CLINICOPATHOLOGICAL SPECTRUM OF NEPHROTIC SYNDROME IN ADULTS: A STUDY OF 50 CASES FROM CHENNAI

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CERTIFICATE

This is to certify that this dissertation entitled "CLINICOPATHOLOGICAL SPECTRUM OF NEPHROTIC SYNDROME IN ADULTS: A STUDY OF 50 CASES FROM CHENNAI " submitted by Dr.V.JAYAPRAKASH to The TamilNadu Dr. M.G.R. Medical University, Chennai is in partial fulfillment of the requirement of the award of M.D DEGREE BRANCH 1(General medicine) and is a bonafide research work carried out by him under direct supervision and guidance.

Signature of the Unit Chief

Signature of the HOD

Signature of the Dean

DECLARATION

I solemnly declare that the dissertation titled

"CLINICOPATHOLOGICAL SPECTRUM OF NEPHROTIC SYNDROME IN ADULTS: A STUDY OF 50 CASES FROM CHENNAI " was done by me at StanleyMedical College and Hospital during 2007-2009 under the guidance and supervision of **PROF. S. SUNDAR, M.D.**

The dissertation is submitted to The Tamil Nadu Dr. MGR Medical University towards the partial fulfillment of requirements for the award of M.D. DEGREE (BRANCH-I) in General Medicine.

Date:

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CONTENTS

INTRODUCTION

Nephrotic syndrome is a clinical syndrome with a characteristic pentad. They are: (1) proteinuria : adult > 3.5g/day; child >40mg / hour per m2 (2) hypoalbuminemia <3.5 g/dl, (3) edema (4) hypercholesterolemia (5) lipiduria[1]. Nephrotic syndrome is pathognomonic of glomerular disease. Patients may be nephrotic with preserved renal function, but in many circumstances, progressive renal failure will become superimposed when nephrotic syndrome is prolonged.

Independent of the risk of progressive renal failure, the nephrotic syndrome has far reaching metabolic effects that can influence the general health of the patient. Fortunately some episodes of nephrotic syndrome are self limiting and a few respond completely to specific treatment. However, for most patients, it is a chronic condition. Not all patients with proteinuria will have all components of nephrotic syndrome; some have a normal serum albumin and no edema. This difference presumably reflects the varied response of protein metabolism. Some patients sustain an increase in albumin synthesis in response to heavy proteinuria that may even normalise serum albumin.

There are several causes of nephrotic syndrome and causes of nephrotic syndrome in adults are different from that of childhood. Minimal change disease is the major cause of nephrotic syndrome in childhood, whereas in adults the main causes are membranous glomerulonephritis, focal segmental glomerulonephritis, minimal change disease,

diabetic nephropathy, IgA nephropathy and connective tissue disorders. Etiology, clinical pattern, laboratory features vary from one type to another, as also the treatment options and prognosis.

AIMS AND OBJECTIVES

1. To study the varied clinical presentation of nephrotic syndrome in adults.
2. To evaluate in detail the biochemical and other laboratory abnormalities in adult patients with nephrotic syndrome.
3. To find out the etiological profile of nephrotic syndrome in adults in our study population.
4. To compare the etiological profile of nephrotic syndrome in our study population with other similar studies, and to assess whether there is change in etiologic pattern in adult nephrotic syndrome in our institution.

REVIEW OF LITERATURE

The major causes of nephrotic syndrome are:

1. Minimal change disease [MCD].
2. Focal segmental glomerulosclerosis [FSGS].
3. Membranous nephropathy[MN,MGN].
4. Membranoproliferative glomerulonephritis [MPGN].
5. Amyloid.
6. Diabetic nephropathy.
7. Other causes like IgA nephropathy, lupus nephritis, light chain deposition disease, fibrillary immunotactoid disease and Fabry's disease.

The relative frequencies of the different glomerular diseases vary with age.

Age related variation in nephrotic Syndrome[2],[3]

(Data derived from studies done by Cameron JS and Haas M et al)

Prevalence

Child

Young adult

Middle and old age

	<15 Yrs				
	White				
	Black				
	White				
	Black				
Minimal change disease					
	78				
	23				
	15				
	21				
	16				
Focal segmental glomerulo sclerosis					
	8				
	19				
	55				
	13				
	35				
Membranous nephropathy					

	2
	24
	26
	37
	24
Membranoproliferative glomerulonephritis	
	6
	13
	0
	4
	2
Others	
	6
	14
	2
	12
	12
Amyloid	

0

5

2

13

11

Etiology of nephrotic syndrome – Changing trends[3]

% of total samples (adults)

	1976-1979	1995-1997
Minimal change disease	23	15
Focal segmental glomerulo sclerosis	15	35
Membranous nephropathy	36	33
Membranoproliferative glomorulonephritis	6	

	2
IgA nephropathy	
	3
	9
Amyloid nephropathy	
	7
	4
Chronic glomerulonephritis	
	5
	<1
Others	
	7
	2

Examination of the incidence of the disease from the above table illustrates both the age dependence of the diagnoses and the changing nature of the underlying lesion. A large series of adults in Chicago is depicted in table, in which was evaluated the renal function of 1000 consecutive patients who presented with the nephrotic syndrome. At this referral center, the relative incidence of different causes of nephrosis is changing with significantly more FSGS and less MCD and MPGN.

HYPOALBUMINEMIA :

It is usually a consequence of urinary losses. The liver responds by increasing albumin synthesis but the compensatory mechanism appears to be blunted in nephrotic syndrome[4]. White bands in nails are a characteristic clinical sign of hypoalbuminemia. The increase in protein synthesis in response to proteinuria is not discriminating; as a result, proteins that are not being lost in the urine may actually increase in concentration in plasma. This is chiefly determined by molecular weight; large molecules will not spill into the urine and will increase in the plasma; smaller proteins, although synthesized to the excess, will enter the urine and be diminished in the plasma. These variations in plasma proteins are clinically important in two areas; hypercoagulability and hyperlipidemia

EDEMA:

At least two major mechanisms are involved in the formation of nephrotic edema: viz, underfill and overfill[5]. The mechanisms are depicted in the diagram.

METABOLIC CONSEQUENCES OF NEPHROTIC SYNDROME:

NEGATIVE NITROGEN BALANCE:

The heavy proteinuria leads to morbid negative nitrogen balance, usually measured in clinical practice by serum albumin. Nephrotic syndrome is a wasting illness, but the degree of muscle loss is masked by edema and not fully apparent until the patient is rendered edema free. Loss of 10% to 20% of the lean body mass is not uncommon. Albumin turnover is increased in response to the tubular catabolism of filtered protein rather than merely to urinary protein loss.

HYPERCOAGULABILITY:

Multiple proteins of the coagulation cascade have altered levels in nephrotic syndrome. In addition, platelet aggregation is enhanced[6]. The net effect is a hypercoagulable state. Venous thromboembolism and also spontaneous arterial thrombosis may occur. In adults, coronary and cerebrovascular events and in children spontaneous thrombosis of upper limb arteries can occur. Thromboembolic events increase markedly if the
serum albumin decreases to <2g/dl. The hypo- and dysproteinemia produce an increase in ESR.

Renal vein thrombosis is an important complication of nephrotic syndrome. It is present in 10 to 50% of patients with nephrotic syndrome; more common in membranous nephropathy.

HYPERLIPIDEMIA AND LIPIDURIA:

Hyperlipidemia is regarded as an integral feature of nephrotic syndrome[7]. It is not uncommon for serum cholesterol to be > 500mg/dl, although triglyceride levels are highly variable.

Several mechanisms account for the lipid abnormalities in nephrotic syndrome, including increased hepatic synthesis of LDL, VLDL and lipoprotein A secondary to hypoalbuminemia; defective peripheral lipoprotein lipase activity resulting in increased VLDL and urinary losses of HDL.

Lipiduria, the fifth component of the nephrotic syndrome, is manifested by the presence of refractile accumulation of lipid in cellular debris and casts.

OTHER METABOLIC EFFECTS:

Vitamin D – binding protein is lost in the urine, resulting in low plasma 25 – hydroxy vitamin D levels, but free vitamin D is usually normal, and overt osteomalacia or uncontrolled hyperparathyroidism is very unusual in nephrotic syndrome in the absence of renal insufficiency. Thyroid binding globulin is lost in the urine and total circulating thyroxine is reduced, but free thyroxine and thyroid stimulating hormone levels are normal and there are no clinical alternation in thyroid status. Drug binding may be altered by the decrease in serum albumin.

INFECTION:

Nephrotic patients are prone to bacterial infection. Primary peritonitis, especially that caused by pneumococci, is characteristic of nephrotic children. It is less common with increasing age.

ACUTE AND CHRONIC CHANGES IN RENAL FUNCTION IN

NEPHROTIC SYNDROME :

ACUTE RENAL FAILURE (ARF):

Patients with nephrotic syndrome are at risk for the development of ARF, by the following mechanisms:[8] (1) Prerenal failure due to volume depletion (2) Acute tubular necrosis due to volume depletion and or sepsis. (3) Intrarenal edema (4) Renal vein thrombosis (5) Transformation of the underlying glomerular disease (6) Adverse effects of drug therapy (7) Acute allergic interstitial nephritis secondary to various drugs (8) Hemodynamic response to drugs like nonsteroidal anti inflammatory agents [NSAIDs], angiotensin converting enzyme inhibitors [ACEIs] and angiotensin receptor blockers [ARBs].

CHRONIC RENAL INSUFFICIENCY :

With the exception of minimal change disease, most causes of nephrotic syndrome are associated with same risk of the development of progressive renal failure. One of the greatest risk factors for progression is the degree of proteinuria. Progression is uncommon if proteinuria is <2g/day. The risk increases in proportion to the severity of the proteinuria, with marked risk of progression when protein excretion is >5g/day.

Disease	**Nephrotic features**	**Nephritic features**
Minimal change disease	+ + + +	-
Membranous nephropathy	+ + + +	+
FSGS	+ + +	+ +

Fibrillary glomerulonephritis

+ + +

+ +

Mesangioproliferative glomeralonephritis

+ +

+ +

MPGN

+ +

+ + +

Proliferative glomerulonephritis

+ +

+ + +

Acute diffuse proliferative glomerulonephritis

+

+ + + +

Crescentic glomerulonephritis

+

+ + + +

Manifestation of nephrotic and nephritic features by glomerular disease:

INVESTIGATIONS :

Disease	Associations	Serological tests helpful in diagnosis
Minimal change disease	Allergy, atopy, NSAIDs, Hodgkin's disease.	None
FSGS	African Americans, HIV, Heroin, Pamidronate	HIV Antibody
Membranous Nephropathy	Drugs: Gold, penicillamine, NSAIDs, Infections : Hepatitis B,C, Malaria. Lupus Nephritis Malignancy : Breast, lung, GIT	Hepatitis B surface Antigen, Anti hepatitis C antibody, Anti-DNA antibody.
MPGN I	C4 Nephritic factor	C3, C4 decreased
MPGN II	C3 Nephritic factor	C3 decreased, C4 normal
Cryoglobulinemic MPGN	Hepatitis C	Anti hepatitis C antibody, Rheumatoid factor, C3↓C4↓, CH50↓
Amyloid		

Myeloma, Rheumatoid arthritis, Bronchiectasis, Crohn's disease, Familial Mediterranean fever

Serum protein electrophoresis, urine immunoelectro- phoresis

Diabetic Nephropathy

Other diabetic microangiopathy

None

Investigations in nephrotic syndrome are aimed to arrive at the diagnosis of nephrotic syndrome by measuring serum albumin and urine protein levels, serum lipid levels and demonstration of oval fat bodies and fatty casts in the urine. Investigations are also directed to rule out the secondary causes of nephrotic syndrome like infections, autoimmune disorders, drugs, malignancies, etc.

TREATMENT:

General Principles

- Edema and volume overload can usually be managed with diuretics, as appropriate and dietary sodium restriction.
- Aggressive treatment of hypertension with a goal BP of <125/75 mmHg is mandatory.
- Proteinuria should be monitored regularly with the use of urinary protein to creatinine ratio or urinary microalbumin. A combination of ACEIs and ARBs is more effective than either agent used alone in reducing proteinuria.
-
- Hyperlipidemia is managed with dietary restriction of cholesterol and saturated fat and statin therapy.
- Deep venous thrombosis occurring in upper and lower limbs and renal veins may warrant anticoagulation with heparin, followed by long term warfarin therapy.
- Dietary sodium restriction and modest protein restriction may be advised.

DISEASE SPECIFIC THERAPY:

The therapy is most often guided by results of renal biopsy and supplemental lab evaluation but frequently involves corticosteroid based therapy for primarily nephrotic disorders and cytotoxic agents plus corticosteroids for primarily proliferative or nephritic disorders

MINIMAL CHANGE DISEASE:

Etiology and pathogenesis:

In a minority of patients with minimal change disease, there is association with factors such as NSAIDS, interferons, lithium, gold, allergy,
pollen, house dust, insect stings, immunization, malignancy, Hodgkin's diseases, mycosis fungoides, CLL. The pathophysiology of the lesion is uncertain. Most agree that there is a circulatory cytokine, related to a T cell response that alters capillary charge and podocyte integrity [9,10,11].

Clinical manifestations:

The nephrotic syndrome is of rapid onset, increasing the risk of hypovolemia, particularly in children. Pleural effusions and ascites are common, especially in children, who may present with abdominal pain, a symptom that may suggest peritonitis. Pericardial effusion may occur. Facial puffiness and genital edema may occur. Edema of the bowel may cause diarrhea with significant albumin loss from the gut. Muehrcke's bands in nails and xanthomata may occur.

Microscopic hematuria is rare in minimal change disease and hypertension can be seen in 30% of adults with minimal change disease. Complications include peritonitis in children, mainly by *Str. pneumoniae, H. influenzae* and other encapsulated bacteria[12]. Venous and arterial thrombo embolism may occur.

Renal function is generally preserved. Hypovolemia and aggressive diuretic therapy can cause acute renal failure.

Pathology :

Renal biopsy shows no obvious glomerular lesion by light microscopy and is negative for deposits by immunofluorescent microscopy or occasionally show deposits of IgM in the mesangium. Electron microscopy demonstrates effacement of the foot processes supporting the epithelial podocytes with weakening of slit pore membranes.

TREATMENT:

All children and adults with minimal change disease are treated with steroids [13]. Approximately 80% of adults with MCD respond to prednisone 1mg /kg/d PO, with a decrease in proteinuria to <3g/day or a remission of the nephrotic syndrome. NSAID induced MCD usually responds well to discontinuation of NSAIDs. In patients who respond, steroids should be tapered over 3 months and then discontinued. Treatment with cytotoxic agents may be indicated in patients who are deemed steroid dependent, steroid resistant, or frequent relapsers. Cyclophosphamide, 2mg/kg/d PO for 8 weeks; chlorambucil 0.2mg/kg/d PO for 6-12 months, are typical regimens [14].

FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSGS):

FSGS, a histologic pattern of glomerular injury, defines a number of cilincopathologic glomerular syndromes that may be primary or secondary to diverse etiologies. FSGS is the leading cause of nephrotic syndrome in adults as shown by review of renal biopsy archives from Chicago, Spring field, Massacheusetts[15,16,17,18]. A similar pattern has been noted among children [19]. In India, the prevalence of FSGS on kidney biopsy rose from 20% to 47% during the 1990s [20,21].

Worldwide, there is considerable heterogeneity in the relative incidence of FSGS compared to the other causes of adult nephrotic syndrome, ranging from 10% to 45%. Factors contributing to this variability include population genetic differences, renal biopsy practices and environmental factors including HIV-1 infection. There are also striking racial differences in the incidence of FSGS ESRD. Blacks are at approximately four fold increased risk for FSGS ESRD compared to Whites, Hispanics and native Americans.

Etiology and pathogenesis:

1. Primary FSGS
2. Secondary FSGS: Causes include viruses (HIV, hepatitis B, parvovirus), hypertensive retinopathy, reflux nephropathy, cholesterol emboli, drugs (heroin, analgesics), renal dysgenesis, Alport's syndrome, sickle cell disease, lymphoma, radiation nephritis, familial podocytopathies (mutation in nephrin, podocin, cation channel, actin), Fabry's disease.

The pathogenesis of FSGS is largely multifactorial. Possible mechanisms include a T cell- mediated circulating permeability factor, TGF-β mediated cellular proliferation and matrix synthesis, and podocyte abnormalities associated with genetic mutation.

Clinical manifestations:

The patients present with asymptomatic proteinuria or full nephrotic syndrome [22, 23]. The incidence of nephrotic range proteinuria at onset in children is 70-90% while only 50-70% adults with FSGS present with nephrotic syndrome. Edema is the most common manifestation.
Hypertension is present in 30-50% of children and adults with FSGS at the time of diagnosis; microscopic hematuria is seen in 25 to 75% of patients and reduced GFR is noted at presentation in 20 to 30% Daily urine protein excretion ranges from <1 to >30 g/day. Proteinuria is non selective. Complement and other serologic tests are normal.

Pathology:

The pattern of injury is characterised by segmental glomerular scars that involve some but not all glomeruli. The pathologic changes of FSGS are most prominent in glomeruli located at the corticomedullary junction, so if the renal biopsy specimen is from superficial tissue, the lesion can be missed, which sometimes leads to the misdiagnosis of MCD. In addition to the focal and segmental scarring, other variants have been described.

Morphologic variants of FSGS:[24]

1. FSGS, classic type,
2. FSGS, perihilar variant,
3. FSGS, cellular variant,
4. FSGS, collapsing variant (rapid decline of GFR)
5. FSGS, tip variant (better prognosis)

Treatment:

1

Subnephrotic proteinuria without symptoms

Optimal BP control

Treat with ACEI /ARBs, statins.

Avoid high protein diet.

2.

Symptomatic nephrotic syndrome

As above + Prednisone 1mg/ kg/day for 6-8 weeks;

Subsequent taper of dose and continuing therapy until remission or upto 6 months

Alternative therapy for steroid resistant cases

- Oral cyclosporine 4-6mg/kg/day for 4-6 months
- Oral cyclophosphamide 2mg / kg/ day for 2-4 months
- Oral MMF 1-1.5g BD for 4-6 months.

MEMBRANOUS NEPHROPATHY (MN, MGN):

MN represents the most common cause of nephrotic syndrome in elderly adults, representing upto 30% of all cases in patients over age 50[15,25,26]. It occurs most commonly in isolation (idiopathic MN, 80%), but
may be a feature of an underlying disease (secondary MN, 20%) most often either autoimmune, infections or malignant [27]. The peak incidence is between the age of 30-50 years and M: F ratio is 2:1.

Etiology and pathogenesis:

1. Primary / idiopathic membranous nephropathy.
2. Secondary membranous nephropathy.

Causes include 1) Infections (Hepatitis B,C syphilis, malaria, schistosomiasis, leprosy, filariasis), 2) Cancer (breast, colon, lung, stomach, kidney, oesophagus, neuroblastoma) 3) Drugs (gold, mercury, penicillamine, NSAIDs, probenecid), 4) Autoimmune diseases (SLE, Rheumatiod arthritis, primary biliary cirrhosis), dermatitis herpetiformis, bullous pemphygoid, myasthenia gravis, Sjogren's syndrome, Hashimoto's thyroiditis) 5) Others (Fanconi syndrome, sickle cell anemia, diabetes, sarcoidosis, Crohn's disease)

Work in Heyman nephritis, an animal model of MGN, suggests that glomerular lesions result from in situ formation of immune complexes with megalin receptor – associated protein as the putative antigen [28].

Clinical manifestations:

The onset is insidious. There is gradual development of peripheral edema without other signs or symptoms. MGN is uncommon in patients younger than age 50 years. There is male preponderance. Individual peaks occur between ages 30 and 40 years and again between 50 and 60 years. 80% of patients have overt nephrotic syndrome at the time of presentation with urine protein > 3.5g/day, reduced serum albumin levels, elevated serum lipids, as well as fluid retention and edema. 20% of patients are asymptomatic with non nephrotic proteinuria. Proteinuria is always non selective, 5-15g/day range; >15 gram is more suggestive of MCD. Microscopic hematuria is seen in 50% of adults, but macroscopic hematuria and RBC casts are extremely unusual. Hypertension is not a feature of MN. It is present in 30% of cases. Renal function is usually preserved at the onset of the disease. Reduction in renal function develops slowly in MGN.

Treatment:

In addition to the treatment of edema, dyslipidemia and hypertension, inhibition of renin – angiotensin system is recommended for patients with primary MGN and persistent proteinuria (>3g/ 24 hours). The choice of
immunosuppressive drugs is controversial, but current recommendations are to treat with steroids and cyclophosphamide, chlorambucil and cyclosporine.

MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS (MPGN):

It is also called mesangiocapillary glomerulonephritis or lobar glomerulonephritis. MPGN is rare in African Americans. Epidemiologic data indicate that MPGN is a rare disease (4.5% among the histologically proven primary glomerulonephritis) and that its incidence has decreased in the developed countries of the world since the early 1980s [29, 30].

Etiology, pathogenesis and pathology:

MPGN is subdivided pathologically into Type 1, Type 2 and Type 3 disease.

Type 1 disease (most common):

1) Idiopathic, 2) Subacute bacterial endocarditis, 3) SLE, 4) Hepatitis C ± cryoglobulinemia, 5) mixed cryoglobulinemia, 6) Hepatitis B, 7) Cancer of lung, breast and ovary.

Type 2 disease (Dense deposit disease):

1) Idiopathic, 2) C3 nephritic factor associated, 3) Partial lipodystrophy

Type 3 disease :

1) Idiopathic, 2) Complement receptor deficiency
Type I, the most proliferative of the three types, shows mesangial proliferation with lobular segmentation on renal biopsy and mesangial interposition between the capillary basement membrane and endothelial cells, producing a double contour sometimes called tram tracking. Subendothelial deposits with low serum levels of C3 are typical. Low serum C3 and a dense thickening of the GBM containing ribbons of dense deposits and C3 characterise type II MPGN. The glomerular tuft has a lobular appearance. Proliferation of type III MPGN is less common than other types and is often focal.

Type I MPGN is secondary to glomerular deposition of circulating immune complexes or their in situ formation. Type II and III MPGN may be
related to ‘nephritic factors’, which are antibodies that stabilize C3 convertase and allow it to

activate serum C3.

Clinical manifestations:

Patients with MPGN present with proteinuria, hematuria or pyuria (30%), systemic symptoms of fatigue and malaise that are more common in children with type 1 disease , or an acute nephritic picture with RPGN and speedy deterioration in renal function in upto 25% of patients. Chronic HCV infection may present with triad of weakness, arthralgia and purpura. Low serum levels of C3 are common. 50% of patients with MPGN develop ESRD 10 years after diagnosis and 90% have renal insufficiency after 20 years.

Treatment:

In the presence of proteinuria, treatment with ACEIs is prudent. There is some evidence supporting the efficacy of treatment of primary MPGN with steroids, particularly in children [31]. In secondary MPGN, treating the associated infection, autoimmune disease or neoplasm is of demonstrated benefit.

MESANGIOPROLIFERATIVE GLOMERULONEPHRITIS:

It is characterized by expansion of the mesangium; sometimes with mesangial hypercellularity; single contoured capillary walls, and mesangial immune deposits. Clinically presents with varying degrees of proteinuria and commonly hematuria. It is seen in IgA nephropathy, P.falciparum malaria, resolving PIGN and class II lupus nephritis, all of which have a similar histologic appearance. With these secondary entities excluded, the diagnosis of primary mesangioproliferative glomerulonephritis is made in <15% of renal biopsies. Patients with isolated hematuria may have a very benign course, and those with heavy proteinuria occasionally progress to renal failure. Treatment is with renin-angiotensin system inhibitors, steroid therapy and cytotoxic agents.

IgA NEPHROPATHY:

IgA nephropathy is one of the most common form of glomerulonephritis worldwide [32]. 5% of IgA nephropathy patients present with nephrotic syndrome. There is a male preponderance, a peak incidence in the second and third decade of life, and rare familial clustering. There are geographic differences in the prevalence of IgA nephropathy, with 30% prevalence along the Asian and Pacific rim and lower prevalence in Northern Europe and North America.

Etiology, pathogenesis and pathology:

There are close similarities between Henoch- Schoenlein purpura and IgA nephropathy. IgA nephropathy is an immune complex mediated glomerulonephritis defined by the presence of diffuse mesangial IgA deposits often associated with mesangial hypercellularity. IgM, IgG, C3 or immunoglobulin light chains may be codistributed. Abnormalities have been described in IgA production by plasma cells; in IgA clearance predominantly in the liver. Immunofluorescent pattern of IgA on renal biopsy defines IgA nephropathy in proper clinical context. Deposits of IgA are also found in the glomerular mesangium in a variety of systemic diseases, including chronic liver disease, Crohn’s disease, GI adenocarcinoma, leprosy, dermatitis herpetiformis and Sjogren’ syndrome.

Clinical manifestations:

It is classically characterized by episodic hematuria associated with the deposits of IgA in the mesangium. The two most common presentations are recurrent episodes of macroscopic hematuria during or immediately following an upper respiratory infection in children or asymptomatic microscopic hematuria most often seen in adults. Between episodes, the urinalysis is normal. Proteinuria without hematuria is uncommon. Rarely patients can present with ARF or RPGN. IgA nephropathy is a benign disease for the majority of patients with progression to renal failure seen in only 25-35% over 20-25 years.

Treatment :

ACE inhibitors are used in patients with proteinuria or declining renal function. When presenting as RPGN, patients typically receive steroids, cytotoxic agents and plasmaphresis[33].

LUPUS NEPHRITIS:

Various rheumatologic diseases have been described in association with membranous nephropathy [34,35]. SLE is common among rheumatologic
diseases producing nephrotic syndrome. About 15-25% of patients with lupus nephritis are classified with a class V (membranous) lesion with predominantly subepithelial deposits [36].

Clinical manifestations:

The majority of these patients are young females and in a substantial number the onset of nephrotic syndrome predates the development of other signs of SLE. Upto 25 to 50% of patients have negative ANA levels, and if present, is of low avidity. Complement levels are usually normal. The clinical course of lupus MN mimics that of the idiopathic form with an excellent long term prognosis, in excess of 85% renal survival at 10 years [37,38].

It can present as slowly progressive azotemia with urinary abnormalities, as nephrotic syndrome or as RPGN. Hypocomplementemia is often present during flares of nephritis.

Pathology:

Renal biopsy is useful in SLE for evaluating disease activity and assessing irreversible changes such as glomerular sclerosis, tubular atrophy and interstitial fibrosis. The clinical presentation is a poor predictor of the class of lupus nephritis involved.

International Society of Nephrology/ Renal Pathologic Society (ISN/RPS) classification (2004):

Class I – Minimal mesangial deposits
Class II – Mesangial proliferation
Class III – Focal nephritis
Class IV – Diffuse nephritis
Class V – Membranous nephritis
Class VI – Sclerotic nephritis

Immunofluorescence is commonly positive for IgA, IgG, IgM, C3 and C4.

Treatment:

For patients with severe renal disease, treatment is with methyl prednisolone 500gm i.v. q12h, for 3 days, followed by oral predinsone, 0.5 –1mg/kg PO daily. Prednisone should then be tapered over 6-8 weeks.

In moderate to severe lupus nephritis, induction with mycophenolate mofetil 1000mg PO TID or cyclophosphamide 0.5-1g/m^2 monthly for 6 months, improves the likelihood of remission and appears to reduce the progressive renal failure. Rituximab and i.v.gamma globulin are alternative agents.

DIABETIC NEPHROPATHY:

Diabetic nephropathy can present as nephrotic syndrome. Approximately 25-45% of patients with type 1 diabetes develop clinically evident diabetic nephropathy during their lifetime, and this is the leading cause of ESRD [39]. The risk of nephropathy seems to be equivalent in the two types of diabetes [40].

Clinical presentation:

Patients are often asymptomatic. Hence screening for microalbuminuria is mandatory. Microalbuminuria precedes proteinuria (>300mg albumin / day) by several years in type 1 and type 2 DM. The mean duration from the diagnosis of type 1 DM to the development of proteinuria is 17 years and the time from the occurrence of proteinuria to ESRD averages 5 years. In type 2 diabetes, microalbuminuria can be present at the time of diagnosis.

Annual screening should be performed in type 1 patients who have had diabetes for >5 years and all type 2 diabetes patients starting at diagnosis. Measurement of microalbumin to creatinine ratio (Normal is <30 mg albumin/ g creatinine) in a random urine sample is recommended for screening [41].

Pathology:

Renal biopsy is not routinely indicated in the evaluation of diabetic nephropathy. Indications for biopsy include type 1 DM for <10 years, no retinopathy, nephrotic range proteinuria without progression through microalbuminuria, macroscopic hematuria and red cell casts. Biopsy features include GBM thickening which can be upto three times normal. Nodular glomerular intercapillary lesions, which are considered pathognomonic for diabetes, called Kimmelstein Wilson nodules are seen in 10-50% of biopsies in both type 1 and type 2 diabetes.

Management:

Intensive control of diabetes and hypertension is an effective intervention for incipient or established diabetic nephropathy. Drugs that delay the progression of nephropathy include ACEIs, ARBs, non dihydropyridine CCBs, β-blockers and diuretics [42]. Dietary protein restriction may be beneficial in some patients

OTHERS:

GLOMERULAR DEPOSITION DISEASE:

Light chain deposition disease, renal amyloidosis and fibrillary – immunotactoid glomerulopathy can cause nephrotic syndrome in a proportion of patients. Both AA amyloidosis and AL amyloidosis can progress to nephrotic syndrome. Biopsy of the kidney or liver is diagnostic.
In primary amyloidosis, melphalan and autologous hematopoietic stem cell transplantation can be tried. For secondary amyloidosis, which is also relentless, primary disease should be controlled.

FABRY'S DISEASE:

This is an X-linked inborn error of globotriosylceramide metabolism secondary to deficient lysosomal α-galactosidase A activity. Many organs including kidneys are involved. Zebra bodies are seen in electron microscopy. The patients present in third decade with mild to moderate proteinuria, sometimes with microscopic hematuria and nephrotic syndrome, Renal biopsy may show features of FSGS. Treatment is with recombinant α galactosidase A.

MATERIALS AND METHODS

Place : Department of Medicine and Department of Nephrology, Government Stanley Hospital.
Design : Observational Study.
Period : October 2007 to October 2009.
Sample size : 50 patients.

INCLUSION CRITERIA :

1. Age >18 years of age.
2. Newly admitted patients with clinical and laboratory findings suggestive of nephrotic syndrome.

EXCLUSION CRITERIA :

1. Nephrotic syndrome in children and adolescents.
2. Known patients with nephrotic syndrome admitted with relapses and complications.
3. Patients with diabetic nephropathy, who do not require biopsy.
4.
5. Other causes of volume overload like cardiac and hepatic causes, renal causes other than nephrotic syndrome, malnutrition, etc.

METHODS:

Detailed history was taken from all patients admitted with features suggestive of nephrotic syndrome. This included presenting complaints and history of presenting illness, significant past medical history and history suggestive of complications of nephrotic syndrome. The patients were then examined thoroughly and biochemical investigations were carried out to establish the diagnosis of nephrotic syndrome. Also, investigations to establish the etiology of nephrotic syndrome were done. After obtaining patients' consent, renal biopsy was done to find out the etiology and to decide on the therapy. The patients were treated accordingly and were advised to get reviewed periodically. All relevant data, clinical, laboratory and biopsy details were recorded and were analysed at the end of the study. The proforma used for the same is attached.

Ethical Committee approval was obtained.

OBSERVATIONS AND DATA ANALYSIS:

Total number of patients – 50
Male – 22
Female – 28
Age group range – 19 to 53 years
Mean age – 31 years.

The most common clinical features observed in our study were pedal edema (84%), facial puffiness (94%), abdominal distension (40%). A combination of pedal edema and facial puffiness occurred in 38% of cases, a combination of pedal edema, facial puffiness and abdominal distension occurred in 40% of cases, facial puffiness done in 16% cases and pedal edema alone in 6% cases.

Duration of onset of illness to the time of presentation to the hospital ranged from 1 week to 20 weeks. Mean duration of presenting complaints was 6 weeks.

Table – 1
Age Distribution of Nephrotic Syndrome in our Study

Age (Years)	Male	Female	Total (n=50)
19-30	8	19	27 (54%)
31-40	11	6	17 (34%)
41-50			

2

2

4 (8%)

>50

1

1

2 (4%)

22 (44%)

28(56%)

50

In our study population, females constituted 56% and males 44%. Majority of the patients belonged to 19-30 years age group (54%). 31- 40 years group constituted 34% of cases. Only 8% cases belonged to 41-50 years age group and 4% cases in >50 years age group. Among females, the majority of patients belonged to the 19-30 years age group (38%) but among males, majority belonged to 31-40 years age group (22%) followed by 19-30 years age group (16%). Nephrotic syndrome was uncommon in age group
> 40 years and only 12% cases in males and females belonged to that age pool.

None of the patients had fever or any other history suggestive of infectious diseases at presentation. As per our protocol, patients with similar illness in the past, who were already evaluated, did not participate in our study. None of the patients were diabetics in our study.

History of hypertension was present in 2 cases. None of the patients presented with features suggesting complications of nephrotic syndrome
like abdominal pain, fever, swelling of limbs, chest pain or history suggestive of focal neurological deficit.

Three patients gave history of SLE during admission and one patient had NSAID intake for pain at presentation.

On examination, systemic hypertension was present in 19 cases (38%). Stage 1 hypertension was present in 26% and stage 2 in 12% of cases. Among patients with systemic hypertension, 7 cases were females (14%) and 12 were males (24%). Systemic hypertension was present in 50% of cases with histological subtypes, MGN and MPGN and less common in other subtypes.

STAGE 1
STAGE 2
TOTAL
MGN
6
2
8
FSGS
2
2
4
MCD
1
0
1
MPGN
1
1
2
OTHERS
3
1
4

13
6
19

Table 2 : **Systemic hypertension in nephrotic syndrome**

Clinical examination did not reveal any complications of nephrotic syndrome like peritonitis, arterial or venous thrombotic sequlae.

Table 3 : Severity of Proteinuria in our study population

	3-6g/d	**6.1-9 g/d**	**9.1-12g/d**	**12.1-15g/d**	**Mean**
MGN	5	5	1	7.98	
FSGS	6	3	2	-	6.32
MCD					

2

-

-

2

9.22

MPGN

1

3

-

-

6.6

Others

12

3

-

-

4.76

Total

26

14

7

3

6.64

Urine protein excreted over 24 hours ranged from 3g / day to 15g/day. The mean value was 6.64 grams. The proteinuria was in the range of 3-6 g/day in 28% of cases, 6.1 - 9 g/day in 28% of cases,9.1- 12 g/day in 14% of cases and > 12 g/day in 6% of cases. Among histologic subtypes, mean proteinuria was highest (9.22 g/day) for minimal change disease.

Severity of Proteinuria in our study population

Table 4 : Hypercholesterolemia in our study population

<200mg/ dl	
200-250 mg/dl	
250-300 mg/dl	
>300 mg/dl	
Mean	
MGN	
1	
6	
5	
4	

260

FSGS

1

4

5

1

253

MCD

-

1

1

2

277

MPGN

-

4

-

-

221

OTHERS

3

4

8

-

245

TOTAL

5

19

19

7

251.2

Hyperlipidemia was present in majority of the patients. Serum cholesterol levels >300 mg% were found in 7 cases (14%); levels between 250-300mg % were found in 19 cases (38%), levels <250mg % were found in 24 cases (48%). Levels between 200-250 mg% were present in 19 (38%) cases and 5 cases (10%) had levels <200mg%. The mean value was 251 .2mg/dl.

Hypercholesterolemia in our study population

Urea and creatinine were elevated in 7 cases (14%). Renal failure was present in 27% of cases with FSGS, 25% of MPGN patients and 37% of lupus patients. No patient with MCD and MGN had renal dysfunction.

Renal biopsy was done in all patients. The etiology based on renal biopsy findings was as follows

Table 5: Etiology of nephrotic syndrome

Etiology

Males

Females

Total (n=50)

Membranous nephropathy

8

8

16(32%)

FSGS

5

6

11 (22%)

MCD

1

3

4(8%)

MPGN

3

1

4(8%)

Others*

5

10

15(30%)

*Includes mesangioproliferative glomerulonephritis and proliferative glomerulonephritis

Membranous nephropathy was the commonest cause of nephrotic syndrome in adults. It constituted 32% of cases and M: F ratio was 1.1. FSGS constituted 22% of cases. Among patients of FSGS 6 (12%) were females and 5(10%) were males. Minimal changes disease was the cause of nephrotic syndrome in 8% of cases and M: F ratio was 1:3. MPGN constituted the same 8% of cases but the M: F ratio was 3:1.

A significant proportion of patients had biopsy findings classified as ‘others’, which included mesangioproliferative glomerulonephritis and proliferative glomerulonephritis (30%). Serologic tests and biopsy findings suggested the etiology in these cases as either IgA nephropathy (16%) or lupus nephritis (14%)

Nephrotic syndrome was primary or idiopathic in 43 (86%) of cases and secondary to other disorders in 7 cases (14%). Lupus was the primary disorder in all these cases.

Etiological profile of Nephrotic Syndrome

DISCUSSION

In our study clinical characteristics and biopsy findings of 50 patients were analysed. Males were 22 (44%) and females 28 (56%). Maximum number of cases occurred in the third decade among females and in fourth decade among males.

In our study, etiology was nephrotic syndrome was analysed. Majority of the patients in our study had membranous nephropathy as the etiology (32%), followed by FSGS (22%). Several studies conducted elsewhere demonstrate changing trends in the etiology of nephrotic syndrome in adults. **Haas M et al** [3] evaluated the renal function of 1000 consecutive patients who presented with nephrotic syndrome. At the center, the relative incidence of different causes of nephrosis is changing with significantly more FSGS and less MCD and MPGN. Similar results were obtained in studies done by **Dragovic D et al** [16]**, Borzilla Felix M et al** [19]**.** In India also, studies done by **Gulate S et al** [20] demonstrated increased prevalence of FSGS in the 1990s. Similar study done by **Adhikari et al** [21] concluded with similar results. FSGS was the common histopathologic type in similar studies done by **Jacob C K et al**[43] (Vellore) and **Sakhuja V et al**[44] (Chandigarh). Our study is discordant with the results of the above mentioned studies and is concordant with the study done by **Pathak R et al**[45] (Jaipur), which demonstrated increased prevalence of membranous nephropathy in adults. **A R Reshi et al** [46] (Srinagar) reported increased incidence of minimal change disease in adults, followed by focal segmental glomerulosclerosis and then by membranous nephropathy.
Branden et al [15] noted that membranous nephropathy represents the most common cause of nephrotic syndrome in elderly adults, representing upto 30% of all cases in patients over 50 years of age. Similar results were obtained from studies done by **Yamagata K et al** [25] and **Preston RA et al**[26]. But the above mentioned studies could not be compared with our study because our study population comprises all individuals > 18 years of age, whereas the above studies included older individuals in study population.

In the study conducted at Vellore by **Jacob C K et al** [43], males dominated all histologic subtypes barring lupus nephritis. In our study, females dominated in all histologic subtypes except in MPGN, where males dominated and MGN, where both males and females were affected in equal numbers.

Haas M et al Study results (1995-97)

Our study results

95% confidence interval

Study population

1000

50

1. MCD

15%

8%

4.16%-11.84%

2. FSGS

35%

22%

16.14%-27.86%

3. MGN

33%

32%

25.4%-38.6%

4. MPGN

2%

8%

4.16%-11.84%

5. Others

15%

30%

23.5%-36.5%

The standard error for MCD,FSGS,MGN,MPGN and 'others' in our study respectively are 3.84, 5.86, 6.6, 3.84, 6.5. The incidence with 95% confidence interval is given in the table. With this confidence interval, the incidence of MCD and FSGS in our study is lesser than their incidence in

Haas M et al[3] study, the incidence of MGN is almost equal and the incidence of MPGN and 'others' is greater in our study when compared to **Haas M et al**[3] study results.

Worldwide, there is considerable heterogeneity in the relative incidence of FSGS compared to the other causes of adult nephrotic syndrome, ranging from 10% - 45%. Factors contributing to the variability
include population genetic differences, renal biopsy practices and environmental factors including HIV infection. There are also striking racial differences in the incidence of FSGS ESRD. Blacks are at approximately four fold increased risk for FSGS ESRD compared to Whites, Hispanics and Native Americans.
No one with HIV infection participated in our study. Differences in ethnicity and differences in biopsy practices can be the factors that can be attributed the reduced incidence of FSGS compared to MGN in our study population.
In the study conducted by **Jayakumar et al** [47]**,** in FSGS patients, hypertension was present in 13.3% of cases and renal insufficiency in 23.3% of cases. In our study population, hypertension was present in 4 cases (36.4%) and renal insufficiency in 3 cases (27.3%).
The incidence of MCD in our study was 8%. This is lesser when compared to studies conducted by **Cameron J S et al** [2] and **Hass M et al** [3]**,** where the incidence of MCD was in the range of 15%.
The incidence of MPGN was 8% in our study population and is comparable with studies conducted by **Cameron J S et al** [2]**, Haas M et al** [3]**, Simo P et al** [29] and **Gesualdo L et al** [30]**.**

Mesangioproliferative glomerulonephritis and proliferative glomerulonephritis occurred in a sizeable proportion in our study population. Etiologies were found to be IgA nephropathy and lupus nephritis. IgA nephropathy occurred in 16% of patients in our study. In studies done by **Hass M et al**, the prevalence of IgA nephropathy was 9%. All patients in our study had hematuria in urinalysis.

Various rheumatologic diseases have been described in association with membranous nephropathy. The majority of these patients are young females and in a substantial number the onset of the nephrotic syndrome predates the development of other signs of SLE. Biopsy findings were suggestive of lupus nephritis in 14% of cases (7 cases). Among these, one had focal nephritis, 4 patients had diffuse proliferative glomerulonephritis (DPGN) and 2 patients had membranous nephritis. All patients with lupus in our study were females. 3 among 7 patients participated in the study were known SLE patients. Other patients presented with features of nephrosis and after evaluation, found to be having SLE. 4 patients tested positive for ANA, 2 for ds DNA and 3 patients had reduced complement levels.

SUMMARY AND CONCLUSIONS

[1] 50 adult patients with nephrotic syndrome participated in the study. Males constituted 44% and females 56% of cases.

[2] The commonest presenting complaint was facial puffiness, which occurred in 94% of cases. Pedal edema occurred in 84% and abdominal distension on 40% of cases.

[3] Systemic hypertension was present in 38% of cases. Males constituted 24% of cases and females 14%. Systemic hypertension was present in 50% of cases with histological subtypes, MGN and MPGN and less common in other subtypes.

[4] 24 hours urine protein excretion ranged from 3 g to 15 g/ day. The mean value was 6.64 g/day. Proteinuria was severe with histopathological subtype, minimal change disease (mean -9.22 g/day).

[5] Hypercholesterolemia was present in 90% of cases. The mean value was 251.2 mg%.

[6] Renal failure was present in 14% of cases. Renal failure was present in 27% of cases with FSGS, 25% of MPGN patients and 37% of lupus patients.

[7] The commonest histopathological subtype was membranous nephropathy. It occurred in 32% of cases. FSGS was the etiology in 22% of
cases, MCD and MPGN in 8% of cases, IgA nephropathy in 16% of cases and lupus nephritis in 14% of cases.

[8] In our study, females dominated in all histologic subtypes except in MPGN, where males dominated and in MGN, where both males and females were affected in equal numbers.

[9] In patients with FSGS, hypertension was present in 4 cases (36.4%) and renal insufficiency in 3 cases (27.3%).

[10] All patients with IgA nephropathy had hematuria on urinalysis.

[11] Nephrotic syndrome was primary or idiopathic in 86% of cases and secondary in 14% of cases. Lupus nephritis was the primary etiology in all these cases.

[12] All patients with lupus in our study were females. Among these patients with lupus nephritis, one patient had focal nephritis, 4 patients had diffuse proliferative glomerulonephritis (DPGN) and 2 patients had membranous nephritis.

I. BIBLIOGRAPHY

1. Orth S R, Ritz E: The nephrotic syndrome. N Eng J Med 1998; 338; 1201-1212.
2. Cameron J S: Nephrotic syndrome in the elderly. Semin Nephrol 1996; 16: 319-329.
3. Haas M, Meehan S M, Karison T G, Spargo BH: Changing etiologies of unexplained adult nephrotic syndrome. A comparison of renal biopsy findings from 1976-1979 and 1995-1997 Am J Kidney Dis 1997; 30: 621-631.
4. Kaysen G. Gambertoglio J. Felts J, Hutchison F: Albumin synthesis, albuminuria and hyperlipidemia in nephrotic syndrome. Kidney Int 1987; 31: 1368-1376.
5. Humphrey's M H: mechanisms and management of nephrotic edema. Kidney Int 1994; 45: 266-281.
6. Rabelink T J, Zawginga T J, Kooman's H A, Sixma J J: Thrombotic hemostasis in renal disease: Kidney Int 1994;46: 287-296.
7.
8. Wheeler D C, Bernard D B: Lipid abnormalities in nephrotic syndrome. Am J Kidney Dis 1994; 23: 331-346.
9. Smith J D, Hayslett J P; Reversible renal failure in the nephrotic syndrome. Am J Kidney Dis 1992; 19: 201-213.
10. Jenette J C, Mandal A K. The Nephrotic syndrome. Diagnosis and management of renal diseases and hypertension. Carolina Academic Press. Durban NC, 1994.
11. Koyama A. Fujisaka M, Kobayashim et al. A glomerular permeability factor produced by human T cell hybrindoma. Kidney Int 1991;40 : 453-460.
12. Cheung P K, Klok P A, Baller J F, Bakker W W: Induction of experimental proteinuria in vivo following infusion of human plasma hemopexin. Kidney Int 2000; 57: 4512-4520.
13. Feinstein E I, Chesney R W, Zelikovic I: Peritonitis in childhood renal disease. Am J Nephrol 1998; 8:247- 265.
14. The primary nephrotic syndrome in children. Identification of patients with minimal change nephrotic syndrome from initial response to prednisone: A report of the International study of kidney disease in children. J Pediatr 1981; 98: 461-464.
15.
16. Latta K, Von Schnakenburg C, Ehrich J H: A meta analysis of cytotoxic treatment for frequently relapsing nephrotic syndrome in children; Pediartr Nephrol 2001 : 16 : 371-382.
17. Braden G L, Muthem J G, O'shea M H, et al; Changing incidence of glomerular diseases in adults. Am J Kidney Dis 2000; 35:878.
18. Dragovic D, Rosenstock J L, Wahl S J, et al. Increasing incidence of focal segmental

glomerulosclerosis and an examination of demographic pattern. Clin Nephrol 2005; 63:1

19. Kitiyakava C, Eggers P, Kopp J B: Twenty one year trends in ESRD due to FSGS in the United States. Am J Kidney Dis 2004; 44: 815-825.

20. Bahiense- Oliveira M, Saldanha L B, Andrade Mota E L, et al: Primary glomerular disease in Brazil. 1979-1999. Is the frequency of FSGS increasing? Clin Nephrol 2004 ; 61: 90-97

21. Borilla Felix M, Parra C, Dajani T I et al: Changing patterns in the histopathology of idiopathic nephrotic syndrome in children. Kidney Int 1999; 55: 1885.

22. Gulate S, Sharma A P, Sharma R K et al. Changing trends of histopathology in childhood neptrotic syndrome. Am J Kidney Dis 1999; 34:646.

23.

24. Adhikari M, Bhimma K, Cooradia H M: FSGS in children from Kwazulu/ Natal, South Africa, Clin Nephrol 2001: 55:16.

25. Chun M J, Korbet S M, Schwatz M M, Lewis E J: FSGS in nephrotic adults : Presentation, prognosis and response to therapy of the histologic variants. J Am Soc Nephrol 2004; 15: 2167-2177.

26. Appel GB, Glassock RJ: Glomerular, vascular and tubulointersitital diseases. Nephrology self Assessment Program 2005; 4: 117-153.

27. D'Agati V D, Fogo A B, Bruijn J A, Jennette J C : Pathologic classification of focal segmental glomerulosclerosis : A working proposal. Am J Kidney Dis 2004; 43: 1223 – 1241.

28. Yamagata K. A long term follow up study of asymptomatic hematuria and or proteinuria in adults Clin Nephrol 1996; 4 : 281.

29. Preston R A et al. Renal biopsy in patients 65 years of age or older; an analysis of the results of 334 biopsies. J Am Geriatric Soc 1990; 38: 669.

30. Abrass C, Couser W. Pathogenesis of membranous nephropathy. Annu Rev Med 1998; 39: 517.

31.

32. Kerganchki D: Pathomechanisms and molecular basis of membranous glomerulopathy. Lancet 2004; 364: 1194 – 1196.

33. Simo P, et al. Epidemiology of primary glomerular diseases in a French region. Variation according to period and age. Kidney Int 1994; 46: 1192.

34. Gesualdo L et al. The Italian experience of the national registry of renal biopsies. Kidney Int 2004; 66: 905.

35. Levin A: management of MPGN. Evidence based recommendations. Kidney Int 2006; 69: 504-511.

36. Suzuki K, Honda K, Tanabe K, et al: Incidence of latent mesangial IgA deposition in renal allograft donors in Japan. Kidney Int 2003; 63: 2286-2294.

37. Pozzi C, Andralli S, Del Vecchio L, et al: Corticosteroid effectiveness in IgA nephropathy: Long term results of a randomized, controlled trial. J Am S Nephrol 2004; 15 : 157-163.

38. Balow J E, Austin H A: Therapy of membranous nephropathy in SLE. Seminal Nephrol 2003;

23:886.

39.

40. Pasquali S et al. Lupus membranous nephropathy. Long term outcome. Clin Nephrol 1993; 39:175.

41. Huong D L, et al. Renal involvement in SLE : A study of 180 patients from a single center. Medicine (Baltimore) 1999; 78: 148.

42. Bakir A A, Levy P S, Dunea G. The prognosis of lupus nephritis in African Americans: A restrospective analysis. Am J Kidney Dis 1994; 24:159.

43. Sloan R P, et al. Long term outcome in SLE membranous glomerulonephritis. J Am Soc Nephrol 199 ; 7:299.

44. Jawa A, Kcomt J, Fonseca V A. Diabetic nephropathy and retinopathy. Med Clin North Am 2004; 88: 1001-1036.

45. Rossing P, Rossing K, Jacobsen P et al. Unchanged incidence of diabetic nephropathy in IDDM patients. Diabetes 1995; 44: 739-743.

46. Diabetic nephropathy: American Diabetes Association. Diabetes care 2003; 26: S94-S98.

47. Molich M E, Defronzo R A, Franz M J, et al. Diabetic nephropathy. Diabetes Care 2204; 27: S79-S83.

48. Balakrishnan N, John G T, Korula A, Visalakshi J, Talulikar G S, Thomas P P, Jacob C K; Spectrum of biopsy proven renal disease and

49. changing trends in a tropical tertiary care centre 1990-2001. Indian Journal of Nephrology, 2003:12(5).

50. Sajith N, Sud K, Kohil H S, Gupta K L, Joshi K, Sakhuja V. Adolescent onset nephrotic syndrome in India: Clinical features and histopathological spectrum. Indian Journal of Nephrology, 2001; 1(3).

51. Hareesha Babu, Sharma L C, Agarwal D, Pathak R. Profile of Renal Histopathology from a Tertiary hospital in Rajasthan. Indian Journal of Nephrology, 2005;15(3).

52. Reshi A R, Bhat M A, Najar M S, Banday K A, Naik M A, Singh D P, Wani F. Etiologic profile of nephrotic syndrome in Kashmir. Indian Journal of Nephrology, 2008; 18:9-12

53. Nagarajan P, Kandasamy S, Muthukumar T, Edwin Fernando M, Manorajan R, Venkatraman R, Sreedhar S, Jayakumar M. Idiopathic adult FSGS: Outcome of long term steroid therapy and clinicopathological correlation. Indian Journal of Nephrology, 2004: 14(3).

II.PROFORMA

Name:
Age:
Sex:
Presenting complaints with duration:
Pedal edema:
Facial puffiness:
Abdominal distension:
Significant past history:
H/O similar episodes in the past:
H/O Diabetes mellitus:
H/O Systemic hypertension:
H/O Connective tissue disorder:
H/O Drug history:
H/O Substance abuse:
H/O Premarital and extramarital contact:
H/O suggestive of Infectious diseases:
H/O malignancy in the past:
H/O Radiation therapy:

Blood pressure:
Urine Routine:
Albumin:
Sugar:
Deposits:
Blood sugar:
Blood urea:
Serum creatinine:
Serum albumin:
Serum cholesterol:
Coagulation profile:
Viral markers (HbsAg, Anti HCV, HIV Elisa):
ANA:
Others (Complement assay, dsDNA, Hb electrophoresis, peripheral Smear, etc.)
Ultrasound abdomen:
Renal biopsy:

III. MASTER CHART

S No	Name	Age (yrs)	Sex	Pedal edema (wks)	Abdominal distension	Facial puffiness	Past h/o	BP (mmHg)	Urine Alb	Urine Sugar	Urine deposit	24 hr urine protein (g)
1	Ganesh	30	M	3	-	4	-	160/110	3+	-	2+R	6.6
2	Ammu(459/07)	29	F	6	-	1	-	120/76	3+	-	2+P	7.8
3	Samundeeswari	24	F	-	-	4	SLE 2yrs	140/84	2+	-	4+P	3.5
4	Pappi	27	F	4								

-
4
SHT 1yr
130/94
2+
-
5+P
5.3
5
Jalammal
45
F
12
-
4
-
130/80
3+
-
2+P
7.5
6
Praveen Banu
25
F
20
4
4
SLE 2yrs
110/70
3+
-
2+R
4.5
7
Sanma
40
F
4
-
4
-
132/80
1+
-
2+P
15
8
Chandra
52
F
3
-
-
-
116/76
3+
-

-
4
9
Vimala
27
F
-
-
2
-
146/96
3+
-
2+R
10
10
Jagadeesan
21
M
3
3
3
-
130/86
3+
-
1+P
5.6
11
Valli
28
F
8
2
4
-
140/80
2+
-
1+P
12
12
Vadamalli
28
F
6
2
2
-
134/80
3+
-
1+R
5.8
13
Mariya
21
F

-
-
2
-
110/84
3+
-
-
3.6
14
Rajeswari
23
F
1
-
4
-
160/90
3+
-
2+R
8.2
15
Vivekanandan
37
M
12
4
4
-
200/120
4+
-
2+R
9
16
Nagaraj
37
M
16
4
4
-
150/100
3+
-
1+R
4.9
17
Jayalakshmi
26
F
3
-
4
-
140/100
3+

-
2+R
8.3
18
Shakila
23
F
8
-
2
-
150/104
3+
-
2+R
11.2
19
Rajathi
35
F
12
8
12
SLE 10yr
130/90
3+
-
-
3
20
Ramanathan
19
M
12
4
4
-
134/80
3+
-
2+P
6.6
21
Sankar
38
M
2
-
-
-
140/96
3+
-
3+
6.5

22
Kumar

24
M
3
-
-
-
120/90
3+
-
3+R
7
23
Nithyanandam
45
M
12
4
8
-
150/100
3+
-
2+R
11
24
Shanthamma
25
F
3
-
1
-
150/90
3+
-
2+R
7.8
25
Sowmya
19
F
8
4
8
-
104/80
2+
-
-
5.4
26
Kalyani
37
F
2
-
-
-

140/90
3+
-
1+P
4.3
27
Prakash
34
M
10
6
6
-
160/110
3+
-
3+R
12.6
28
Bhavani
19
F
4
-
6
-
132/90
3+
-
1+P
9.3
29
Karupasamy
53
F
16
4
4
-
130/100
3+
-
-
10.8
30
Mani
40
M
4
-
4
-
130/84
3+
-
1+P
4.2
31

Subramani
30
M
-
-
2
-
170/110
3+
-
1+R
3.8
32
Padma
22
F
8
1
1
-
110/70
3+
-
1+P
4
33
Bavanandam
45
M
8
-
2
-
140/90
3+
-
2+R
6.2
34
Santhya
24
F
4
-
1
-
120/80
3+
-
-
5
35
Chitra
37
F
-
-
2

-
110/80
3+
-
2+R
4.8
36
Ashok
34
M
4
4
4
-
150/90
3+
-
1+P
4.6
37
Naresh
21
M
2
-
4
-
124/80
3+
-
1+P
5.4
38
Thiagu
34
M
8
8
8
-
140/100
3+
-
2+R
10.2
39
Samsath
20
F
4
-
8
-
120/80
3+
-
2+P
6.3

40
Muthamizh
24
F
2
2
2
-
120/82
3+
-
2+P
6.2
41
Ravi
36
M
4
-
4
-
160/96
4+
-
6+R
4
42
Krishnaraj
36
M
4
4
4
-
130/80
3+
-
-
7.6
43
Sivakumar
31
M
-
-
2
-
126/80
3+
-
1+R
4.5
44
Thangam
48
F
8
2

2
-
130/90
3+
-
2+P
6
45
Ammu(501/09)
22
F
8
2
2
-
130/100
4+
-
-
5.8
46
Shanthi
40
F
-
-
2
SHT 1.5yr
140/90
2+
-
1+P
4
47
Jayanthi
33
F
16
-
4
NSAIDs
130/80
4+
-
4+R
3.8
48
Shanmugam
28
M
12
2
2
-
120/80
3+
-
2+R

4.2

49
Vinoth Kumar
19
M
-
-
1
-
110/70
3+
-
1+P
4.8
50
Abdul Sathar
40
M
4
-
-
-
120/80
3+
-
2+R
9.6

S No
Name
Blood sugar
Blood urea
Sr creatinine
Sr albumin
Sr cholesterol
Viral markers
ANA
Others
USG
Renal biopsy
1
Ganesh
124
28
0.8
3.3
265
Neg
Neg
-
Normal size kidneys
MGN
2
Ammu(459/07)
94
32
1

3.2
318
Neg
Neg
-
Normal size kidneys
MGN
3
Samundeeswari
98
53
1.5
3.4
289
Neg
1:40 +
dsDNA 1:10+, C3,C4↓
RK-9.6;LK-10.6,Mild ↑ in cortical echoes
DPGN
4
Pappi
85
21
1.1
3.2
252
Neg
Neg
-
RK-10.7;LK-10.5
DPGN
5
Jalammal
112
34
1.1
3.2
243
Neg
Neg
-
Normal size kidneys
FSGS
6
Praveenbanu
91
15
0.8
3.6
237
Neg
1:40+ speck
C3,C4↓
RK,LK-11.8, Normal echoes
MGN Class5
7
Sanma
88

60
1.1
3.0
254
Neg
Neg
-
Normal size kidneys
MCD
8
Chandra
80
18
0.8
3.6
236
Neg
Neg
-
Normal size kidneys
FSGS
9
Vimala
102
20
0.9
3.1
242
Neg
Neg
-
Normal size kidneys
MGN
10
Jagadeesan
94
24
1
3.8
230
Neg
Neg
-
Normal size kidneys
MCD
11
Valli
83
16
0.8
3.5
308
Neg
Neg
-
RK-10.1;LK-10.6
MCD
12

Vadamalli
92
20
0.8
3.2
214
Neg
Neg
-
Normal size kidneys
MGN
13
Mariya
60
15
0.8
3.5
284
Neg
Neg
-
RK-11.9;LK-11.7, Mild ↑ in cortical echoes
FSGS
14
Rajeswari
96
44
1.6
3.3
270
Neg
Neg
-
Normal size kidneys
FSGS
15
Vivekanandan
110
88
3.2
3.5
228
Neg
Neg
-
RK,LK-10,Grade 1 echo
MPGN
16
Nagaraj
84
34
0.9
3.3
257
Neg
Neg
-
Normal size kidneys

MGN

17
Jayalakshmi
93
16
0.9
3.2
282
Neg
Neg
-
RK-9.4;LK-9.7;PCS-N
MGN
18
Shakila
98
42
1.1
3
246
Neg
Neg
-
Normal size kidneys
MGN
19
Rajathi
117
16
0.9
3.4
274
Neg
1:40+
dsDNA +
RK,LK-10;N echoes
MGN Class5
20
Ramanathan
121
38
1.1
3.8
212
Neg
Neg
-
Normal size kidneys
MPGN
21
Sankar
94
50
1.1
3.6
206
Neg

Neg
-
RK,LK-9.8;N echoes
IgA N
22
Kumar
80
40
1
3.2
270
Neg
Neg
-
RK,LK-10.3;N echoes
IgA N
23
Nithyanandam
110
36
1.1
3.0
295
Neg
Neg
-
Normal size kidneys
MGN
24
Shanthamma
108
34
0.9
3.7
256
Neg
Neg
-
Normal size kidneys
FSGS
25
Sowmya
76
40
0.9
3
181
Neg
Neg
-
RK-10.4;LK-9.8
FSGS
26
Kalyani
123
20
1
3.7

316
Neg
Neg
-
RK,LK-10.8;N echoes
MCD
27
Prakash
93
18
0.9
3
197
Neg
Neg
-
RK-12.3,LK-13;PCS-N
MGN
28
Bhavani
90
26
0.8
3
260
Neg
Neg
-
Normal size kidneys
MGN
29
Karupasamy
129
62
1.5
3
331
Neg
Neg
-
Renal parenchymal dis
FSGS
30
Mani
90
30
0.8
3.5
270
Neg
Neg
-
Normal size kidneys
FSGS
31
Subramani
96
36

0.9
3.8
268
Neg
Neg
-
RK,LK-9.5, N echoes
IgA N
32
Padma
78
22
0.6
40
190
Neg
Neg
-
RK-9,8,LK-9.9,N echo
IgA N
33
Bavanandam
104
46
1.2
3.3
264
Neg
Neg
-
RK,LK-10.3;N echoes
IgA N
34
Santhya
70
24
0.7
3.8
198
Neg
Neg
-
RK,LK-10;N echoes
IgA N
35
Chitra
80
30
0.8
3.5
240
Neg
Neg
-
RK,LK-9.6:N echoes
IgA N
36
Ashok

98
46
1.1
3.8
236
Neg
Neg
-
Normal size kidneys
MPGN
37
Naresh
86
28
0.7
3.6
228
Neg
Neg
-
Normal size kidneys
MGN
38
Thiagu
108
26
1.1
3.1
306
Neg
Neg
-
Normal size kidneys
MGN
39
Samsath
85
18
0.8
3.2
208
Neg
Neg
-
RK,LK-11.1;N echoes
MGN
40
Muthamizh
86
26
0.9
3.8
210
Neg
Neg
-
Normal size kidneys
FSGS

41
Ravi
115
20
1
3.6
210
Neg
Neg
-
RK-8.9,LK-8.4;Grade I echoes
FSGS

42
Krishnaraj
89
30
0.9
3.4
304
Neg
Neg
-
Normal size kidneys
MGN
43
Sivakumar
96
28
1
3.2
288
Neg
Neg
-
Normal size kidneys
FSGS
44
Thangam
116
34
1.1
3.3
320
Neg
Neg
-
Normal size kidneys
MGN
45
Ammu(501/09)
76
22
1
3.1
298
Neg
Neg

C3,C4-N; dsDNA- Neg
RK-11.3,LK-11.1; Grade I echoes
DPGN
46
Shanthi
98
50
1.3
3.8
190
Neg
1:100+
dsDNA-Pos; C3,C4-↓
RK,LK-9.6, Grade I echoes
FN
47
Jayanthi
96
65
1.4
3.6
256
Neg
Neg
C3,C4- N
RK,LK-11.8; Grade 3 echoes
DPGN
48
Shanmugam
106
24
0.7
3.6
244
Neg
Neg
-
RK,LK-10.1;N echoes
IgA N
49
Vinoth Kumar
91
30
0.8
37
219
Neg
Neg
-
Normal size kidneys
MGN
50
Abdul Sathar
112
82
3.5
3.1
216

Neg
Neg
-
RK-10.3,LK-10.8
FSGS

ABBREVIATIONS

1. MGN – Membranous nephropathy
2. FSGS – Focal and segmental glomerulonephritis
3. MCD – Minimal change disease
4. MPGN – Membranoproliferative glomerulonephritis
5. IgA N – IgA Nephropathy
6. FN – Focal nephritis
7. DPGN – Diffuse proliferative glomerulonephritis
8. ANA – Anti nuclear antibody
9. RK – Right kidney
10. LK – Left kidney
11. N – Normal
12. Neg – Negative
13. Pos - Positive
14. R – RBCs
15. P – Pus cells
16. Speck – Speckled pattern