic syndrome and response to proteinuria with end stage renal disease warranted dialytic support( $P<0.001$).Of which T score and those respond to proteinuria(as complete remission <300mg/day, partial remission 300-3000mg/day, nil remission >3000 mg/dl) had better significance($P=0.1$ and 0.0002 respectively).

# SUMMARY

1. Mean age at presentation was 27.3 years.
2. Nephrotic syndrome was present in 22.9%
3. Renal failure at diagnosis was 59.4%
4. There was significant correlation with mesangial score (M >0.5), segmental score (S1), tubular atrophy/interstitial fibrosis score (T1&T2) with renal failure at presentation
5. Treatment response to proteinuria had statistical correlation with those progressed to chronic kidney disease. Patients achieved nil remission significantly progressed to chronic kidney disease.
6. Of the MEST scoring, segmental score (S1) had significant correlation with the progression of chronic kidney disease.
7. Crescents were not significantly associated with either renal failure at diagnosis of IgA nephropathy or with progression of chronic kidney disease.
8. T score and nil response to proteinuria had statistically significance of developing of end stage renal disease.

# CONCLUSION

1. Nephrotic syndrome is the most common clinical presentation in IgA nephropathy.
2. Majority of the patients presented with renal failure at entry into study.
3. Severe MEST scoring was significantly associated with renal failure at presentation.
4. Non- responders of proteinuria and those who had severe S and T scores in MEST scoring system progressed to chronic kidney disease.
5. Those who had either complete or partial remission of proteinuria had less chance to progression of CKD during the follow up period.

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| Age | NAME | sex | wt | MICROHEMTURIA | MACROHEMATURIA | OEDEMALEG | OLIGURIA/ANURIA | BP | HTENCEPHOLOPATHY/FUNDUS | PCR /ADMISSION | URINE PROTEIN/AD | URINE RBC/ADMISS | HB Gms/dl | PCR /ADMISSION | B.UREA/ ADMISSION | S.CREATINIE | e GFR( cockcroft gault) | S.URIC ACID mg/dl | NEPHROTIC SYNDROME |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 18 | SATHIANARAYANAN | M | 52 | P | A | P | P | P(170/110) | F | 4.28 | 3+ | 6-8 RBC | 11 gm/dl | 4.28 | 68 | 4.8mg/d | 17.2 | 7.4mg/dl | yes |
| 24 | SATIYA | F | 42 | P | A | A | A | N(120/80) | N | 6.56 | 4+ | 8-10 RBC | 7.7 | 6.56 | 80 | 1.8 | 17.8 | 8.2 | yes |
| 18 | SRINIVASAN | M | 56 | A | P | P | P | P(140/90 | N | 4 | 4+ | NIL | 11.2 | 4 | 78 | 1.4 | 60 | 5.7 | yes |
| 27 | MANJULA | F | 51 | A | A | P | A | N | N | 7.8 | 3+ | NIL | 9.8 | 7.8 | 68 | 2.1 | 16.9 | 5.9 | yes |
| 42 | VIJAYKARUNAGARAN | M | 42 | P | A | P | A | P(180/100) | E | 6.8 | 3+ | NIL | 10.8 | 6.8 | 86 | 8.1 | 9 | 7.8 | yes |
| 18 | INDIRAN | M | 62 | A | P | P | A | N | N | 4.5 | 3+ | plenty | 10.6 | 4.5 | 46 | 1.1 | 94.1 | 4.2 | yes |
| 40 | BAHRINUSHA | F | 46 | A | P | P | P | P(170/120 | E | 5.6 | 3+ | plenty | 9.8 | 5.6 | 50 | 2 | 16.8 | 6.1 | yes |
| 12 | THRILOKCHANDAR | M | 51 | P | A | P | P | P(180/100) | F | 4.8 | 3+ | 8-10 RBC | 11.8 | 4.8 | 64 | 1 | 28.2 | 4.8 | yes |
| 16 | UMA | F | 14 | A | A | P | A | N(110/80) | N | 1.4 | 1+ | plenty | 9 | 1.4 | 16 | 1.1 | 48.4 | 4.8 | NO |
| 20 | SUMATHY | F | 44 | A | P | A | A | N(120/80) | N | 1.1 | 1+ | plenty | 12 | 1.1 | 56 | 1 | 70 | 4 | NO |
| 16 | SUCHITRA | F | 56 | A | P | P | A | P140/100 | N | 0.2 | NIL | plenty | 9.8 | 0.2 | 52 | 1.6 | 21.9 | 4.1 | NO |
| 41 | PARAMASIVAM | M | 64 | A | P | P | P | P190/100 | N | 4.2 | 3+ | 10-12 RBC | 6.8 | 4.2 | 126 | 4.8 | 24 | 6.8 | NO |
| 15 | TAMILARASAN | M | 61 | A | A | A | P | P(160/100) | F | 2.6 | 2+ | NIL | 10 | 2.6 | 98 | 1.6 | 70 | 5.2 | NO |
| 46 | KARPAGAM | M | 56 | A | P | A | A | N | N | 2 | 2+ | plenty | 9.2 | 2 | 60 | 2 | 14 | 4.5 | NO |
| 16 | JYOTHI | F | 17 | A | P | A | A | N | N | 1.15 | 1+ | plenty | 12 | 1.15 | 46 | 0.9 | 96 | 4 | NO |
| 17 | ANNAVEL | M | 47 | A | A | P | A | N | N | 0.51 | 1+ | NIL | 12.8 | 0.51 | 40 | 1.2 | 96 | 4.6 | NO |
| 28 | PADMAVATHY | M | 42 | A | P | P | P | P160/100 | F | 1.81 | 2+ | plenty | 12 | 1.81 | 46 | 1.2 | 96 | 4.8 | NO |
| 20 | BHARATHI | M |  | A | P | A | A | N | N | 1.5 | 1+ | plenty | 10 | 1.5 | 40 | 1.5 | 90 | 1.8 | NO |
| 18 | KOTHANDAM | M | 52 | A | P | A | A | N | N | 0.8 | 1+ | plenty | 11.6 | 0.8 | 52 | 1.2 | 86 | 5.2 | NO |
| 24 | TAMLSELVAN | M | 46 | P | A | A | P | N | N | 0.02 | NIL | 8-10 RBC | 9.6 | 0.02 | 42 | 2.8 | 14 | 4.7 | NO |
| 26 | CHRISTIANA | F | 45 | A | P | A | P | N | N | 2.08 | 2+ | plenty | 12.2 | 2.08 | 10 | 1.1 | 96 | 5.6 | NO |
| 28 | MUTHUKUMARAN | M | 44 | A | A | P | P | N | N | 1.6 | 2+ | NIL | 8.8 | 1.6 | 40 | 1.8 | 56 | 4.9 | NO |
| 19 | RAJU | M | 52 | A | A | P | P | P(160/100) | N | 0.02 | NIL | NIL | 11.6 | 0.02 | 12 | 1.8 | 51.5 | 1.8 | NO |
| 28 | YAM BAGADUR | M | 47 | A | A | A | P | P(170/110) | F | 2.9 | 2+ | NIL | 11.6 | 2.9 | 56 | 1.1 | 15 | 4.1 | NO |
| 14 | SATHISH | M | 26 | A | P | P | A | N(120/80) | N | 1.85 | 1+ | plenty | 12 | 1.85 | 64 | 1.4 | 16 | 6.2 | yes |

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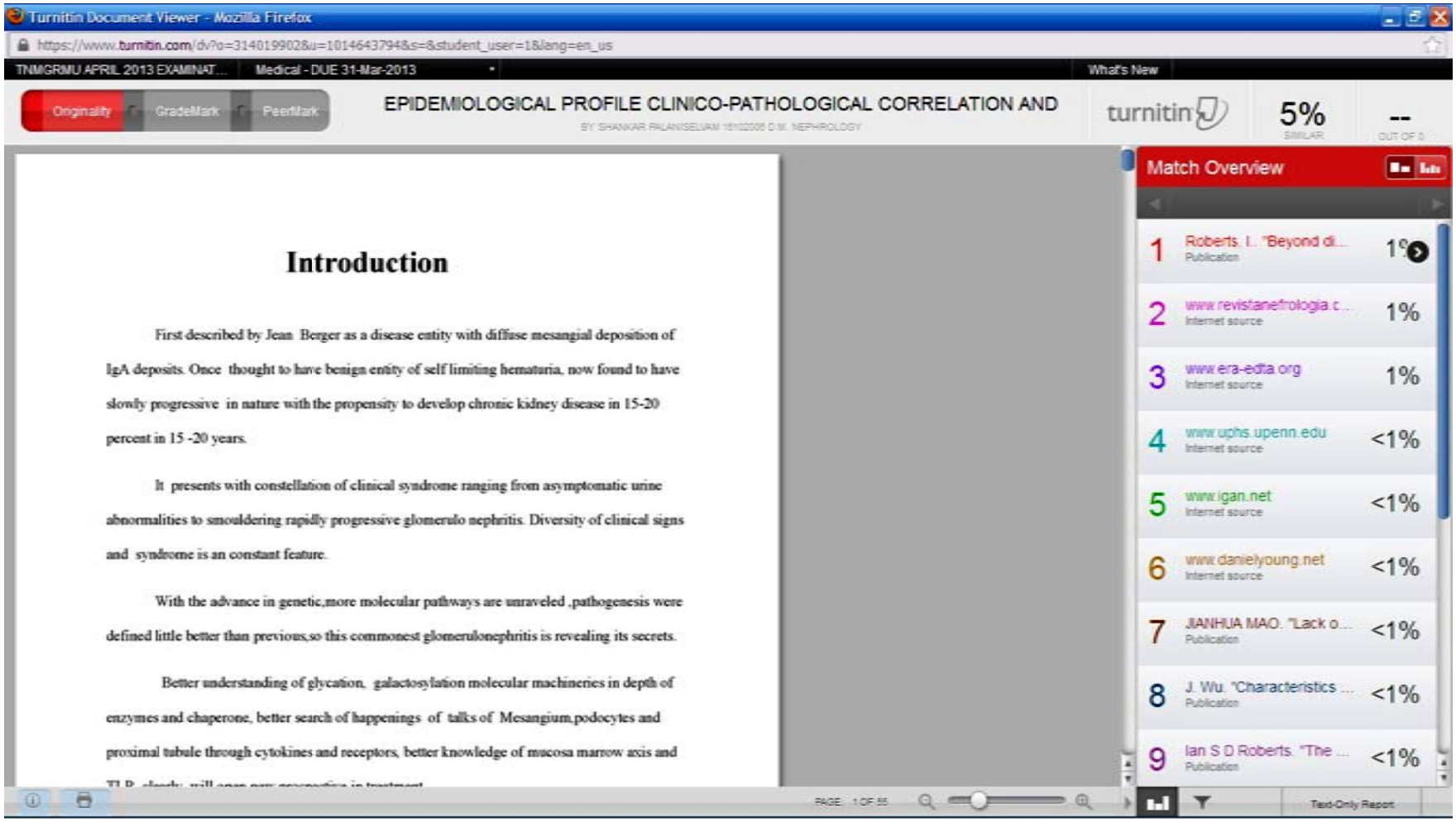
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 18 | REVATHI | F | 46 | A | A | P | A | P(140/100) | N | 5.2 | 4+ | 1-5 RBC | 8.7 | 5.2 | 108 | 2.56 | 25.9 | 5.9 | yes |
| 18 | SURESH | M | 58 | A | A | A | P | N(110/70) | N | 4.7 | 4+ | NIL | 7.8 | 4.7 | 42 | 1.7 | 70.2 | 6 | yes |
| 40 | BANNISHA | F | 64 | A | A | P | P | P(170/110) | F | 5.6 | 4+ | NIL | 10.8 | 5.6 | 62 | 1.5 | 50.6 | 6.8 | yes |
| 21 | SANGEETHA | F | 58 | P | A | P | P | P(180/100) | F | 4.5 | 4+ | 10-12 RBC | 11 | 4.5 | 40 | 1.2 | 15.5 | 7 | yes |
| 29 | SATHYAMOORTHY | M | 58 | A | A | A | P | P(180/100) | E | 7.9 | 4+ | NIL | 12 | 7.9 | 112 | 1.1 | 68.6 | 4.6 | yes |
| 18 | NANDINI | F | 40 | P | P | P | P | P(170/120) | F | 4.8 | 3+ | 10-15 RBC | 10 | 4.8 | 48 | 2.2 | 90.6 | 6.2 | yes |
| 20 | ABIRAMI | F | 44 | A | A | A | A | P(140/90) | N | 4.6 | 4+ | NIL | 9 | 4.6 | 80 | 1.4 | 64 | 1.8 | yes |
| 15 | KANNIAPPAN | M | 56 | A | A | P | P | P(200/100) | E,F | 5.5 | 4+ | NIL | 9.6 | 5.5 | 82 | 2.9 | 40 | 6.5 | yes |
| 17 | SIVAPOOSHNAM | M | 42 | A | P | P | A | N | N | 5.26 | 4+ | plenty | 10 | 5.26 | 60 | 1.1 | 92 | 4.8 | yes |
| 46 | PRABAKARAN | M | 62 | A | A | P | P | P190/100 | F IV, | 4.2 | 4+ | NO | 8.8 | 4.2 | 68 | 1.2 | 27.5 | 7.2 | yes |
| 46 | RAJESWARI | F | 62 | A | A | P | P | P(200/100) | E | 6.6 | 4+ | NIL | 8.5 | 6.6 | 108 | 4.8 | 19.1 | 5.8 | yes |
| 21 | POORNIA | F | 41 | P | A | P | A | N | N | 5.2 | 4+ | 8-10 RBC | 12.2 | 5.2 | 62 | 1.6 | 74.9 | 4.8 | yes |
| 28 | KARTHIKEYAN | M | 51 | A | A | P | P | N | N | 4.8 | 1+ | NIL | 10.8 | 4.8 | 82 | 2.1 | 45 | 1.8 | yes |
| 41 | KUMAR | M | 52 | A | A | A | P | N | N | 5.28 | 3+ | NIL | 11.2 | 5.28 | 64 | 2.47 | 40 | 5.2 | yes |
| 29 | SHANTHI | F | 42 | A | A | P | P | N | N | 5.2 | 4+ | NIL | 9.6 | 5.2 | 52 | 5.2 | 14 | 4.6 | yes |
| 21 | UMA | F | 21 | A | A | A | A | N | N | 2 | 1+ | NIL | 12.2 | 2 | 46 | 1.1 | 90 | 4.4 | yes |
| 39 | SATIYAMOORTY | M | 52 | P | A | P | P | P(180/100) | F | 1.8 | 1+ | 10-12 RBC | 10 | 1.8 | 64 | 2.2 | 40 | 6.2 | yes |
| 10 | USHADEVI | F | 41 | A | A | P | P | N | N | 4.18 | 3+ | NIL | 10.4 | 4.18 | 26 | 1 | 74 | 1.9 | yes |
| 19 | RAM | M | 50 | A | P | P | P | N | N | 6.24 | 4+ | plenty | 12.8 | 6.24 | 16 | 2.8 | 18.8 | 4.1 | yes |
| 27 | SURESH KUMAR | M | 42 | A | A | P | P | P(150/90) | N | 5.16 | 4+ | NIL | 8.4 | 5.16 | 62 | 1.9 | 50 | 5.2 | yes |
| 20 | KRISHNARAJ | M | 40 | P | P | P | P | N | N | 8.5 | 4+ | plenty | 8.4 | 8.5 | 114 | 1.2 | 10 | 8.2 | yes |
| 28 | MANOHARI | F | 46 | P | P | P | P | N | N | 7.8 | 4+ | plenty | 9.6 | 7.8 | 87 | 2.1 | 40 | 6.5 | yes |
| 45 | VANAJA | F | 52 | P | A | A | P | P(140/96) | N | 4.2 | 3+ | 10-12RBC10. | 10.4 | 4.2 | 56 | 1.49 | 24.8 | 5.6 | yes |
| 41 | CHINNHAMBI | M | 41 | A | A | P | P | N | N | 1.25 | 2+ | NIL | 15.6 | 1.25 | 26.4 | 1.1 | 76 | 4.1 | yes |
| 17 | MANIKANDAN | M | 11 | A | P | A | P | N | N | 1.16 | 2+ | plenty | 15 | 1.16 | 51.4 | 5.2 | 18 | 4.7 | yes |
| 27 | KANNAN | M | 52 | A | A | A | A | P | F | 4.19 | 3+ | NIL | 9.2 | 4.19 | 100.8 | 1.15 | 26 | 6.7 | yes |
| 18 | ILANGOVAN | M | 56 | A | P | P | P | P | N | 2.42 | 2+ | plenty | 11 | 2.42 | 41 | 4.6 | 18 | 5.1 | yes |
| 16 | SUBRAMANI | M | 17 | A | A | P | P | N | N | 1.92 | 1+ | NIL | 12.8 | 1.92 | 79 | 2.1 | 28 | 4.5 | yes |
| 21 | GANSEH BABU | M | 41 | P | P | P | P | P(170/100) | F | 5.1 | 4+ | plenty | 10 | 5.1 | 61 | 5.1 | 16 | 8.1 | yes |
| 51 | CHANDRASEKARAN | M | 61 | A | A | A | A | N(110/80) | N | 1.1 | 4+ | NIL | 12 | 1.1 | 42 | 2.72 | 28.6 | 7.2 | NO |
| 24 | MUNIAMMAL | F | 46 | A | P | P | P | N(110/70) | N | 2.6 | 1+ | plenty | 9.2 | 2.6 | 54 | 2.27 | 27.8 | 7 | NO |
| 38 | SYED | M | 62 | A | A | P | A | P(160/100) | F | 1.8 | 2+ | NIL | 12 | 1.8 | 22 | 1.2 | 58.1 | 4.6 | NO |
| 12 | RAMAN | M | 52 | P | A | A | A | N | N | 2.4 | 4+ | 6-8 RBC | 11.8 | 2.4 | 48 | 1.2 | 19.1 | 4.4 | NO |
| 10 | GOVINARAJ | M | 60 | P | N | A | A | P(200/110 | E | 2.8 | 2+ | 10-15 RBC | 10.8 | 2.8 | 64 | 2 | 40.2 | 5.8 | NO |

| | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 50 | GOWRI | M | 68 | A | P | P | A | P(180/100) | E | 0.4 | 2+ | NIL | 9.8 | 0.4 | 42 | 0.9 | 94 | 4 | NO |
| 14 | SASIKALA | F | 52 | A | P | P | A | P(140/100) | N | 1.6 | 2+ | plenty | 8.8 | 1.6 | 18 | 0.8 | 90 | 4.8 | NO |
| 18 | KRISHNAMOORTHY | M | 62 | A | A | P | P | P(140/100) | N | 2.6 | 1+ | NIL | 9.8 | 2.6 | 60 | 2.6 | 42 | 4.7 | NO |
| 39 | VIJAYA | F | 55 | A | A | P | A | P140/100 | N | 1.4 | 4+ | NIL | 12 | 1.4 | 46 | 1.8 | 40 | 5.6 | NO |
| 14 | MYSORE RAHMAN | M | 61 | A | A | P | P | P(210/110 | E | 2.7 | 1+ | NIL | 8.4 | 2.7 | 64 | 4.8 | 26 | 6.2 | NO |
| 54 | JEGANATHAN | M | 62 | P | A | P | P | N | N | 2.6 | 2+ | 8-10 RBC | 11 | 2.6 | 16 | 1 | 94 | 4 | NO |
| 18 | RAVI | M | 52 | P | A | P | P | P(180/100) | F | 2.4 | 2+ | 10-12 RBC | 10.8 | 2.4 | 40 | 1 | 24 | 6.2 | NO |
| 11 | MUTHUKUMAR | M | 55 | A | A | P | P | P(150/100) | F,E | 2.4 | 2+ | NIL | 12 | 2.4 | 46 | 1.8 | 70 | 4.2 | NO |
| 39 | POONGOTHAI | F | 56 | A | A | P | P | N | N | 0.06 | NIL | NO | 10.8 | 0.06 | 42 | 2.1 | 67 | 4.1 | NO |
| 21 | ARCHANA | F | 16 | P | A | P | P | N | N | 2.2 | 2+ | 15-20RBC | 12.8 | 2.2 | 56 | 1.72 | 41 | 4.6 | NO |
| 38 | RAJESH | M | 56 | A | P | P | A | N | N | 0.04 | NIL | plenty | 12.8 | 0.04 | 48 | 2.1 | 47 | 4.1 | NO |
| 42 | KAILAINATHAN | M | 42 | A | P | P | P | P(160/90) | N | 0.06 | NIL | plenty | 10.2 | 0.06 | 44 | 2.8 | 26 | 4 | NO |
| 17 | NANDAKUMAR | M | 12 | A | P | P | P | N | N | 2.4 | 2+ | plenty | 10.6 | 2.4 | 41.2 | 2.1 | 25 | 4.7 | NO |
| 24 | THIRUMALAI | M | 18 | A | P | P | P | P(140/96) | N | 1.8 | 2+ | plenty | 12.8 | 1.8 | 54 | 1.1 | 42 | 5.6 | NO |
| 11 | KAMATCHI | F | 47 | A | A | P | P | P(190/110) | F | 1.71 | 2+ | NIL | 10.2 | 1.71 | 56 | 2.1 | 52 | 5.7 | NO |
| 45 | RAMAMOORTHY | M | 50 | A | A | P | P | P(160/100 | F | 1.2 | 1+ | NIL | 9.8 | 1.2 | 24 | 2.8 | 16 | 5.6 | NO |
| 54 | IBRAHIMN | M | 54 | A | P | P | P | P(160/90) | N | 1.8 | 1+ | plenty | 12.8 | 1.8 | 64 | 1.2 | 90 | 4.7 | NO |
| 14 | GOPINATH | M | 61 | A | P | P | P | P(180/106) | F | 1.8 | 2+ | plenty | 11.2 | 1.8 | 68 | 1.4 | 101 | 4 | NO |
| 54 | PALANI | M | 17 | P | A | P | P | P(164/90) | F | 1 | 1+ | 6-8RBC | 10.2 | 1 | 58 | 2.8 | 17.15 | 1.8 | NO |
| 20 | SURYA | M | 16 | A | P | P | A | N | N | 0.02 | NIL | plenty | 12.4 | 0.02 | 64 | 1.6 | 26 | 4.2 | NO |
| 42 | ELUMALAI | M | 56 | A | A | P | P | P140/100 | N | 2.8 | 2+ | NIL | 10.4 | 2.8 | 47 | 1.4 | 46 | 6.9 | NO |
| 56 | MARIAMMAL | F | 50 | A | P | P | P | N | N | 2.76 | 2+ | plenty | 11.8 | 2.76 | 62 | 1.8 | 90 | 5.7 | NO |
| 18 | RENUGA | M | 16 | A | A | P | P | N | N | 2.4 | 2+ | NIL | 11.8 | 2.4 | 98 | 2.1 | 40 | 4.7 | NO |
| 52 | MOORTY | M | 62 | A | P | P | P | P | F | 0.02 | NIL | plenty | 12.8 | 0.02 | 67 | 1.1 | 44 | 5.1 | NO |
| 41 | SENTHIL | M | 49 | A | P | P | P | P | N | 2.6 | 2+ | plenty | 10.4 | 2.6 | 54 | 2.1 | 41.7 | 6.7 | NO |
| 14 | JEYAVEL | M | 56 | A | P | P | P | P | N | 2.8 | 1+ | plenty | 11.8 | 2.8 | 62 | 2.1 | 40 | 6.1 | NO |
| 16 | SULOCHANA | F | 51 | P | A | P | P | P | N | 1.8 | 2+ | 8-10 RBC | 11.6 | 1.8 | 57 | 2.6 | 40.6 | 4.5 | NO |
| 60 | VELAYUTHAM | M | 62 | A | P | P | P | N | N | 2.6 | 2+ | 12-14 RBC | 14.2 | 2.6 | 78 | 2.1 | 17 | 1.6 | NO |

| NON NEPHROTIC | NEPHRITIC | Nnis | AKD | HT | CKD | IF igM | IF IgA | IgG | C1Q | IF C1 | M SCORE | E SCORE | S SCORE | T SCORE | CRESENTS | ACEI/ARB/STATIN | S.CREATINIE | STEROID | CYCLOPHOSPHAMIDE | ANTIHT | PCR/FW | URINE RBCF/W | S.CREATININE F/W | GFR FINAL |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| NO | yes | yes | NO | YES | No | 1+ | 4+ | NO | NO | 1+ | M1 | E0 | S1 | T1 | NO | GIVEN | 4.8mg | 1 | NO | YES | 1.4 | NIL | 1.7 | 41.1 |
| NO | yes | yes | NO | No | No | No | 1+ | NO | NO | NIL | M1 | E0 | S0 | T1 | YES(1/6) | GIVEN | 1.8 | 1 | GIVEN | No | 5.5 | NIL | 5.22 | 5.6 |
| NO | NO | NO | NO | YES | NO | 2+ | 1+ | NO | NO | 2+ | M0 | E0 | S1 | T2 | NO | GIVEN | 1.4 | 2 | NO | YES | 0.8 | NIL | 0.8 | 99.2 |
| NO | NO | NO | NO | NO | NO | 1+ | 4+ | 1+ | NO | NO | M1 | E1 | S1 | T1 | NO | GIVEN | 2.1 | 2 | NO | NO | 2.47 | NIL | 1.4 | 50.5 |
| NO | NO | NO | NO | YES | NO | 1+ | 4+ | 1+ | NO | NO | M1 | E1 | S0 | T2 | NO | GIVEN | 8.1 | 1 | MMF | YES | 4.2 | NIL | 6.8 | 9.5 |
| NO | yes | yes | YES | No | No | 1+ | 4+ | NO | NO | NO | M0 | E1 | S0 | T2 | NO | GIVEN | 1.1 | 1 | NO | No | 0.06 | 2-4 RBC | 0.7 | 114 |
| NO | yes | yes | NO | YES | No | No | 4+ | NO | NO | 1+ | M1 | E1 | S1 | T2 | PARTIAL | GIVEN | 2 | 1 | GIVEN | YES | 2.6 | 2-4RBC | 1 | 64 |
| NO | yes | yes | NO | YES | No | No | 4+ | NO | NO | 1+ | M0 | E0 | S1 | T1 | YES4/10 | GIVEN | 1 | 1 | GIVEN | YES | 4.4 | NIL | 1.6 | 47.8 |
| YES | YES | NO | NO | No | No | No | 4+ | 1+ | NO | 1+ | M1 | E0 | S0 | T2 | NO | GIVEN | 1.1 | 2 | NO | No | 0.4 | NIL | 0.7 | 124 |
| YES | yes | yes | NO | No | No | 1+ | 4+ | NO | NO | 1+ | M0 | E1 | S0 | T0 | NO | GIVEN | 1 | 2 | NO | No | 0.8 | NIL | 0.8 | 80 |
| NO | yes | NO | YES | YES | NO | No | 1+ | NO | NO | NIL | M1 | E0 | S0 | T0 | NO | NO | 1.6 | 2 | NO | No | 0.2 | NIL | 0.7 | 98 |
| NO | yes | YES | NO | YES | NO | 2+ | 1+ | NO | NO | 2+ | M1 | E0 | S0 | T2 | YES10/14 | GIVEN | 4.8 | 1 | NO | No | 4 |  | 2.8 | 10.8 |
| YES | NO | NO | NO | YES | NO | 1+ | 4+ | NO | NO | NO | M0 | E1 | S1 | T2 | NO | GIVEN | 1.6 | 2 | NO | No | 0.8 | NIL | 0.9 | 101.7 |
| YES | yes | NO | NO | No | No | No | 1+ | 1+ | NO | NO | M1 | E1 | S0 | T2 | PARTIAL | GIVEN | 2 | 1 | NO | No | 0.02 | NIL | 0.6 | 121 |
| YES | Yes | NO | NO | No | No | No | 1+ | NO | NO | NO | M0 | E1 | S0 | T2 | NO | NO | 0.9 | 2 | NO | No | 0.1 | NIL | 0.7 | 75 |
| YES | NO | NO | NO | No | No | No | 1+ | 1+ | NO | NO | M0 | E1 | S0 | T1 | NO | GIVEN | 1.2 | 2 | NO | No | 0.04 | NIL | 0.8 | 84 |
| YES | yes | NO | NO | YES | No | No | 1+ | NO | NO | NO | M1 | E1 | S1 | T0 | NO | GIVEN | 1.2 | 2 | NO | No | 0.29 | NIL | 0.8 | 82 |
| YES | NO | NO | NO | No | No | 2+ | 4+ | 1+ | NO | 1+ | M0 | E0 | S1 | T0 | NO | GIVEN | 1.5 | 2 | NO | No | 0.1 | NIL | 0.9 | 74 |
| YES | yes | NO | NO | No | No | No | 1+ | NO | NO | 1+ | M1 | E0 | S0 | T2 | NO | GIVEN | 1.2 | 2 | NO | No | 0.2 | NIL | 0.8 | 92.6 |
| NO | yes | NO | NO | No | No | No | 4+ | NO | NO | NO | M1 | E1 | S0 | T2 | YES4/11 | NO | 2.8 | 1 | NO | No | 0.02 | 2-4RBC | 0.8 | 92.1 |
| YES | yes | NO | NO | NO | NO | 1+ | 4+ | NO | NO | 1+ | M1 | E0 | S1 | T0 | NO | GIVEN | 1.1 | 2 | NO | No | 0.9 | NIL | 0.6 | 120.8 |
| NO | NO | NO | NO | NO | NO | 1+ | 4+ | NO | NO | 1+ | M1 | E0 | S0 | T1 | NO | GIVEN | 1.8 | 2 | NO | No | 0.2 | NIL | 0.8 | 86 |
| NO | NO | NO | YES | YES | No | No | 1+ | NO | NO | NO | M1 | E0 | S0 | T2 | NO | NO | 1.2 | 2 | NO | No | NIL | NIL | 1 | 79 |
| YES | NO | NO | NO | NO | NO | NO | 1+ | NO | NO | 2+ | M1 | E0 | S1 | T1 | YES(4/15 | GIVEN | 1.1 | 1 | NO | No | 0.21 | NIL | 0.9 | 81.2 |
| NO | yes | yes | NO | No | No | No | 4+ | NO | NO | NIL | M0 | E0 | S0 | T0 | YES(4/10) | GIVEN | 1.4 | 1 | GIVEN | No | 1.2 | NIL | 0.7 | 65 |

| | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| NO | NO | NO | NO | YES | No | 2+ | 4+ | NO | NO | 1+ | M0 | E1 | S0 | T1 | YES(4/9) | GIVEN | 2.56 | 1 | NO | No | 0.6 | NIL | 1.29 | 65 |
| NO | NO | NO | NO | NO | NO | No | 1+ | NO | NO | NIL | M1 | E1 | S0 | T2 | YES(2/6) | GIVEN | 1.7 | 1 | NO | No | 1.8 | NIL | 1.5 | 21.5 |
| NO | NO | NO | NO | YES | No | No | 1+ | NO | NO | 2+ | M1 | E1 | S1 | T1 | YES(6/25) | GIVEN | 1.5 | 1 | NO | No | 4.1 | NIL | 1.2 | 61 |
| NO | YES | YES | NO | YES | No | 1+ | 1+ | 1+ | 1+ | 2+ | M0 | E1 | S0 | T1 | YES(1/10) | GIVEN | 1.2 | 1 | NO | No | 0.4 | NIL | 1 | 94.1 |
| NO | NO | NO | NO | YES | No | 1+ | 1+ | 2+ | NO | NO | M1 | E1 | S1 | T2 | NO | GIVEN | 1.1 | 1 | NO | No | 4.2 | NIL | 0.8 | 111.8 |
| NO | YES | YES | NO | YES | NO | No | 4+ | NO | 1+ | NO | M0 | E0 | S1 | T2 | YES(1/12) | GIVEN | 2.2 | 1 | NO | No | 2.2 | 5-8RBC | 5.8 | 11.5 |
| NO | NO | NO | NO | NO | NO | 2+ | 4+ | NO | NO | 1+ | M1 | E1 | S1 | T0 | YES(1/8) | GIVEN | 1.4 | 1 | MMF | No | 0.56 | NIL | 0.8 | 91.7 |
| NO | NO | NO | NO | YES | NO | NO | 1+ | 1+ | NO | 1+ | M1 | E1 | S0 | T2 | NO | GIVEN | 2.9 | 1 | NO | No | 1.8 | NIL | 4.2 | 19.4 |
| NO | yes | yes | NO | No | No | No | 4+ | 1+ | NO | 1+ | M1 | E1 | S1 | T0 | YES1/21 | GIVEN | 1.1 | 1 | NO | No | 0.86 | NIL | 1 | 62 |
| NO | NO | NO | NO | YES | No | 2+ | 4+ | 2+ | NO | 1+ | M1 | E0 | S1 | T1 | NO | GIVEN | 1.2 | 1 | NO | No | 9.6 | NIL | 12 | 12 |
| NO | NO | NO | NO | YES | No | 1+ | 1+ | 2+ | NO | 1+ | M0 | E0 | S1 | T1 | NO | GIVEN | 4.8 | 1 | NO | No | 2 | NIL | 7.2 | 9.8 |
| NO | yes | yes | NO | No | No | 1+ | 4+ | 1+ | NO | NO | M0 | E1 | S1 | T2 | NO | GIVEN | 1.6 | 1 | NO | No | 0.08 | NIL | 1 | 70 |
| NO | NO | NO | NO | No | No | No | 1+ | 1+ | NO | NO | M1 | E1 | S0 | T1 | NO | GIVEN | 2.1 | 1 | NO | No | 1.4 | NIL | 1.2 | 68.7 |
| NO | NO | NO | NO | No | NO | 2+ | 1+ | NO | NO | 2+ | M1 | E1 | S1 | T2 | NO | GIVEN | 2.47 | 2 | NO | No | 1.61 | NIL | 2.6 | 28 |
| NO | NO | NO | NO | NO | NO | NO | 1+ | 1+ | NO | NO | M1 | E1 | S0 | T1 | NO | GIVEN | 5.2 | 1 | GIVEN O | No | 0.2 | NIL | 0.8 | 68.8 |
| NO | NO | NO | NO | NO | NO | NO | 4+ | NO | NO | NO | M1 | E1 | S1 | T2 | NO | GIVEN | 1.1 | 2 | NO | No | 0.78 | NIL | 0.7 | 46 |
| NO | yes | yes | NO | YES | NO | 1+ | 4+ | 1+ | NO | NO | M1 | E0 | S1 | T1 | NO | GIVEN | 2.2 | 1 | NO | No | 0.01 | NIL | 1 | 70.8 |
| NO | NO | NO | NO | NO | NO | No | 1+ | NO | NO | 1+ | M1 | E1 | S1 | T0 | NO | GIVEN | 1 | 2 | NO | No | 0.12 | NIL | 0.9 | 62 |
| NO | yes | yes | NO | No | No | No | 1+ | NO | NO | 1+ | M1 | E1 | S1 | T2 | NO | GIVEN | 2.8 | 1 | NO | No | 4 | NIL | 1.8 | 19 |
| NO | NO | NO | NO | YES | NO | No | 1+ | NO | NO | 1+ | M0 | E1 | S1 | T1 | YES | GIVEN | 1.9 | 1 | NO | No | 1.9 | NIL | 1.5 | 19 |
| NO | yes | Yes | NO | NO | NO | NO | 1+ | NO | NO | NO | M1 | E1 | S1 | T1 | NO | GIVEN | 1.2 | 1 | NO | No | 4.2 | NIL | 5.6 | 12 |
| NO | YES | YES | NO | NO | NO | 2+ | 4+ | NO | NO | N0 | M1 | E0 | S1 | T2 | NO | GIVEN | 2.1 | 1 | NO | No | 2.48 | NIL | 1.6 | 18 |
| NO | YES | YES | NO | No | No | 1+ | 1+ | NO | 1+ | 1+ | M1 | E0 | S1 | T2 | NO | GIVEN | 1.49 | 1 | NO | No | 0.8 | NIL | 1.1 | 51 |
| NO | NO | NO | NO | NO | NO | 1+ | 4+ | N0 | NO | 1+ | M1 | E1 | S0 | T1 | NO | GIVEN | 1.1 | 2 | NO | No | 0.11 | NIL | 0.8 | 68.7 |
| NO | yes | yes | NO | No | NO | 2+ | 4+ | NO | NO | 1+ | M1 | E1 | S0 | T2 | YES | GIVEN | 5.2 | 1 | NO | No | 0.46 | NIL | 0.9 | 62.6 |
| NO | NO | NO | NO | YES | NO | NO | 1+ | NO | NO | NO | M0 | E0 | S0 | T2 | NO | GIVEN | 1.15 | 1 | NO | No | 2.7 | NIL | 1.86 | 41.9 |
| NO | yes | yes | NO | YES | No | 1+ | 4+ | NO | NO | NO | M1 | E1 | S0 | T2 | YES | GIVEN | 4.6 | 1 | NO | No | 1.6 | NIL | 2.1 | 14 |
| NO | NO | NO | NO | NO | NO | 1+ | 1+ | NO | NO | 1+ | M0 | E0 | S0 | T1 | NO | GIVEN | 2.1 | 1 | GIVEN | No | 1.07 | NIL | 0.8 | 80 |
| NO | yes | yes | NO | YES | NO | 1+ | 4+ | 1+ | NO | 1+ | M0 | E1 | S1 | T1 | NO | GIVEN | 5.1 | 1 | NO | No | 2.6 | NIL | 1.6 | 44.6 |
| YES | NO | NO | NO | No | No | No | 1+ | NO | NO | NIL | M1 | E1 | S1 | T2 | NO | GIVEN | 2.72 | 2 | NO | No | 0.8 | NIL | 1.1 | 78 |
| YES | yes | NO | NO | NO | NO | 1+ | 1+ | 1+ | NO | NIL | M0 | E1 | S0 | T2 | NO | GIVEN | 2.27 | 1 | NO | No | 0.06 | NIL | 0.8 | 78.8 |
| YES | NO | NO | NO | YES | No | 2+ | 4+ | NO | NO | NIL | M0 | E1 | S1 | T1 | NO | GIVEN | 1.2 | 2 | NO | No | 4.8 | NIL | 4.2 | 24 |
| NO | yes | NO | NO | No | No | No | 1+ | 1+ | NO | NIL | M1 | E0 | S0 | T1 | NO | NO | 1.2 | 2 | NO | No | 0.2 | NIL | 0.7 | 111.4 |
| YES | yes | NO | NO | YES | No | 1+ | 1+ | NO | NO | NIL | M1 | E0 | S0 | T1 | NO | GIVEN | 2 | 1 | NO | No | 0.2 | NIL | 0.8 | 114.6 |

| | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| NO | YES | NO | NO | YES | NO | 1+ | 4+ | NO | NO | 2+ | M0 | E1 | S0 | T0 | NO | NO | 0.9 | 2 | NO | No | NIL | NIL | 0.8 | 106 |
| NO | yes | NO | NO | YES | NO | 2+ | 4+ | NO | NO | 1+ | M0 | E1 | S1 | T2 | NO | NO | 0.8 | 2 | NO | No | 0.2 | 4-8 RBC | 0.7 | 91 |
| YES | NO | NO | NO | YES | No | No | 1+ | NO | NO | NO | M1 | E0 | S0 | T2 | NO | NO | 2.6 | 2 | NO | No | 1.4 | NIL | 1.4 | 62.7 |
| NO | NO | NO | NO | YES | NO | 2+ | 4+ | NO | NO | 1+ | M1 | E1 | S1 | T2 | NO | GIVEN | 1.8 | 2 | NO | No | 0.28 | NIL | 1.2 | 54.1 |
| YES | NO | NO | NO | YES | No | No | 4+ | 1+ | NO | NO | M1 | E1 | S1 | T1 | NO | GIVEN | 4.8 | 1 | NO | No | 2 | NIL | 5.2 | 18.6 |
| YES | yes | NO | NO | No | No | No | 4+ | 1+ | NO | NO | M0 | E1 | S0 | T1 | NO | GIVEN | 1 | 2 | NO | No | 0.2 | NIL | 0.8 | 92.6 |
| YES | yes | NO | NO | YES | No | NO | 1+ | NO | NO | NO | M1 | E1 | S0 | T1 | NO | GIVEN | 1 | 1 | NO | No | 1.6 | NIL | 1.6 | 46 |
| YES | NO | NO | NO | YES | No | 1+ | 1+ | 1+ | NO | NO | M0 | E0 | S0 | T0 | NO | GIVEN | 1.8 | 2 | NO | No | 0.04 | NIL | 1 | 81.4 |
| NO | NO | NO | YES | No | No | 1+ | 4+ | NO | NO | NO | M0 | E0 | S0 | T0 | NO | NO | 2.1 | 2 | NO | No | NIL | NIL | 0.6 | 74.9 |
| YES | NO | NO | NO | No | No | 2+ | 1+ | 1+ | NO | 1+ | M1 | E1 | S1 | T2 | PARTIAL | GIVEN | 1.72 | 1 | NO | No | 0.8 | NIL | 0.8 | 84.1 |
| NO | YES | NO | YES | NO | NO | 1+ | 4+ | NO | NO | NO | M1 | E1 | S0 | T2 | NO | NO | 2.1 | 2 | NO | No | NIL | NIL | 0.6 | 108 |
| NO | yes | NO | YES | NO | NO | NO | 4+ | 1+ | NO | NO | M1 | E0 | S0 | T2 | NO | NO | 2.8 | 2 | NO | No | 0.04 | NIL | 0.8 | 70.4 |
| YES | yes | NO | NO | No | No | 1+ | 1+ | NO | NO | 2+ | M1 | E1 | S0 | T1 | NO | GIVEN | 2.1 | 1 | NO | No | 0.8 | NIL | 0.7 | 79 |
| YES | yes | NO | NO | NO | NO | 1+ | 1+ | 1+ | NO | 1+ | M1 | E0 | S1 | T2 | NO | NO | 1.1 | 2 | NO | No | 0.14 | NIL | 0.9 | 68 |
| YES | NO | NO | NO | YES | No | No | 1+ | NO | NO | 1+ | M1 | E0 | S0 | T1 | NO | NO | 2.1 | 2 | NO | No | 0.2 | NIL | 1.1 | 61 |
| YES | NO | NO | NO | YES | NO | 2+ | 1+ | NO | NO | 1+ | M1 | E0 | S1 | T1 | NO | NO | 2.8 | 1 | NO | No | 0.06 | NIL | 0.8 | 82.5 |
| YES | Yes | NO | NO | No | No | No | 4+ | NO | NO | NO | M0 | E0 | S0 | T0 | NO | NO | 1.2 | 2 | NO | No | 1.2 | NIL | 1 | 70 |
| YES | yes | NO | NO | YES | NO | 2+ | 4+ | NO | NO | 1+ | M0 | E0 | S1 | T0 | NO | NO | 1.4 | 2 | NO | No | 1.4 | NIL | 1.1 | 92.8 |
| YES | yes | NO | NO | YES | No | No | 1+ | NO | NO | NO | M1 | E0 | S1 | T2 | NO | NO | 2.8 | 1 | NO | No | 0.2 | NIL | 0.8 | 60 |
| YES | yes | NO | NO | No | No | 2+ | 4+ | 1+ | 1+ | 1+ | M1 | E0 | S0 | T2 | NO | NO | 1.6 | 1 | NO | No | 0.02 | NIL | 0.9 | 67 |
| YES | NO | NO | NO | No | No | No | 1+ | NO | NO | NO | M1 | E0 | S0 | T2 | NO | GIVEN | 1.4 | 2 | NO | No | 0.8 | NIL | 1 | 85.8 |
| NO | yes | NO | NO | NO | NO | 1+ | 4+ | NO | NO | NO | M0 | E0 | S1 | T0 | NO | NO | 1.8 | 2 | GIVEN | No | 0.06 | NIL | 0.9 | 70.8 |
| YES | NO | NO | NO | No | NO | No | 1+ | 1+ | 1+ | 1+ | M1 | E0 | S1 | T1 | N0 | GIVEN | 2.1 | 1 | NO | No | 0.26 | NIL | 0.9 | 67.8 |
| NO | YES | NO | NO | YES | NO | NO | 1+ | 1+ | NO | 1+ | M1 | E0 | S1 | T2 | NO | GIVEN | 1.1 | 1 | NO | No | 0.02 | NIL | 0.8 | 94.7 |
| NO | yes | NO | NO | YES | No | 1+ | 4+ | NO | NO | N0 | M1 | E0 | S1 | T2 | NO | GIVEN | 2.1 | 1 | NO | No | 0.06 | NIL | 1 | 74 |
| YES | YES | NO | NO | YES | 2 | 1+ | 1+ | 2+ | 1+ | 1+ | M1 | E0 | S0 | T2 | NO | NO | 2.1 | 1 | NO | No | 0.06 | NIL | 1.2 | 62 |
| YES | YES | NO | NO | NO | 2 | 1+ | 4+ | 1+ | 1+ | NO | M1 | E0 | S0 | T1 | N0 | GIVEN | 2.6 | 1 | NO | No | 0.06 | NIL | 1 | 77 |
| YES | YES | NO | NO | NO | NO | 1+ | 2+ | NO | NO | NO | M1 | E0 | S0 | T1 | NO | GIVEN | 2.1 | 2 | NO | No | 0.4 | NIL | 0.8 | 110.9 |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Introduction
First described by Jean Berger as a disease entity with diffuse mesangial deposition of IgA deposits. Once thought to have benign entity of self limiting hematuria, now found to have slowly progressive in nature with the propensity to develop chronic kidney disease in 15-20 percent in 15 -20 years.
It presents with constellation of clinical syndrome ranging from asymptomatic urine abnormalities to smouldering rapidly progressive glomerulo nephritis. Diversity of clinical signs and syndrome is an constant feature.
With the advance in genetic,more molecular pathways are unraveled ,pathogenesis were defined little better than previous,so this commonest glomerulonephritis is revealing its secrets.
Better understanding of glycation, galactosylation molecular machineries in depth of enzymes and chaperone, better search of happenings of talks of Mesangium,podocytes and proximal tubule through cytokines and receptors, better knowledge of mucosa marrow axis and
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Match Overview
1 Roberts, I.. "Beyond di... Publication 1%
2 www.revistanefrologia.c... Internet source 1%
3 www.era-edta.org Internet source 1%
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9 Ian S D Roberts. "The ... Publication <1%
Text-Only Report

**FIGURE 1:SEX RATIO**

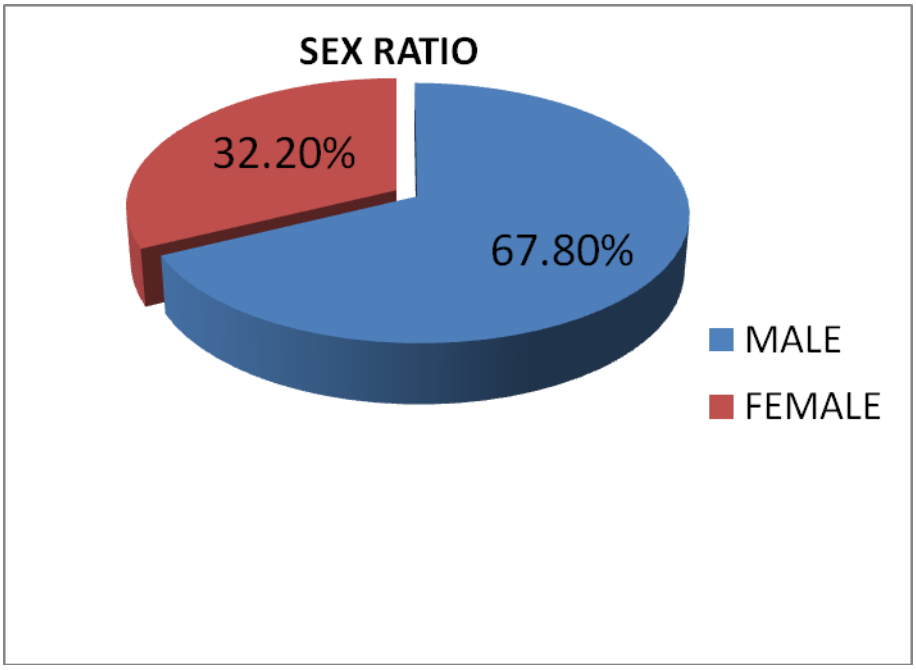



**FIGURE 2: SYNDROMIC PRESENTATION OF IgA (IN PERCENTAGE)**

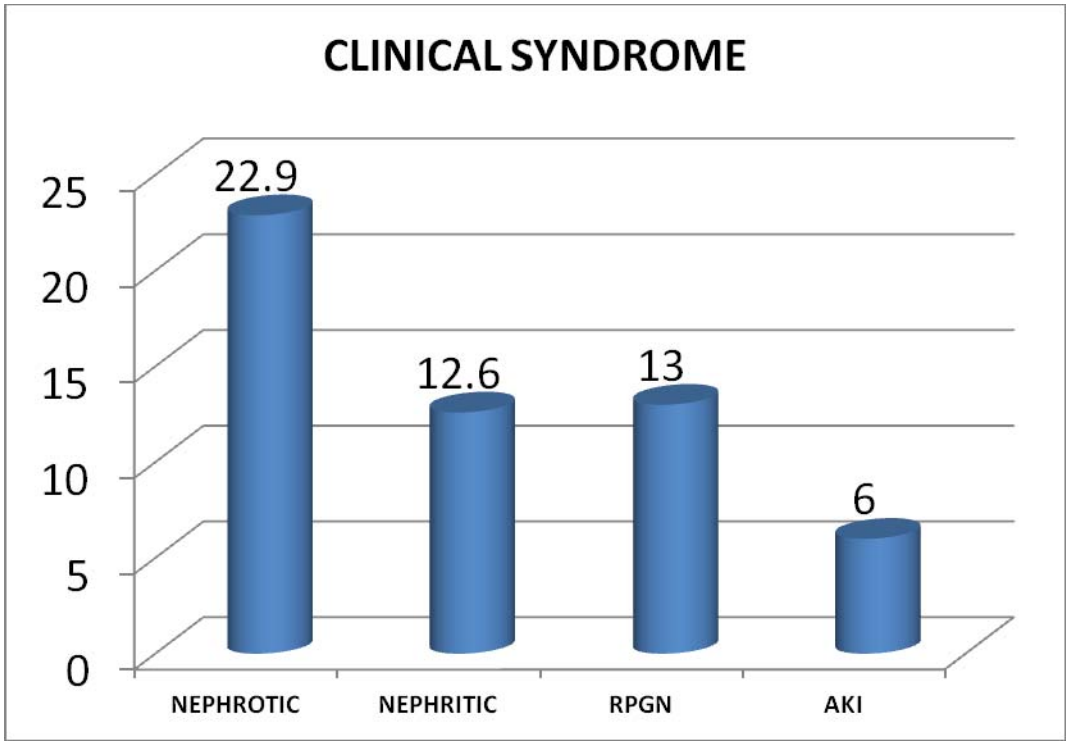


**FIGURE 3: BIOPSY FINDING IN IgAN(MEST SCORING) IN PERCENTAGE:**

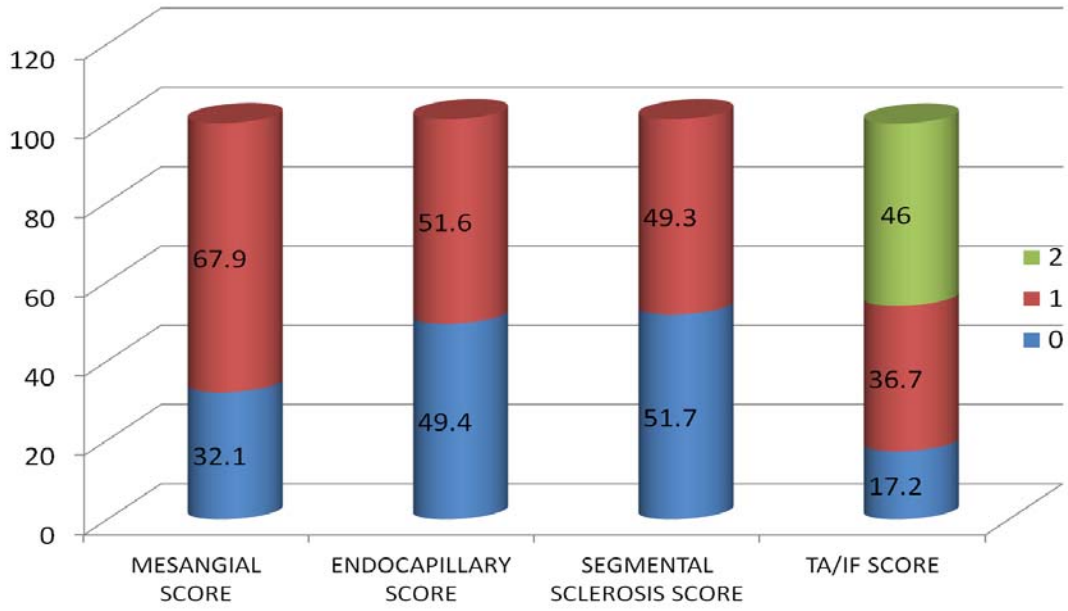



**FIGURE 4: VARIABLES ANALYSED IN PATIENTS PRESENTED WITH RENAL FAILURE:**

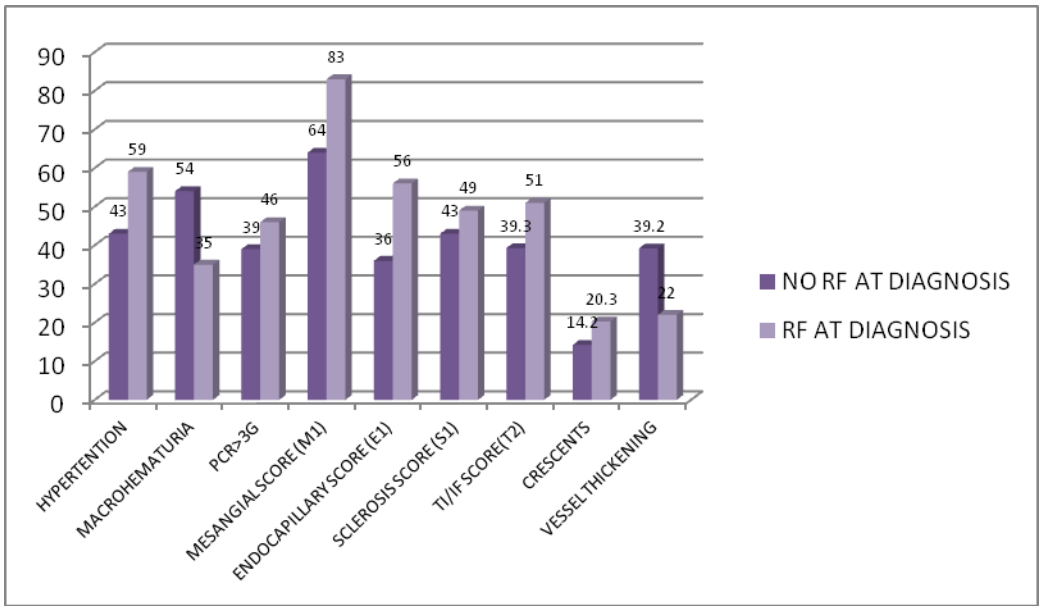
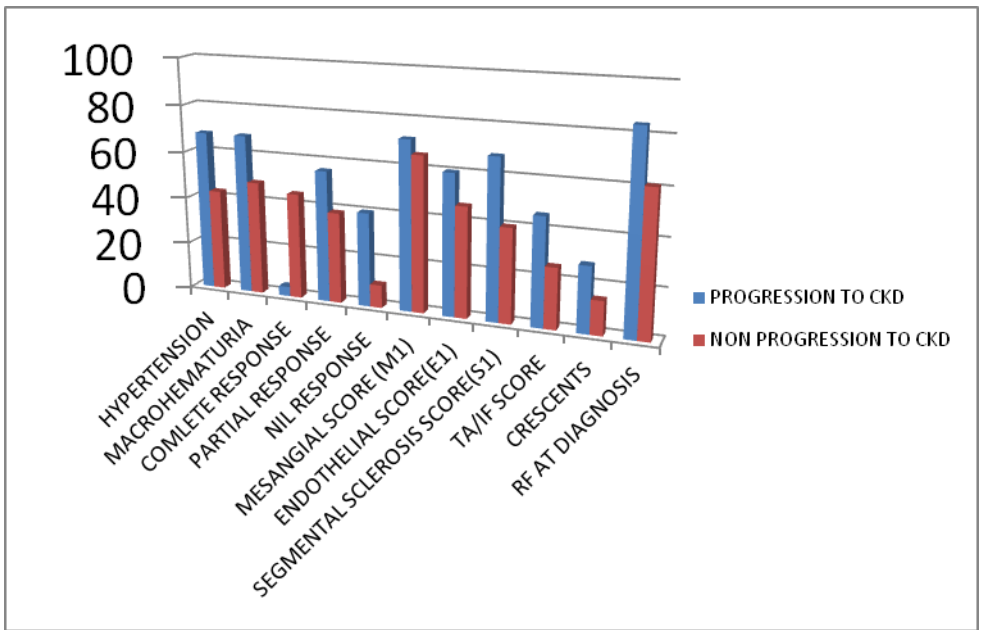


**FIGURE 5.VARIABLES ANALYSED IN PROGRSESSION TO CKD**



Name: Sex: Age:

I P No: Address:

DOA:

| PRESENTATION | DURATION | |
|---|---|---|
| 1.Hematuria(Micro/Macro) | | |
| 2.Edema legs | | |
| 3.Oliguria/Anuria | | |
| 4.Hypertension | | |
| 5.AKI | | |
| 6.CKD(Duration of renal failure) | | |
| 7.Duration of follow up | | |
| 8.Family h/o | | |

| INVESTIGATION | | | | RESP TO Rx |
|---|---|---|---|---|
| URINE | | | | |
| PROTEIN | | | | |
| RBC | | | | |
| DEPOSITS | | | | |
| PCR | | | | |
| C/S | | | | |
| Hb | | | | |
| Tc | | | | |
| PLATELETS | | | | |
| UREA | | | | |
| CREATININE | | | | |
| SUGAR | | | | |
| URIC ACID | | | | |
| T.PROTEIN | | | | |

| | | | | |
|---|---|---|---|---|
| ALBUMIN | | | | |
| BILIRUBIN | | | | |
| OT | | | | |
| PT | | | | |
| ALP | | | | |
| C3/C4 | | | | |
| Na/K/ | | | | |
| USG ABD | | | | |

Biopsy findings:

LM:

IF:

MEST SCORE

TREATMENT

| DRUGS | DOSE | DURATION |
|---|---|---|
| ACEI/ARB/STATIN | | |
| STEROIDS | | |
| CYCLOPHOSPHAMIDE | | |
| MMF | | |
| AZATHIOPRINE | | |

**INSTITUTIONAL ETHICS COMMITTEE**
**MADRAS MEDICAL COLLEGE, CHENNAI -3**

Telephone No : 044 25305301
Fax : 044 25363970

## CERTIFICATE OF APPROVAL

To
Dr. Shankar .P
PG in DM Nephrology
Madras Medical College, Chennai -3

Dear Dr. Shankar .P

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "Epidemiological profile, clinicopathological correlation and treatment response in adult patients with IgA nephropathy" No. 14122011

The following members of Ethics Committee were present in the meeting held on 22.12.2011 conducted at Madras Medical College, Chennai -3.

| | | |
|---|---|---|
| 1. | Prof. S.K. Rajan. MD | -- Chairperson |
| 2. | Prof. R. Nandhini MD<br>Director, Institute of Pharmacology ,MMC, Ch-3 | -- Member |
| 3 | Prof. Pregna B. Dolia MD<br>Director , Institute of Biochemistry, MMC, Ch-3 | -- Member |
| 4. | Prof. S. Regunanthan, MD<br>Prof of Internal Medicine, MMC, Ch-3 | -- Member |
| 5. | Prof. Md Ali MD. DM<br>Prof & Head , Dept. of MGE, MMC,Ch-3 | -- Member |
| 6. | Thiru. S. Govindsamy. BA BL | -- Lawyer |

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee