"CLINICAL, BIOCHEMICAL AND HISTOPATHOLOGICAL FEATURES OF ADULT NEPHROTIC SYNDROME – A CROSS SECTIONAL STUDY"

By

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M. D. MEDICINE

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I hereby declare that this dissertation entitled **"CLINICAL, BIOCHEMICAL AND HISTOPATHOLOGICAL FEATURES OF ADULT NEPHROTIC SYNDROME - A CROSS SECTIONAL STUDY"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. M. S. KHANPET** $_{\text{MD, DNB}}$ Associate Professor, Department of Medicine, Jawaharlal Nehru Medical College, Nehru Nagar, Belgaum – 590010.

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LIST OF ABBREVIATIONS USED

Abd Dist	–	Abdominal distention
AL	–	Amyloid Light Chain
ACE	–	Angiotensin Converting Enzyme
ACEI	–	Angiotensin Converting Enzyme Inhibitor
Apo (a)	–	Apolipoprotein (a)
Apo-B-100	–	Apolipoprotein B 100
C1q	–	Complement Component 1q
C_3	–	Compliment Factor C3
C_4	–	Compliment Factor C4
CD2Ap	–	CD2 Associated Protein
Factor B	–	Complement Factor B
Factor D	–	Complement Factor D
FFAs	–	Free Fatty Acids
FITC	–	Fluorescein Isothiocyanate
FMD	–	Flow Mediated Dilatation
FSGS	–	Focal Segmental Glomerulo Sclerosis
GBM	–	Glomerular Basement Membrane
GFR	–	Glomerular Filtration Rate
gm/dl	–	grams per deci litre
HIV	–	Human Immuno Deficiency Virus
HDL	–	High Density Lipoprotein
IDL	–	Intermediate Density Lipoprotein
IgA	–	Immunoglobulin A
IgA N	–	Immunoglobulin A Nephropathy

IgE	–	Immunoglobulin E
IgG	–	Immunoglobulin G
IgM	–	Immunoglobulin M
INR	–	International Normalised Ratio
Kd	–	Kilo Dalton
Kg	–	Kilogram
LCAT	–	Lecithin Cholesterol Acyltransferase
LDL	–	Low Density Lipoprotein
Lp (a)	–	Lipoprotein a
LpL	–	Lipoprotein Lipase
LN	–	Lupus Nephritis
MCN	–	Minimal Change Nephropathy
MCNS	–	Minimal Change Nephrotic Syndrome
Mg	–	Milligram
mg/dl	–	mili grams per deci litre
MMF	–	Mycophenolate Mofetil
MN	–	Membranous Nephropathy
MPGN	–	Membrano Proliferative Glomerulo Nephritis
No.	–	Number
NOS	–	Not Otherwise Specified
NS	–	Nephrotic Syndrome
PAS	–	Periodic Acid - Schiff
POF	–	Puffiness Of Face
SLE	–	Systemic Lupus Erythematosus
T3	–	Triiodothyronine

T4	–	Thyroxine
TC	–	Total Cholesterol
TG	–	Triglycerides
TSH	–	Thyroid Stimulating Hormone
VAD	–	Vincristine Adriamycin Daunorubicin
VLDL	–	Very Low Density Lipoprotein
WHO	–	World Health Organisation

ABSTRACT

Background and Objectives

There is currently little information in literature about the pattern of nephrotic syndrome in adults in our country. The occurrence of different histopathological lesions in adult patients with nephrotic syndrome is different from that seen in paediatric population. The objectives of the present study were to know the clinical features, biochemical and histopathological spectrum in the adult onset nephrotic syndrome and to correlate the clinical and biochemical parameters with histopathological diagnosis.

Methods

The present one year cross sectional study was conducted in the Department of Nephrology and Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum, on 30 patients clinically diagnosed to have adult onset nephrotic syndrome during the period of January 2007 to December 2007. Data was collected by relevant history, clinical examination, relevant biochemical investigation and renal biopsy.

Results

Out of 30 patients 19 (63.33%) were males and 11 (36.66%) were females. Mean age was 31.1 years. Primary glomerular disease was predominant and accounted for 76.6%. Of which MCN was the most common histological lesion (60%), followed by FSGS (17%). Among secondary glomerular disease amyloid was the most common (57%) followed by SLE (42%). The commonest presentation was pedal oedema, puffiness of face and oliguria. 33.33% patients

had hypertension, of which 50% were MCN, 20% were SLE and 10% were FSGS. 33.33% had haematuria of which 40% were MCN, 20% were FSGS and 20% were MN. All patients had nephrotic range proteinuria, hypoalbuminemia and high lipid profile with low HDL levels.

Conclusion and interpretation

MCN was the most common primary glomerular disease followed by FSGS and amylodosis is the most common secondary glomerular disease followed by SLE. The common presentation was pedal oedema, puffiness of face and oliguria. Hypertension was more prevalent among MCN and FSGS. Renal biopsy is of paramount importance in diagnosing underlying histopathology adult nephrotic syndrome.

Keywords

Nephrotic syndrome; Minimal change nephropathy; Focal segmental glomerular sclerosis; Amyloidosis; Lupus nephritis;

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INTRODUCTION

Nephrotic syndrome refers to a classic tetrad of proteinuria, hypoproteinemia, edema and hyperlipidemia.[1] Relationship among these findings was recognized as early as 15th century.[1] Adult Nephrotic syndrome arises from a variety of causes of glomerular damage which inturn leads to considerable persistent proteinuria, either arising apparently primary to the kidney, or as part of systemic disease and leading to identical clinical manifestations, the most important of which is the accumulation of edema but also involving hyperlipidemia, hypercoagulability and possibly renal damage from increased protein traffic through glomeruli and tubules. Despite considerable advances in health care, glomerular disease constitutes one of the leading cause of renal failure resulting in considerable morbidity and mortality. Even though glomerular diseases are less common in adults than in children, it accounts for 20 to 25% of End Stage Renal Disease (ESRD).[2]

Even though Nephrotic Syndrome is a disease of children, considerable number of cases are seen in adults as well. The clinical features between children and adults do not vary much. Adults have higher prevalence of Hypertension and decline of renal function. In children primary glomerular disease constitutes more than 90% and less than 30% in adults. In adults secondary glomerular disease constitutes more than 50% and less than 30% in children.[1]

The patterns of the glomerular disease varies from continent to continent and from place to place in same continent. Changing pattern of Glomerular disease is noted very much these days within the same country.

Spectrum of Nephrotic syndrome varies in different ethnic populations, age groups and socio economic strata. For instance IgA nephropathy is common in northwest regions of Italy, far east and eastern Europe,[3,4] while FSGS appear to be more prevalent in USA and Saudi Arabia.[5,6] In Italy, Japan, China, Singapore, Hong Kong and Taiwan IgA nephropathy is the most common primary glomerulonephropathy, followed by MGN and FSGS.[3,7,8,] In Iraq, FSGS followed by MCD represents the most common primary glomerular diseases.[9] In Vietnam and Indonesia MCD represents the most common primary glomerular disease.[10]

Secondary glomerular diseases accounted for 54% of all glomerular diseases in Jamaica.[11] Hepatitis-B was associated with 80% of glomerular diseases in Zimbabwe.[12] Lupus nephritis accounted for 20.4% in Hawaii.[13]

In India the pattern varies according to demographic location, mesangio proliferative glomerular nephritis represents the most common cause of Adult Nephrotic Syndrome in south India,[14] MCD dominates Northern India and Eastern India,[15,16] where as IgA nephropathy is common in western India.[17] Lupus Nephritis followed by Diabetic nephropathy are the leading Secondary glomerular diseases in Southern India.[14]

Hence in this study an attempt is made to note the clinical features, biochemical, and histopathological spectrum in the adult nephrotic syndrome.

OBJECTIVES

The objectives of the present study were;

1. To study the clinical features, biochemical and histopathological spectrum in the adult onset nephrotic syndrome.

2. To correlate the clinical and biochemical parameters with histopathological diagnosis.

REVIEW OF LITERATURE

Nephrotic syndrome classically presents with heavy proteinuria, hypoalbuminemia, hypercholesterolemia, edema, and hypertension.[18] If left undiagnosed or untreated, some of these syndromes will progressively damage enough glomeruli to cause a fall in GFR, producing renal failure.[19] The nephrotic syndrome results from greater than 3.5 grams per day of proteinuria or 50 mg per kg of body weight per day.[18] In addition to primary (idiopathic) glomerular diseases, the nephrotic syndrome may be secondary to a large number of identifiable disease states. Despite the differences in these causes, the loss of substantial amounts of protein in the urine results in a shared set of abnormalities that comprise the nephrotic syndrome.[18]

Pathophysiology of the Nephrotic Syndrome

Virtually every abnormality observed in primary nephrotic syndrome can be traced directly or indirectly to the urinary loss of protein. Thus, the mechanisms responsible for this proteinuria have systemic consequences that are manifested in the clinical signs and symptoms of nephrosis.[1]

Proteinuria

The renal factors contributing to albumin homeostasis include both glomerular filtration and tubular reabsorption. In its simplest form, the glomerulus functions as a means to promote fluid and solute flux from the blood vessel to the urinary space, from where most constituents of the filtrate are then reabsorbed. This model acquires significant complexity as solute particles

approach the size limits that are characteristic of the glomerular filter. Further, recent progress in understanding tubular handling of protein has demonstrated that the reabsorptive component also has a significant impact on albumin homeostasis.[1]

The glomerular filtration barrier is composed of endothelial cells, basement membrane, and podocytes. The glomerular basement membrane is composed of a multitude of proteins, including collagen IV, heparan sulfate proteoglycans, and laminin. The slit diaphram, which is seen as a membrane covering the space between adjacent foot processes close to the basement membrane, is an extremely important structure with a crucial role in permselectivity of the filtration barrier. Its composition is now understood to consist primarily of a unique protein called nephrin. Mutations in the gene-encoding nephrin are known to result in the Finnish type of nephrotic syndrome. The exact mechanism by which nephrin controls permselectivity is not yet clear, but it is known to interact with several podocyte proteins including CD2AP, podocin, and alpha-actinin-4. Abnormalities of any of these proteins may result in proteinuria. The role of nephrin and its associated proteins in the pathogenesis of common acquired glomerulopathies in humans is still under investigation.[20]

Nephrotic proteinuria does not result from a simple defect in glomerular filter steric hindrance. Several theories have been advanced to account for albumin loss. A prominent one is a decrease in glomerular electrostatic charge selectivity.[1]

Alteration of podocyte architecture also may account for the generally decreased fractional clearance of smaller macromolecules in nephrotic syndrome.[1]

In addition to the urinary losses of albumin in the nephrotic syndrome, glomerular permeability causes the loss of proteins of similar molecular weight. Not all proteins are lost in the urine, especially larger proteins such as IgM, fibrinogen, alpha-1 and alpha-2 macroglobulin, and larger lipoproteins that never traverse the glomerular capillary wall and thus are of normal or increased concentration in the plasma.

Consequences of Proteinuria

It is generally accepted that the central feature of the nephrotic syndrome, irrespective of its underlying renal cause, is hypoalbuminemia resulting from urinary loss. There is increased fractional catabolism of albumin in nephrotic syndrome, mostly within the renal tubule after increased filtration of plasma proteins. Rates of hepatic synthesis of albumin are increased, but this increase is inadequate to compensate for urinary losses.[1]

Edema

Edema is the most common presenting symptom of patients with the nephrotic syndrome. Various theories for the cause of nephrotic edema have been proposed. Hypovolemia as a consequence of reduced plasma oncotic pressure has long been considered the proximal cause of salt and water retention by the kidney. Enhanced tubular sodium reabsorption is thought to be a function of multiple mediator systems responding to the “perceived volume depletion” with

activation of the renin-angiotensin-aldosterone, sympathetic nervous, and vasopressor systems.[18]

Although there is evidence to support the "underfilling" hypothesis of edema formation, other investigators have suggested that a primary disorder of the kidney results in increased intravascular volume and subsequent suppression of renin angiotensin aldosterone access and elevated natriuretic peptide levels ("over fill" theory). The literature is unclear whether plasma volume is low or high. Hypovolemia plays an important role in the retention of salt and water by the kidney. High blood pressure argues against hypovolemia and, in fact, suggests hypervolemia.[18]

Regardless of whether underfilling or overflow is paramount, another model suggests that hormonal mechanisms are of primary importance. Initial studies of the pathophysiology of nephrosis suggested that fluid redistribution results in aldosterone-mediated sodium retention designed to replenish vascular volume. Accordingly, aldosterone activity was thought to be more important in the genesis of fluid retention than either serum albumin or colloid osmotic pressure.[1]

Recently, a hypothesis has been advanced that sodium and water retention in the nephrotic syndrome is due to over-excretion of vasopressin as a consequence of either volume or osmotic stimuli. This vasopressin-dependent process results in fluid retention.

Calcium and vitamin D levels are typically altered in the nephrotic syndrome. Vitamin D binding protein is a relatively small protein of 59 kD that is

filtered as readily as albumin. 25-hydroxyvitamin D, the precursor of Calcitriol, is bound to vitamin D binding proteins and is lost in the urine with the nephrotic syndrome. Similarly, there may be low serum concentrations of total 1,25-dihydroxyvitamin D. With the loss of vitamin D binding protein, it is important to measure free 1,25-dihydroxyvitamin D levels to accurately assess the status of this factor in these patients. Further, hypoalbuminemia results in low total serum calcium concentration.[18]

Hormone-binding proteins are typically lost in the urine resulting in several endocrine or metabolic abnormalities. The urinary loss of thyroid binding globulins and thyroxine results in a low T4, both free and bound, in about one half of all patients with the nephrotic syndrome and a normal glomerular filtration rate. Additionally, TSH will be elevated, total T3 levels are reduced probably because of decreased binding to thyroid binding globulins. Total reversed T3 levels tend to be normal in the nephrotic syndrome, but the free reverse T3 level is elevated. Despite these abnormalities, most patients remain clinically euthyroid.

Hyperlipidemia

Lipemic serum has long been recognized as a cardinal feature of the nephrotic syndrome. Biochemical evaluation has shown that all lipid components of the plasma are increased. Hyperlipidemia may persist well into remission, suggesting a residual effect of nephrosis on lipoprotein transport. Hyperlipidemia is one of the cardinal manifestations of NS. Nephrotic hyperlipidemia is marked by elevations of plasma low-density lipoprotein (LDL), very low-density

lipoprotein (VLDL), intermediate-density lipoprotein (IDL), and lipoprotein (a) [Lp (a)]. Nephrotic hyperlipidemia also is frequently accompanied by a reduced or unchanged HDL concentration.[21]

Lipid metabolism is normally accomplished through a series of complex steps. Abnormalities at any step of metabolism from lipid uptake to the enterohepatic secretion of bile could result in the hyperlipidemia of nephrosis. Likely contributing factors include increased hepatic synthesis of lipoprotein; abnormal transport of lipid through the metabolic pathway; and abnormal catabolism secondary to decreased enzyme activity.

Lipoprotein Synthesis

It is clear that hepatic synthesis of lipoproteins is increased in nephrotic patients.[22,23] The signal for this event appears to be related to hypoalbuminemia because daily infusion of albumin into nephrotic patients, sufficient to raise serum levels, also decreases serum lipid, triglyceride, and cholesterol levels.[24]

Lipid Transport

The major cholesterol-transporting protein associated with the LDLs in the plasma is apo B-100.[25] This also has been implicated as a significant apolipoprotein in atherogenesis. A recent study of nephrotic patients found that elevated serum concentrations of cholesterol, triglycerides, and phospholipids resulted mostly from changes in apo B-100-containing lipoproteins. The size of the apo B-100 pool in patients was two to three times that found in healthy subjects or in patients in remission. Fractional catabolism was decreased only

slightly, suggesting that the major problem was overproduction rather than decreased breakdown.[26]

Metabolism of Lipids

Interest regarding catabolism of lipids in nephrosis has focused on two enzymes: LPL [lipoprotein lipase], which facilitates the breakdown of ester bonds in glycerides, and LCAT [lecithin-cholesterol acyltransferase], which catalyzes the reaction of lecithin and cholesterol to form lysolecithin and cholesterol ester.[27] Activity of these enzymes may be affected both directly and indirectly by urinary protein loss. Albumin binds to free fatty acids (FFAs); decreases in serum albumin concentration lead to FFA accumulation, thereby inhibiting LPL activity.[28] LCAT activity is inhibited by the accumulation of triglyceride and cholesterol esters, [29] suggesting that abnormal LCAT activity could be a result, rather than a cause, of nephrotic hyperlipidemia.

Clinical Significance

Regardless of the cause, the clinical significance of the lipid abnormalities in nephrosis must be considered. Hyperlipidemia has been associated with premature coronary atherosclerosis[30] and a high incidence of myocardial infarction and other cardiovascular diseases have been documented in nephrotic subjects, as well as a higher incidence of hypertension in nephrotic men than in control subjects.[31,32] Lp (a) is an independent risk factor for atherosclerotic disease.[18] In patients with the nephrotic syndrome, plasma Lp (a) increases significantly as a consequence of an increased rate of synthesis with a normal fractional catabolic rate. Lp (a) binds to apolipoprotein (a) [Apo (a)] with a

disulfide bond. Apo (a) has a high degree of homology with plasminogen, and Apo (a) interferes with plasminogen-mediated fibrinolysis; thus, an elevation of Lp (a) produces a prothrombotic event.[18]

Sensitive measures of endothelial dysfunction suggest that in patients with the nephrotic syndrome, endothelial function is altered. Postischemic flow-mediated dilatation (FMD) of the brachial artery was significantly lower in nephrotic patients and primary hyperlipidemia patients when compared with control patients.[33] In addition to the cardiovascular risk, there is a risk of the hyperlipidemia promoting progression of renal disease.

Despite the lack of information on lipid lowering and progression of renal disease, patients of nephrotic syndrome should receive lipid lowering therapy to decrease the risk of coronary heart disease.[34]

Disorders of Hemostasis

In a review of 3,377 children with nephrotic syndrome, the incidence of thromboembolic complications was 1.8%.[35] The prevalence of such complications in adult nephrotic subjects is much higher and averaged 26% in eight series of patients.[36] Many of the components of coagulation pathways are altered in nephrosis. In addition, physical conditions of the nephrotic syndrome, such as venous stasis, dehydration, hemoconcentration, increased blood viscosity, and possibly the administration of diuretic and steroids may also contribute to enhanced blood clotting.

Platelet Aggregation

Platelets may play a role in the genesis of the coagulopathy of nephrotic syndrome. Thrombocytosis is commonly found, especially early in the disease course and platelets show markers of activation. Increased Platelet aggregability and platelet degranulation has been described.

Coagulation Factors

Evidence that various functions of blood coagulation are activated in nephrosis is provided by increased concentration of the D-dimer of fibrinogen.[37] Elevated levels of this breakdown product of crosslinked fibrin indicate that both the coagulation and fibrinolytic pathways are concurrently activated. Plasma fibrinogen is consistently elevated in nephrotic syndrome due to increased hepatic synthesis. Chromatography demonstrates both increased polymerization and increased proteolytic derivatives of fibrinogen or fibrin. These changes reverse as patients with nephrotic syndrome enter remission.[38]

Inhibitors of Coagulation

The most well-studied biologic antagonist of coagulation, antithrombin III, is decreased in the plasma of nephrotic patients. [39] This is presumed to be due to urinary loss of antithrombin III, which has a relatively low molecular weight.

Fibrinolysis

Alterations in the concentrations of several of the components of the fibrinolytic system have been documented. Decreased fibrinolytic activity has

been associated with hypertriglyceridemia. Of the individual components of the fibrinolytic system, decreased concentrations of plasminogen have been found,

The thrombotic abnormalities in the nephrotic syndrome are a consequence of hyperfibrinogemia, thrombocytosis, increased platelet aggregability, increased fibrinogen to fibrin transition, decreased levels of antithrombin III, decreased fibrinolysis, increased factors II, V, VII, VIII, X, XIII, increased blood viscosity and hemoconcentration, these abnormalities may result in venous and arterial thrombi.[1]

Infections

Because of the urinary loss of immunoglobulins and defects in the complement cascade, nephrotic patients have an increased susceptibility of infection, particularly peritonitis. Peritonitis caused by either gram-negative or gram-positive organisms remains a serious complication of the nephrotic syndrome. [40] Acquired IgG deficiency due to urinary losses is certainly a cause of enhanced infection. The deficiency of both factor B and D urinary protein loss results in impaired opsonization of these microorganisms.

Hypoalbuminemia

Hypoalbuminemia is a cardinal feature of the nephrotic syndrome. Serum albumin levels are depressed not only as a consequence of loss in the urine, but also because of an increased albumin catabolism. Hepatic albumin synthesis is increased from 145 ± 9 mg/kg/day to 213 ± 17 mg/kg/day in nephrotic patients.[41] Prolonged and massive proteinuria may lead to malnutrition.

Minimal Change Nephropathy

Although MCN is often thought of as a pediatric disease, it is one of the most common cause of nephrotic syndrome in adults as well. Although most children with MCN achieve permanent remission of symptoms by the time they reach puberty, some cases persist into adulthood.[42] However, the relative incidence of MCN as the etiology of nephrotic syndrome decreases with age in both children and adults.[43] Although it is not clear that adult-onset disease represents the same entity as that found in childhood, or that all patients with the clinical picture of MCNS have an identical disease, the clinical course and outcome of pediatric and adult cases appear to be sufficiently similar.[43] In both adult and pediatric patients, malignancies, especially Hodgkin disease, have been associated with the development of MCNS.

Clinical Findings

Edema formation may begin within a few days of the inciting event. Facial edema usually is noted first, by the time medical advice is sought, the patient typically has pitting edema involving the sacrum and the lower extremities. When anasarca is present, periorbital edema can be so severe that the eyelids are swollen shut, scrotal or vulval edema may be marked, and there may be significant abdominal distension. Respiratory embarrassment may occur from accumulation of either pleural or ascitic fluid. The patient may note vague symptoms such as malaise, easy fatigability, irritability, and depression. Rarely the development of cellulitis, peritonitis or pneumonia may be the first indication of an underlying nephrotic syndrome.

On physical examination, dependent edema is the most prominent finding. The retina has a characteristic 'wet' appearance. Subungual edema may reverse the usual color pattern on the fingernails, the normally white lunulae may be pink and the rest of the nail bed white. Horizontal white lines that may be seen on both the fingernails and the toenails are referred to as Muehrcke bands. Inguinal and umbilical hernias may be present, if the patient has had severe ascites for a prolonged period.[1] Hypertension is seen more commonly in adult patients with MCN than in children.

Laboratory Findings

Urinalysis

Clinicians who first characterized the nephrotic syndrome noted that the urine often foams excessively when voided and that it coagulates when heated. These findings result from marked proteinuria, now indicated by a dipstick reading of 3+. The amount of protein in the urine of nephrotic patients can range from less than 1 to more than 25 g per/day. As a consequence of proteinuria, the urine specific gravity is high, often exceeding 1.035.[1]

In primary nephrotic syndrome, most of the urine protein is albumin; in other diseases, such as glomerulonephritis, both albumin and globulins are lost in increased amounts. Patients with MCNS tend to show more selective proteinuria. The urine sediment from nephrotic subjects often contains oval fat bodies and urine with large amounts of protein also contains hyaline casts. Up to one third of patients with MCN may have microscopic hematuria.[1]

Blood investigations

Hypoproteinemia is common to all nephrotic patients and is caused, primarily, by hypoalbuminemia. Total serum protein is characteristically reduced to between 4.5 and 5.5 g/dL; serum albumin concentrations usually fall to below 2 g/dL and in children may be less than 1 g/dL.[1]

IgG levels, may be profoundly decreased. IgM, IgA and IgE levels may be normal or elevated. Complement levels are typically normal in patients with minimal change glomerulopathy.[18]

Serum total cholesterol level is usually elevated, especially when the serum albumin level has fallen to 2 g/dL or less. Values average 400 mg/dL, but levels in excess of 1,000 mg/dL have been recorded.[1] LDL, and triglyceride levels are also increased.

Most often, serum electrolyte concentrations are within the normal range. Factitiously low serum sodium concentrations (~130 mEq/L) may be measured with marked hyperlipidemia. This pseudohyponatremia results from the nonaqueous, nonsodium-containing component of the serum or plasma (lipid) being increased.[1]

Serum calcium may be low and Serum phosphorus is normal unless the nephrotic syndrome is associated with renal insufficiency. Blood urea nitrogen (BUN) and serum creatinine values are usually close to normal in MCN, but may be mildly elevated if decreased intravascular volume leading to prerenal azotemia.[1]

Histopathology

Minimal Change Nephropathy

Light Microscopy (Figure No. 1)

Minimal change glomerulopathy has no glomerular lesions by light microscopy, or only minimal focal segmental mesangial prominence. Capillary walls should be thin and capillary lumens patent. The most consistent tubular lesion is increased protein and lipid resorption droplets in tubular epithelial cells. These droplets are periodic acid-Schiff positive.

Immunofluorescence Microscopy

Glomeruli usually show no staining with antisera specific for IgG, IgA, IgM, C3, C4, or C1q. The most frequent positive finding is low-level mesangial staining for IgM, sometimes accompanied by low-level staining for C3. If the IgM staining is not accompanied by mesangial electron dense deposits by electron microscopy, it is consistent with a diagnosis of minimal change glomerulopathy.

Electron Microscopy (Figure No. 2)

The pathologic sine qua non of minimal change glomerulopathy is effacement of visceral epithelial cell foot processes observed by electron microscopy. The effacement usually is accompanied by microvillous transformation, which is the development of numerous villous projections from the epithelial surface into the urinary space. The effacement also is accompanied by increased density of the cytoskeleton, including actin filaments, in clumps near the basement membrane surface of the visceral epithelial cells.

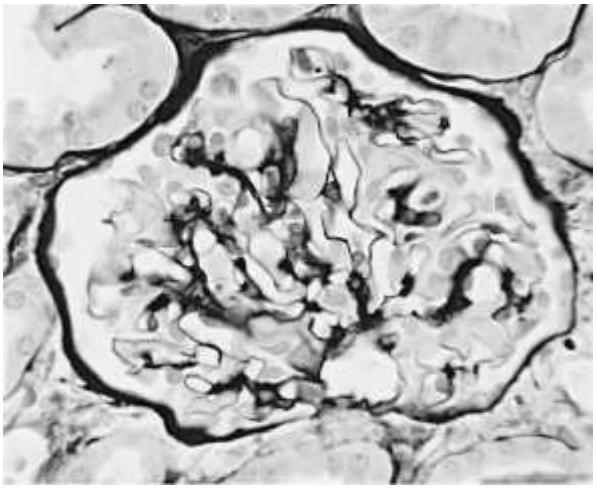


Figure No. 1: Unremarkable light microscopic appearance of minimal change glomerulopathy. Glomerular basement membranes are thin, and there is no glomerular hypercellularity or mesangial matrix expansion. (Jones methenamine silver, ×300.)

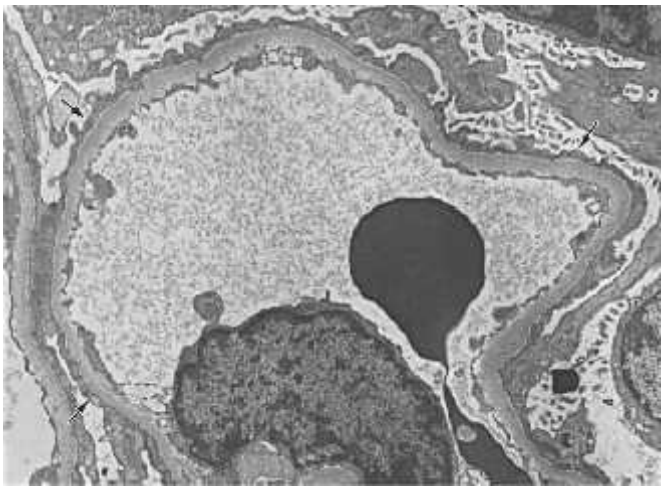


Figure No. 2: Electron micrograph of a glomerular capillary wall from a patient with minimal change glomerulopathy showing extensive foot process effacement (arrows) and microvillous transformation (magnification ×5000).

Treatment of Minimal Change Disease

The optimal treatment for MCN is based on corticosteroids but continues to evolve. It is noteworthy that in the era before current drugs were available, 25% of children with idiopathic nephrotic syndrome underwent a spontaneous remission.[1] Prior to 1940, the mortality rate for nephrotic syndrome was 40%; the major cause of death was infection. After the introduction of antibiotics, mortality was reduced by more than 50%. The development of corticosteroids has further reduced mortality to between 3% and 7%. In the older adult nephrotic patient, the risk of undesirable steroid side effects could outweigh the benefits of these drugs. Despite these caveats, corticosteroids remain the therapeutic agent of choice for MCN in patients of all ages.[1]

Corticosteroid Therapy

The standard dosage regimen for inducing a remission is 2 mg/kg of body weight per day or 60 mg/m^2 of body surface area per day (maximum of 80 mg per day).[1] Typically, patients respond with a diuresis followed by resolution of proteinuria. In most instances, response can be considered to have occurred if the patient has had protein-free urine for at least 3 consecutive days.[1]

After six weeks of daily treatment (rather than the standard 4 weeks of daily treatment) with prednisone, 60 mg/m^2, the patient is switched to 40 mg/m^2 on alternate days. continue prednisone (total of daily and alternate day) for about four to six months and then discontinue the drug.

Frequent Relapse

Attempts to control frequent relapses with steroids may result in their protracted use and possible steroid toxicity. In an effort to minimize these side effects, alternative regimens have been proposed using smaller doses of steroids to treat relapses. Alternatives such as cyclophosphamide and related drugs are now used in frequently relapsing and steroid-dependent nephrotic patients, especially in those with marked steroid side effects. Ideally, cyclophosphamide should not be used until a patient has been diagnosed to have a frequently relapsing course. The original cyclophosphamide regimen used doses of 5 mg/kg per day, but it was associated with a high incidence of leukopenia, hair loss, and cystitis. Most centers obtain satisfactory results with a dosage of 1.5 mg/kg/d for adults (2 mg per kg per day for children) given for 8 to 12 weeks. Approximately 65% of frequently relapsing patients remain in remission for at least five years after a course of cyclophosphamide. [44]

An alternative alkylating agent, chlorambucil, produce a more stable remission than cyclophosphamide does and be effective in some steroid-dependent and cyclophosphamide-resistant nephrotic syndrome and the overall incidence of serious complications with chlorambucil is low, especially when it is used in a dosage of 0.1 to 0.2 mg/kg per day for an eight week course. Cyclosporine and other calcineurin inhibitors can be beneficial in the management of patients with frequent relapses, especially those who do not achieve a long-term remission with an alkylating agent.[1] Mycophenolate mofetil has been reported to successfully treat frequently relapsing minimal change disease in adults and children. [1]

The use of intravenous immunoglobulin as an adjunct to steroids has not resulted in any clinically important extension of the period of remission in patients with frequent relapses. Differences between pediatric and adult patients with MCN may include a less rapid response to corticosteroids in adults,[45] a more effective response in adults to cyclophosphamide used alone and adult patients may be somewhat more prone to steroid complications, particularly in the bones

FSGS and Collapsing Glomerulopathy

Focal segmental glomerulosclerosis (FSGS) is a common cause of nephrotic syndrome in children and adults. FSGS is not a single disease but rather is a diagnostic term for a clinical-pathological syndrome that has multiple etiologies and pathogenic mechanisms.[46] The ubiquitous clinical feature of the syndrome is proteinuria, which may be nephrotic or non-nephrotic and associated with all of the morbid features of the nephrotic syndrome. Hematuria occurs in over half of FSGS patients and approximately one third of patients present with some degree of renal insufficiency. Hypertension is found as a presenting feature in one third of patients. Children tend to present with more proteinuria, while hypertension is more common in adults.[18] The ubiquitous pathologic feature is focal segmental glomerular consolidation or scarring, which my have several distinctive patterns. The collapsing variant of FSGS is a clinically aggressive variant that is much more common in African American than Caucasian populations, and is characterized pathologically by segmental collapse of capillaries accompanied by hypertrophy and hyperplasia of epithelial cells. Over the past two decades, there has been an increased incidence of FSGS. For the past

20 years, the yearly incidence of primary FSGS has risen from less than 10% to approximately 25% of adult nephropathies.[47]

Histopathology

Light Microscopy (Figure No. 3)

FSGS is characterized by focal and segmental glomerular sclerosis. Based on the character and glomerular distribution of lesions, five major structural variants of FSGS can be recognized. The five pathologic variants are collapsing FSGS, tip lesion FSGS, cellular FSGS, perihilar FSGS, and FSGS not otherwise specified (NOS).[46] The collapsing variant of FSGS has segmental to global collapse of capillaries with obliteration of lumens. The collapsing glomerulopathy variant of FSGS is the major pathologic expression of HIV nephropathy, intravenous drug abuse and as an idiopathic process. Tubulointerstitial injury is more severe in collapsing glomerulopathy than in typical FSGS.

The cellular variant of FSGS has lesions that resemble the cellular lesion for the tip variant, but they are distributed throughout the glomerular tuft. Perihilar FSGS is characterized by the perihilar predilection of lesions and the presence of hyalinosis. The NOS FSGS category is a nonspecific category that is used when the lesions do not have the distinctive features of any of the other four distinctive variants.[18]

Immunofluorescence Microscopy

In all of the histologic variants, non-sclerotic glomeruli and segments usually have no staining for immunoglobulins or complement. A minority of patients with focal segmental glomerulosclerosis will have low-level mesangial staining for IgM in non-sclerotic glomeruli. Sclerotic segments typically have irregular staining for C3, C1q, and IgM.[18]

Electron Microscopy (Figure No. 3)

The ultrastructural features of focal FSGS are nonspecific. Foot process effacement in FSGS affects sclerotic and non-sclerotic glomeruli, and usually is more focal than in minimal change glomerulopathy.[18]

Treatment

International Study of Kidney Diseases in Children recommended using an initial course of prednisone. Cytotoxic therapy, including cyclophosphamide and chlorambucil, plays a very limited role in adults with steroid-resistant FSGS and collapsing glomerulopathy. [1] Patients resistant to prednisone may be induced into remission with cyclosporine. Mycophenolate mofetil (MMF) is an appealing alternative therapy. An ACE inhibitor or angiotensin II receptor antagonist sufficiently decreases proteinuria and potentially decreases hyperlipidemia, edema, and other manifestations of persistent loss of protein in the urine in this population with excellent long-term prognosis.

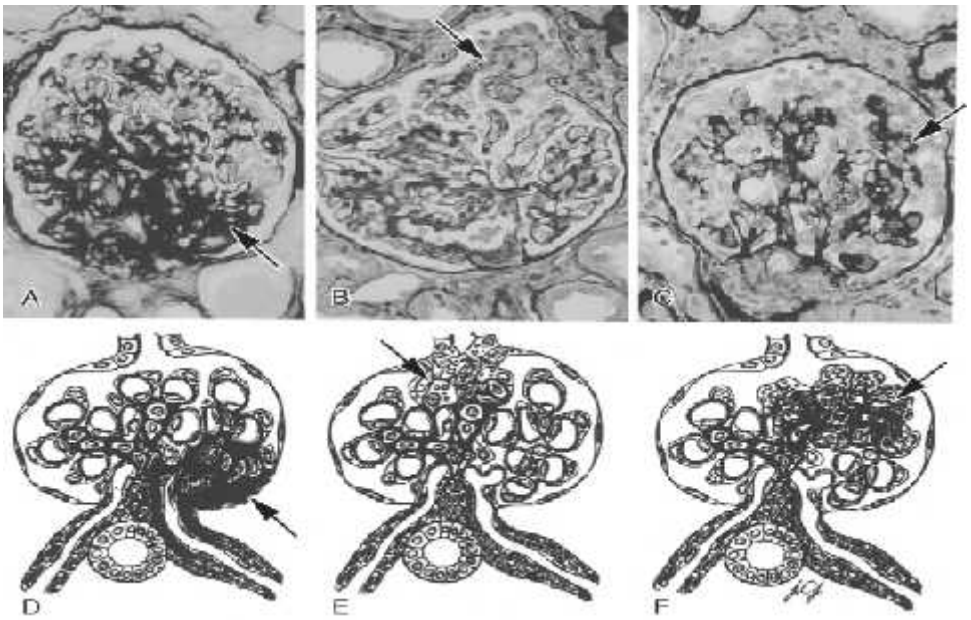


Figure No. 3: Light micrographs and diagrams depicting patterns of FSGS. One pattern (A and D) has a predilection for sclerosis in the perihilar regions of the glomeruli. The glomerular tip lesion variant has segmental consolidation confined to the segment adjacent to the origin of the proximal tubule (B and E). The collapsing glomerulopathy variant has segmental collapse of capillaries with hypertrophy and hyperplasia of overlying epithelial cells (C and F). (Jones methenamine silver, ×100.) [18]

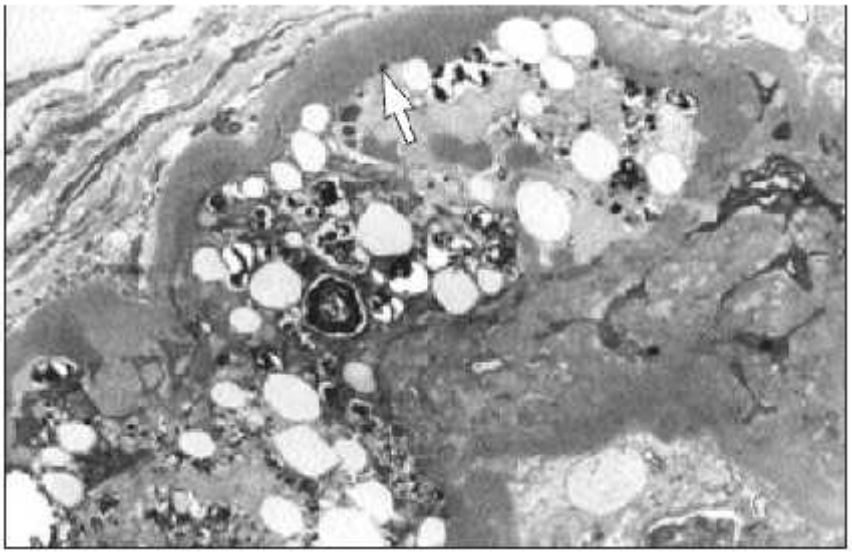


Figure No. 4: Electron microscopy of FSGS. The electron microscopic findings in the involved glomeruli mirror the light microscopic features, with capillary obliteration by dense hyaline "deposits" (*arrow*) and lipids. The other glomeruli exhibit primarily foot process effacement, occasionally in a patchy distribution. [18]

Current Therapeutic Recommendations[1]

For adults with FSGS and serum creatinine less than 2.5 mg/dL and less than 20% interstitial fibrosis area on renal biopsy, a trial of daily prednisone at a dose of 1 mg/kg of ideal body weight (to a maximum dose of 80 mg/day), until complete remission or 8 weeks have been reached. In the case of a complete remission, the recommendation is to prescribe an ~20 week tapering schedule of prednisone on alternate days, tapering at a rate of 20 mg every month. Patients with steroid-resistance would receive 16 weeks of daily prednisone and up to 40 weeks of alternate daily prednisone. Further options during prolonged taper would include cyclosporine for 1 year or oral cyclophosphamide or chlorambucil for 8 to 12 weeks. A newer option that was not included would be mycophenolate mofetil. [1]

Membranous nephropathy (MN)

Idiopathic membranous nephropathy is the most common cause for nephrotic syndrome in adults.[48,49,50] MN occurs as an idiopathic (primary) or secondary disease. Secondary membranous glomerulopathy is caused by various rheumatologic disorders (lupus erythematosus, rheumatoid arthritis, sjogren's syndrome, autoimmune thyroiditis, systemic sclerosis), infection (hepatitis B, hepatitis C, HIV, Malaria, schistosomiasis), drugs (penicillamine, gold, mercury, captopril), and malignancies (colon cancer, lung cancer). Secondary membranous glomerulopathy, especially that caused by hepatitis B [51] and lupus, is more frequent in children than adults. In patients over the age of 60, MN is associated with malignancy in 20% to 30% of patients. The majority of these cancers are carcinomas of the gastrointestinal tract, lung or breast.[52] MN is the cause for nephrotic syndrome in approximately 25% of adults.[53] MN is uncommon in children. The peak incidence is in the fourth or fifth decade of life.[53] Proteinuria is the hallmark of patients with MN (3 to 20 gms / day). Microscopic hematuria is present in 30% to 50% of patients at the time of presentation. Impaired renal function is found in less than 10% of patients at the time of presentation. Serum lipoproteins are characteristically elevated, as they are in other forms of the nephrotic syndrome.

Histopathology[18]

Light Microscopy

The characteristic histologic abnormality is diffuse global capillary wall thickening in the absence of significant glomerular hypercellularity.

Immunofluorescence Microscopy (Figure No. 5)

The characteristic immunofluorescence microscopy finding in membranous glomerulopathy is diffuse global granular capillary wall staining for immunoglobulin and complement. IgG is the most frequent and usually the most intensely staining immunoglobulin, although less staining for IgA and IgM is common. C3 staining is present over 95% but typically is relatively low intensity.

Electron Microscopy (Figure No. 6)

The pathologic sine qua non of MN is the presence of subepithelial immune complex deposits, or their structural consequences.

Treatment [18]

The role of corticosteroids and alkylating agents in the treatment of this disease has been debated for decades. The common therapeutic approaches for new-onset disease include (1) no specific treatment, that is, placebo or supportive care, (2) corticosteroids (usually prednisone or methylprednisolone), and (3) alkylating agents, such as chlorambucil or cyclophosphamide, with or without concurrent corticosteroid treatment

Treatment Recommendations[1]

The current treatment of MN relies on nonspecific antiproteinuric strategies as well as global immunosuppression. Thus, patients with persistent high-grade proteinuria and/or worsening renal function should receive steroids and cytotoxic therapy. In those patients who do not respond to therapy or who are intolerant these drugs, cyclosporine and MMF are additional options.

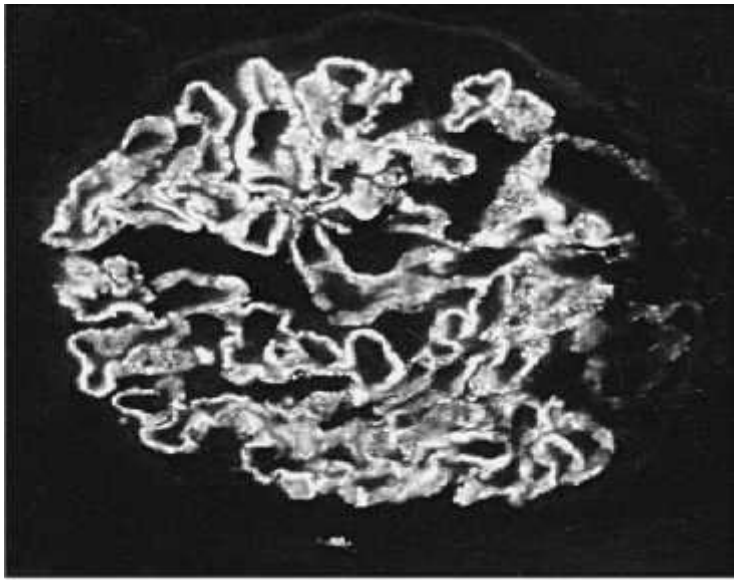


Figure No. 5: Immunofluorescence micrograph showing global granular capillary wall staining for IgG in a glomerulus with membranous glomerulopathy. (FITC anti-IgG, ×300.)

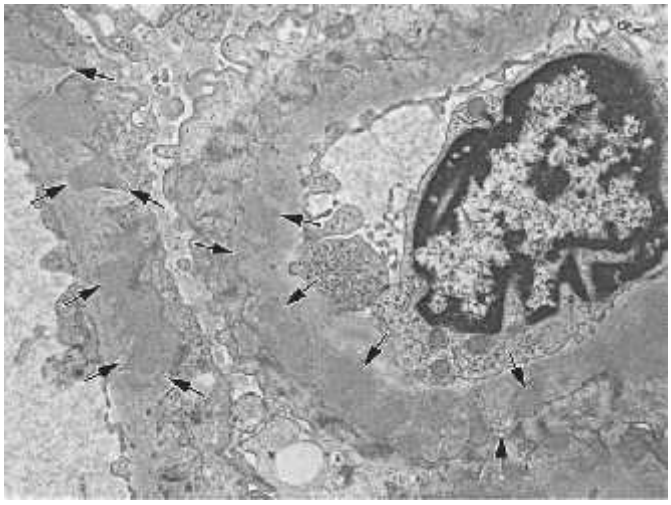


Figure No. 6: Electron micrograph of stage II membranous glomerulopathy with numerous subepithelial dense deposits (straight arrows) and adjacent projections of basement membrane material (curved arrows)

Membranoproliferative Glomerulonephritis

The term membranoproliferative glomerulonephritis (MPGN), or mesangiocapillary glomerulonephritis , refers to the histopathologic entity characterized by (a) intense glomerular hypercellularity, accompanied by increase of mesangial matrix.[54,55] (b) thickening of the peripheral capillary walls by subendothelial deposits (type I) or dense intramembranous deposits (type II) and (c) mesangial interposition into the capillary walls with apparent splitting of the glomerular basement membrane (GBM).[54,55] On the basis of capillary wall lesions, MPGN is subtyped in to types I, II and type III.[1]

The majority of patients with MPGN are children between the ages of 8 and 16 years. MPGN exhibits a distinctive laboratory feature that is unique among the primary glomerular diseases. Reduction of serum C3 in 60% to 70% of cases, and, more rarely, of C4 at time of diagnosis. Adults and children have similar complement profiles.

Histopathology[18]

Type I Membranoproliferative Glomerulonephritis

Light Microscopy (Figure No. 7)

The most common histologic features of type I MPGN are diffuse global capillary wall thickening and endocapillary hypercellularity. Infiltrating mononuclear leukocytes and neutrophils also contribute to the glomerular hypercellularity.

Immunofluorescence Microscopy (Figure No. 8)

The characteristic pattern of staining is peripheral granular to band-like staining for complement, especially C3, and usually immunoglobulins. The staining pattern is less granular and less symmetrical than that usually seen with membranous glomerulopathy. Most specimens have more intense staining for C3 than for any immunoglobulin,

Electron Microscopy

The ultrastructural hallmark of type I MPGN is mesangial interposition into an expanded subendothelial zone that contains electron dense immune complex deposits

Type II Membranoproliferative Glomerulonephritis

An alternative term for type II MPGN is dense deposit disease. This term emphasizes the pathognomonic feature of type II MPGN, which is the development of discontinuous electron dense bands within glomerular basement membranes. These are accompanied by spherical to irregular mesangial dense deposits, and occasional subendothelial and subepithelial deposits, Immunofluorescence microscopy demonstrates intense capillary wall linear to band-like staining for C3, with little or no staining for immunoglobulin.

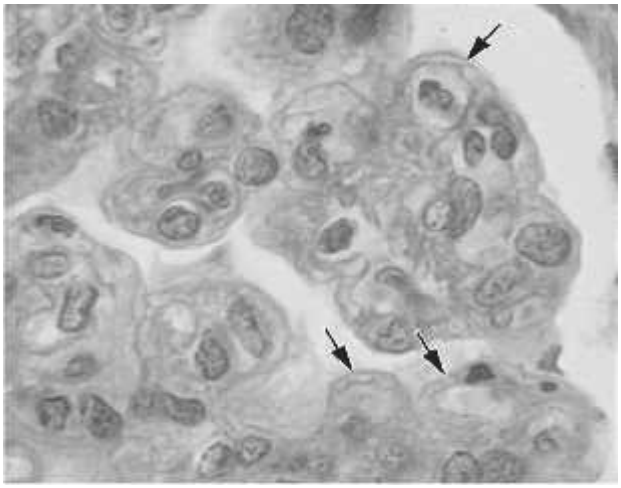


Figure No. 7: Light micrograph of a glomerular segment from a patient with type I membranoproliferative glomerulonephritis (MPGN) demonstrating doubling (arrows) and more complex replication of glomerular basement membranes. (Periodic acid-Schiff [PAS], ×1000.)

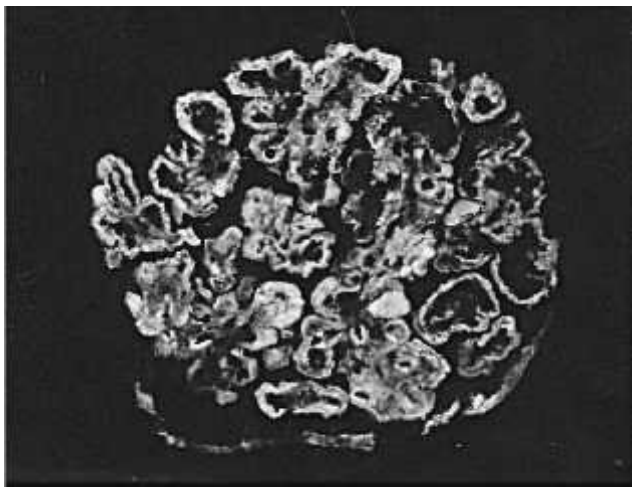


Figure No. 8: Immunofluorescence micrograph of a glomerulus with type I MPGN showing global bandlike capillary wall staining for C3, as well as irregular mesangial staining. (FITC anti-C3, ×300.)

Treatment

In general, one third of patients with type I MPGN will have a spontaneous remission, one third will have progressive disease, and one third will have a disease process that will wax and wane but never completely disappear. [1] The management of type I MPGN is based on the underlying cause of the disease process. Thus, the therapy for MPGN associated with cryoglobulinemia and hepatitis C should be aimed at treating hepatitis C virus infection; whereas, the management of MPGN associated with lupus or with scleroderma should be based on the principles of care of those rheumatological conditions.

From available data three main lines of treatment in idiopathic MPGN, depending on clinical presentation: [1]

- Children with preserved renal function should be given a long-term, alternate-day corticosteroid treatment (a period of 6 to 12 months)

- Adults with proteinuria and reduced GFR, could be treated with a combination of aspirin and dipyridamole. Patients with low proteinuria and normal renal function do not need any treatment, except diet and ACEI [angiotensin-converting enzyme inhibitors].

- In patients with rapidly progressive renal failure or a recent sharp reduction in renal function, aggressive treatment with methylprednisolone pulse therapy followed by oral prednisone plus oral cyclophosphamide is an appropriate therapeutic approach, especially if crescents are present on histologic investigation.

IgA Nephropathy

IgA nephropathy remains one of, if not the most common glomerular lesion of all of the forms of glomerulonephritis. Patients were described based on the finding of predominant IgA deposition in the mesangium with a mesangial proliferation, and with clinical features that span the spectrum from asymptomatic hematuria to rapidly progressive glomerulonephritis.

IgA nephropathy occurs in the second and third decade of life, and it is much more common in males than females. IgA nephropathy is uncommon in children under 10 years of age. The distribution of IgA nephropathy varies in different geographic regions throughout the world.[56] It is the most common form of primary glomerular disease in Asia, accounting for up to 30% to 40% of all biopsies, 20% in Europe, and 10% of all biopsies performed for glomerular disease in North America. Approximately one third of patients with IgA nephropathy present with macroscopic hematuria, one third present with microscopic hematuria (with or without proteinuria) and the final one third of patients have a variety of presentations, including the nephrotic syndrome or chronic glomerular disease. The episodes tend to occur with a close temporal relationship to upper respiratory infection, including tonsillitis or pharyngitis. This synchronous association of pharyngitis and macroscopic hematuria has been given the name “synpharyngitic” nephritis. The angiotensin converting enzyme inhibitors have been demonstrated to be beneficial in IgA in reducing proteinuria, even in normotensive patients with IgA nephropathy. An array of studies, of varying quality, have examined combinations of immunosuppressive agents for

treatment of IgA nephropathy. Results to this point have not been sufficiently clearcut to routinely recommend such an approach.[1]

Histopathology

Immunofluorescence Microscopy[18] (Figure No. 9)

IgA nephropathy can only be definitively diagnosed by the immunohistologic demonstration of glomerular immune deposits that stain dominantly or co-dominantly for IgA compared to staining for IgG and IgM.[57] By definition, 100% of IgA nephropathy specimens stain for IgA. Electron microscopy shows the mesangial deposits often immediately beneath the perimesangial basement membrane. They are accompanied by varying degrees of mesangial matrix expansion and hypercellularity.[18]

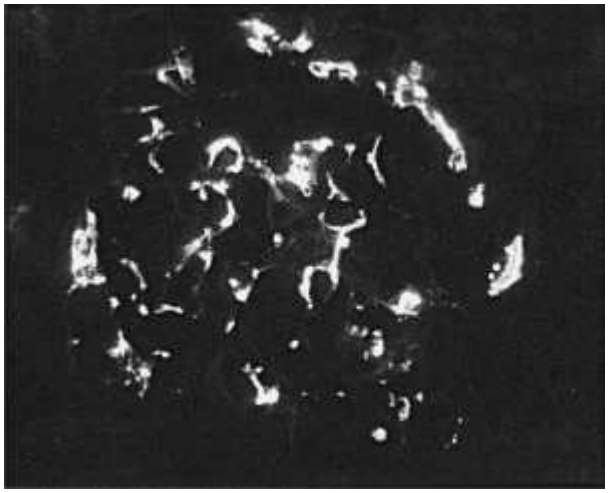


Figure No. 9: Immunofluorescence micrograph of a glomerulus with IgA nephropathy showing intense mesangial staining for IgA.

(FITC anti-IgA, ×300.)[18]

SYSTEMIC LUPUS ERYTHEMATOSUS

Lupus nephritis (LN) is a frequent and potentially serious complication of systemic lupus erythematosus (SLE). Females greatly outnumber males by 8-13:1.[58,59] However, males with SLE have the same incidence of renal disease as do females.[58,59] 85% of patients are younger than 55 years of age..

Class III, focal proliferative LN, is often associated with active lupus serologies. Hypertension and active urinary sediment are commonly present. Proteinuria is often more than 1 g daily, and as many as one quarter to one third of patients with focal LN will have the nephrotic syndrome at presentation.[18]

Patients with Class IV, diffuse proliferative disease, typically presents with the most active and severe clinical features. These patients often have high anti-DNA antibody titers, low serum complement levels, and very active urinary sediment, with erythrocytes, red cell, and other casts on urinalysis.[59] Virtually all have proteinuria and as many as half of the patients will have the nephrotic syndrome. Likewise, hypertension and renal dysfunction are typical, and even when the serum creatinine appears normal, the GFR is usually depressed.[18]

Patients with lupus membranous nephropathy, Class V, typically present with proteinuria, edema, and other manifestations of the nephrotic syndrome.[59]

Modified World Health Organization (WHO) morphologic classification of lupus nephritis[a]

CLASS I Normal glomeruli

a. Nil (by all techniques)
b. Normal by light microscopy, but deposits by electron or immunofluorescence microscopy

CLASS II (12%- 25%) Pure mesangial alterations (mesangiopathy)

a. Mesangial widening and/or mild hypercellularity (+)
b. Moderate hypercellularity (++)

CLASS III (16%- 22%) Focal segmental glomerulonephritis (associated with mild or moderate mesangial alterations)

a. With active necrotizing lesions
b. With active and sclerosing lesions
c. With sclerosing lesions

CLASS IV (37%- 46%) Diffuse glomerulonephritis (severe mesangial, endocapillary or mesangiocapillary proliferation and/or extensive subendothelial deposits)

a. Without segmental lesions
b. With active necrotizing lesions
c. With active and sclerosing lesions
d. With sclerosing lesions

CLASS V (11%- 21%) Diffuse membranous glomerulonephritis

a. Pure membranous glomerulonephritis
b. Associated with lesions of class II
c. Associated with lesions of class III
d. Associated with lesions of class IV

CLASS VI (3%- 4%) Advanced sclerosing glomerulonephritis

[a]Percentages under each WHO class represent frequency of biopsy results in various genes of systemic lupus erythematosus (SLE) patients in which biopsies were systematically performed

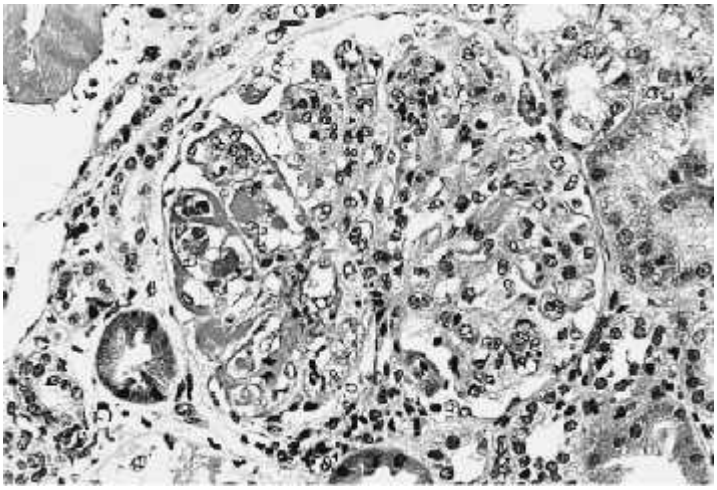


Figure No. 10: Lupus nephritis class IV: There is global endocapillary proliferation with infiltrating neutrophils and segmental wire loop deposits (Hematoxylin-eosin, ×320).

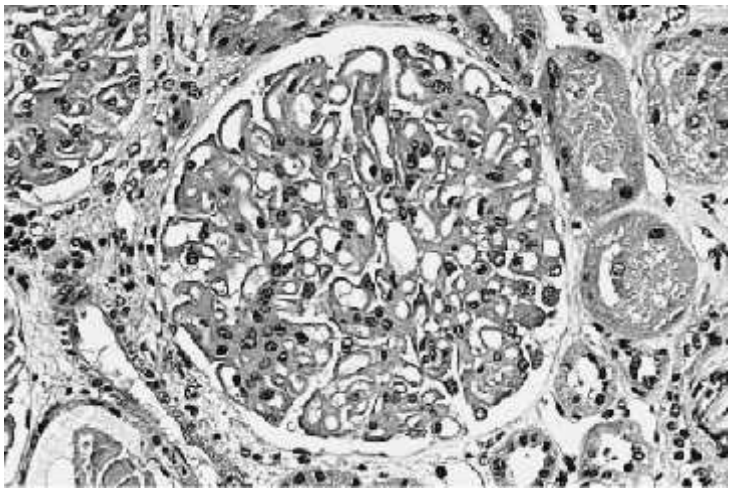


Figure No. 11: Lupus nephritis class V: There is diffuse uniform thickening of glomerular basement membranes accompanied by mild segmental mesangial hypercellularity (Hematoxylin-eosin, ×320).

Pathogenesis

Although numerous immunologic abnormalities have been noted in patients with SLE, it is unclear which factors are directly related to the pathogenesis of the disease itself. SLE is a disease in which abnormalities of immune regulation lead to a loss of self-tolerance and subsequent autoimmune responses. The formation of circulating immune complexes and their deposition with complement activation is important for certain patterns of glomerular damage.[18] Glomerular involvement in SLE has often been considered a human prototype of classic chronic immune complex-induced glomerulonephritis

Management

Patients with Class I and Class II biopsies have an excellent renal prognosis and need no therapy directed at the kidney. Patients with only mild or moderate proliferative lesions involving a few glomeruli, with no necrotizing features and no crescent formation, have a good prognosis and will often respond to a short course of high-dose corticosteroid therapy. Patients with severe segmental lesions and with necrotizing features and crescent formation usually require more vigorous therapy similar to patients with diffuse proliferative LN.

Patients with diffuse proliferative disease, Class IV lesions, require aggressive treatment to avoid irreversible renal damage and progression to ESRD.[59] The precise form of immunosuppressive regimen may include high-dose daily or alternate day corticosteroids, azathioprine, intravenous pulse methylprednisolone, oral or intravenous cyclophosphamide, cyclosporine, mycophenolate mofetil, and rituximab.

AMYLOIDOSIS

Amyloidosis comprises a diverse group of systemic and local diseases characterized by the extracellular deposition of fibrils in various organs. Kidneys are the most common major organ involved by AL amyloid. In patients over the age of 60 years old, as many as 10% to 20% of patients with presumed idiopathic nephrotic syndrome will have amyloidosis on renal biopsy.[60] Multiple myeloma occurs in up to 20% of primary amyloidosis cases.

A Study [61] included 13 cases of renal amyloidosis, oedema of feet and face was the commonest manifestation (100%), two patients (18.18%) also presented with loose motions, ascites and pain in abdomen and one patient had ankylosing spondylitis and cervical spondylitis. About 72.72% cases had some chronic disease in the terms of tuberculosis, ankylosing spondylitis, chronic ulcerative colitis, lepromatous leprosy, rheumatoid arthritis and one patient had carcinoma caecum. Hypertension is found in 20% to 50% of patients [18]

Pathology (Figure No. 12)

By LM there is a glomerular deposition of amorphous hyaline material that usually begins in the mesangium and extends into the peripheral capillary walls. This material is eosinophilic, weakly PAS positive, and non argyrophilic. Congo red stain gives an orange staining reaction and the diagnostic apple green birefringence under polarized light.

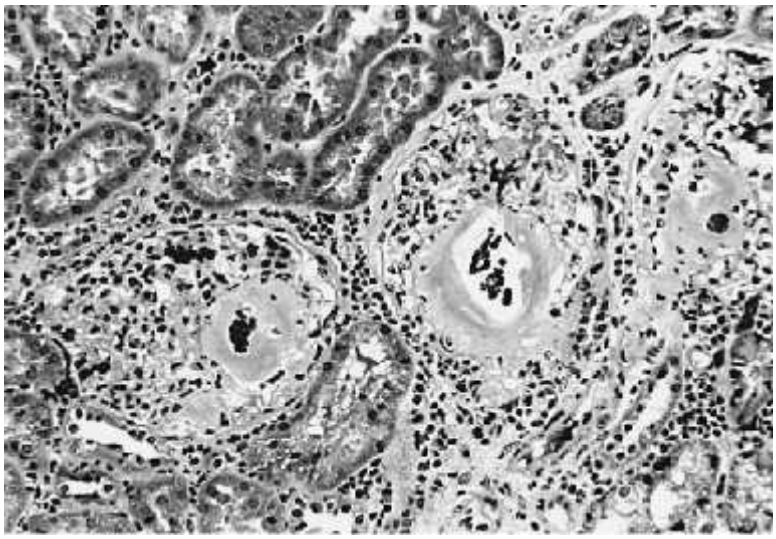


Figure No. 12: Amyloidosis: The glomerular tuft contains segmental deposits of amorphous eosinophilic hyaline material involving the vascular pole and some mesangial regions (Hematoxylin-eosin, ×375).

Treatment

The baseline serum creatinine at diagnosis and the degree of proteinuria are predictive of the progression to ESRD. The median time from diagnosis to onset dialysis is 14 months, and from dialysis to death only 8 months in some series.[62]

A number of treatment strategies using chemotherapeutic drugs such as melphalan and prednisone, cyclophosphamide, or VAD therapy and Colchicine are used to manage AL amyloidosis. Most trials have demonstrated a clear benefit of chemotherapeutic options over colchicine, and even the addition of colchicine to these regimens provided only a small benefit.[63]

Recent reports using high-dose melphalan followed by allogeneic bone marrow transplant or stem cell transplant have given promising results.[63]

METHODOLOGY

The present study was conducted in the Department of Nephrology and Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on patients, clinically diagnosed to have adult onset nephrotic syndrome during the period of January 2007 to December 2007.

Study design

The present one year cross sectional study was conducted on patients, clinically diagnosed to have adult onset nephrotic syndrome.

Study period and duration

The present one year study was conducted during the period of January 2007 to December 2007.

Method of collection of data

Source of Data

All patients admitted in the Department of nephrology and Medicine of KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum who were clinically diagnosed to have adult onset nephrotic syndrome were enrolled in the study.

Sample size

Thirty patients clinically diagnosed to have adult onset nephrotic syndrome were selected for the study.

Sampling procedure

80% of average number of similar cases reported to KLES Dr. Prabhakar Kore Hospital Belgaum, over a period of five years were considered to calculate the sample size. The sample size required was calculated to be of 30 subjects.

Selection criteria

Inclusion Criteria

- All clinically diagnosed adults with nephrotic syndrome.

Exclusion Criteria

- Acute nephritic syndrome
- Patients less than 18 years

Procedure

Patients admitted in the wards of department of Nephrology and Medicine at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum , were evaluated and selected by detailed medical history and physical examination. The study was approved by the Ethical and Research Committee of J. N. Medical College, Belgaum.

After finding the suitability as per inclusion and exclusion criteria, the patients were selected for the study and briefed about the nature of the study, the interventions used and written informed consent was obtained (Annexure–I).

Data was collected and recorded on predesigned and pretested proforma (Annexure-II) by relevant history, clinical examination, relevant biochemical investigation and renal biopsy (done under ultra sound guidance).

Investigations done

- Complete blood count.
- Urine-routine and microscopy.
- 24 hours urinary protein.
- Serum protein and serum albumin.
- Blood urea and serum creatinine.
- Fasting lipid profile.
- Anti nuclear antibody and C3 levels as and when required
- Renal biopsy.

Renal biopsy

In all patients in whom a percutaneous renal biopsy was performed platelet count, prothrombin time (or INR), partial thromboplastin time and Blood Group was established before the procedure was undertaken.

Procedure

Biopsies were performed under the guidance of ultrasonography to permit more accurate localization of the kidney. Biopsy of the lower pole of the left kidney was done. Patients lie on their abdomen (prone position). The entry site was marked, area was cleaned with antiseptic agents, and a local anaesthetic agent was injected. The spring-loaded Biopsy Gun (Biopty, Bard Urological

Division, C.R. Bard, Covington, GA, the long-throw device has a depth of 2.2 cm, yielding a specimen with a potential length of up to 1.8 cm) was inserted through the entry site which was marked. After making the entry of the tip of the needle in to the cortex of the kidney, gun was shot and tissue core was collected in media meant for transport.

After completion of the biopsy, patients were instructed to remain at bed rest for 18 to 24 hours. Blood pressure and pulse were monitored frequently. The patient was asked to save an aliquot of each voided urine in a separate clear-plastic specimen jar labeled with the date and time, which was kept at the patient's bedside for inspection. This provides a visual check for evidence of bleeding into the intrarenal collecting system. Hematocrits were determined six to eight hours after the biopsy and again at 18 to 24 hours, or earlier, if hypotension or gross hematuria was observed.

Statistical analysis

The results were tabulated and the data was analysed using rates, ratios and percentages of different clinical manifestations, biochemical parameters and histopathological diagnosis.

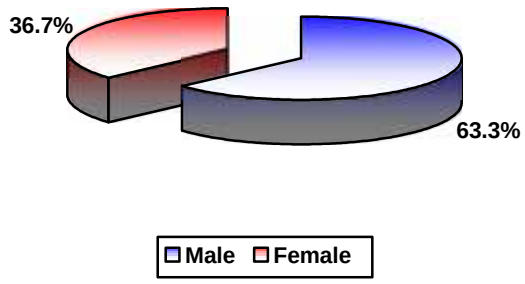
RESULTS

The present one year cross sectional study was conducted in the Department of Medicine and Nephrology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum, on patients clinically diagnosed to have adult onset nephrotic syndrome during January 2007 to December 2007. Finally the data obtained was systematically tabulated as below.

Table No. 1: Sex distribution of patients

Gender	Number of patients	
	Number	Percentage
Male	19	63.30%
Female	11	36.70%
Total	30	100.0%

Graph No. 1: Sex Distribution of patients

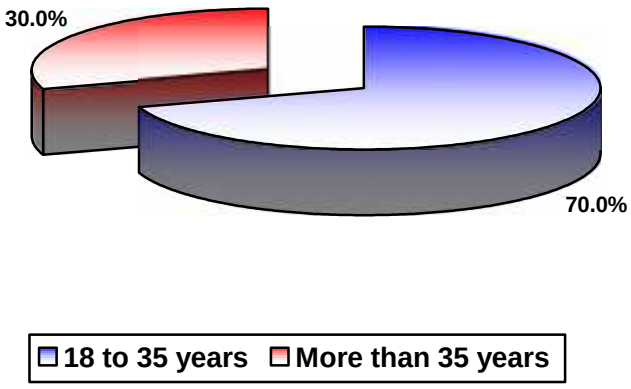


In the present study 30 patients were studied. In this males outnumbered the females. Total number of males were 19 (63.33%) and females were 11 (36.66%). The male to female ratio is 1.72:1

Table No. 2: Age distribution of patients

Age group (In years)	Number of patients	
	Number	**Percentage**
18 to 35	21	70.0%
More than 35	09	30.0%
Total	30	100.0%

Graph No. 2: Age distribution of patients

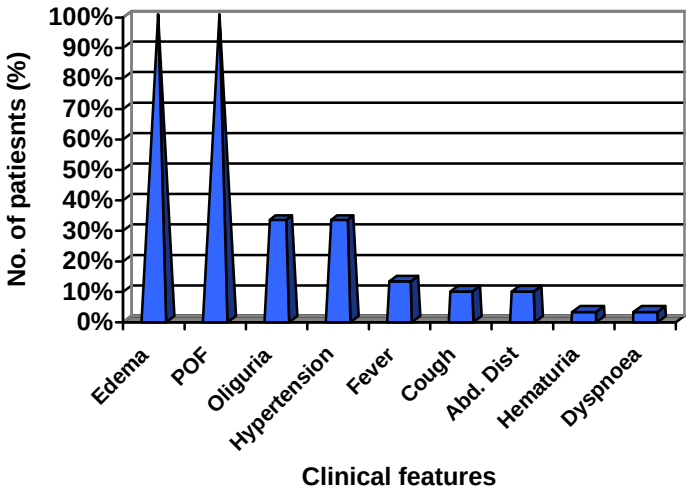


Out of 30 patients studied 70% of subjects were less than 35 years of age and 30% had age more than 35 years. The mean age of presentation was 31.1 years, with a range from 18 to 60 years.

Table No. 3: Distribution of clinical features

Clinical features	Number of patients (n=30)	
	Number	Percentage
Edema	30	100.00%
Puffiness Of Face	30	100.00%
Oliguria	10	33.33%
Hypertension	10	33.33%
Fever	04	13.33%
Cough	03	10.00%
Abdominal distension	03	10.00%
Hematuria	01	3.33%
Dyspnoea	01	3.33%

Graph No. 3:Distribution of clinical features



The commonest clinical presentations were pedal oedema (100%), POF (100%) and oliguria (33.33%) and the average duration of symptoms was three months.

Table No. 4: Biochemical parameters – Proteinuria and serum albumin

Biochemical parameters		Number of patients		Mean values
		Number	Percentage	
Proteinuria* (gms/day)	**2 to 5**	19	63.33%	4.7
	5 to 8	09	30.00%	
	> 8	02	6.67%	
	Total	30	100.0%	
Serum albumin (gms/dL)	**< 1.5**	19	63.33%	1.40
	1.5 to 2.5	09	30.00%	
	2.5 to 3.5	02	6.66%	
	Total	30	100.00%	

*Proteinuria of more than 3.5 gm/1.73 m^2 or 50 mg/kg/day

All subjects studied had 24 hour proteinuria of nephrotic range and serum albumin less than 3.5 mg/dL. The mean 24 hours proteinuria was 4.7 gm/day (range 2-15 gms/day) and the mean serum albumin levels were 1.4 gm/dL.

Table No. 5: Biochemical parameters – Blood urea and serum creatinine

Biochemical parameters		Number of patients		Mean values
		Number	Percentage	
Blood urea (mg/dL)	**< 40**	25	83.40%	27.63
	> 40	5	16.60%	
	Total	30	100.00%	
Serum creatinine	**> 1.3**	05	16.60%	1.10
	< 1.3	25	83.40%	
	Total	30	100.00%	

The mean blood urea and serum creatinine were 27.63 mg/dL and 1.1 mg/dL respectively. 5 (16.6%) subjects had elevated urea and creatinine levels.

Table No. 6: Lipid profile

Lipid Profile*		Number of patients		Mean (mg/dL)
		Number	Percentage	
Total cholesterol (mg/dL)	**> 200**	22	72.66%	240
	< 200	08	27.34%	
	Total	30	100.00%	
Triglycerides (mg/dL)	**> 150**	20	66.66%	170
	< 150	10	33.34%	
	Total	30	100.00%	
LDL cholesterol (mg/dL)	**<130**	06	20.00%	176
	> 130	24	80.00%	
	Total	30	100.00%	
HDL cholesterol (mg/dL)	**< 40**	30	100.00%	30
	> 40	00	0.00%	
	Total	30	100.00%	

* According to American Heart Association Guidelines

In the present study mean total cholesterol was 240 mg/dL and out of 30 patients 22 patients had total cholesterol levels more than 200 mg/dL. The mean triglyceride levels were 170 mg/dL and 20 patients had more than 150 mg/dL. The mean LDL cholesterol was 176 mg/dL and 24 patients had more than 130 mg/dL. Mean HDL cholesterol was 30 mg/dL and in all the 30 patients it was more than 40 mg/dL.

Table No. 7: Urine albumin

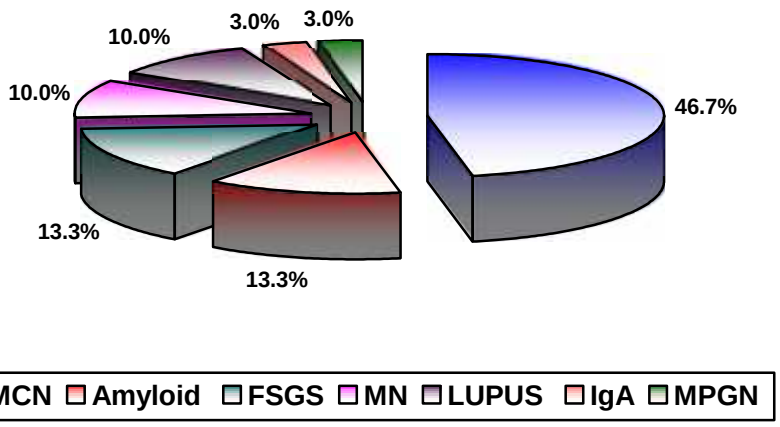
Urine albumin	Number of patients	
	Number	**Percentage**
+2	12	40.00%
+3	12	40.00%
+4	06	20.00%
Total	30	100.00%

In the present study all the patients had urine albumin more than or equal to 2+. Out of 30 patients, 12 (40%) patients had urine albumin 2+, 12 patients had urine albumin 3+ and six patients (20%) had urine albumin 4+.

Table No. 8: Histopathology

Histopathology	Male (n=19)		Female (n=11)		Total (n=30)	
	No.	%	No.	%	No.	%
MCN	09	64.0%	05	36.0%	14	46.66%
AMYLOID	03	75.0%	01	25.0%	04	13.33%
FSGS	03	75.0%	01	25.0%	04	13.33%
MN	02	66.6%	01	33.4%	03	10.00%
Lupus nephritis	00	0.0%	03	100.0%	03	10.00%
IgA	01	100.0%	00	0.0%	01	3.00%
MPGN	01	100.0%	00	0.0%	01	3.00%

Graph No. 4: Histopathology

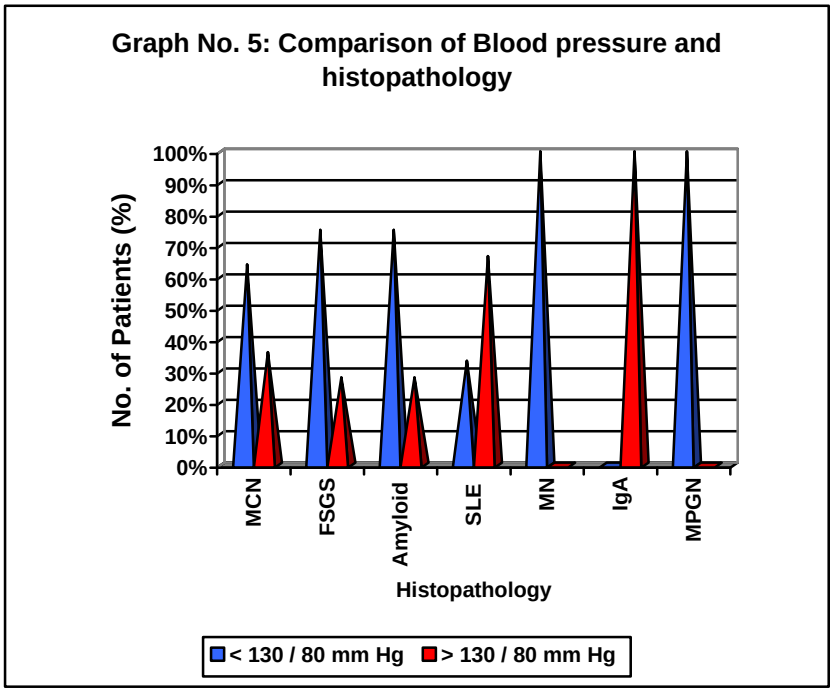


Out of 30 study patients, the predominant histopathological variety was MCN, which accounted for 46.6%. FSG and amyloid accounted for 13.3% each, SLE and MN were 10% each and IgA and MPGN were 3.0% each.

Table No. 9: Comparison of blood pressure and histopathology

Histopathology	Blood Pressure*			
	BP < 130 / 80 mm of Hg		BP > 130 / 80 mm of Hg	
	Number	Percentage	Number	Percentage
MCN	09	64.0%	05	36.0%
FSGS	03	75.0%	01	25.0%
AMYLOID	03	75.0%	01	25.0%
SLE	01	33.3%	02	66.6%
MN	03	100.0%	00	0.0%
IgA	00	0.00%	01	100.0%
MPGN	01	100.0%	00	0.0%

* According to JNC-7 guidelines

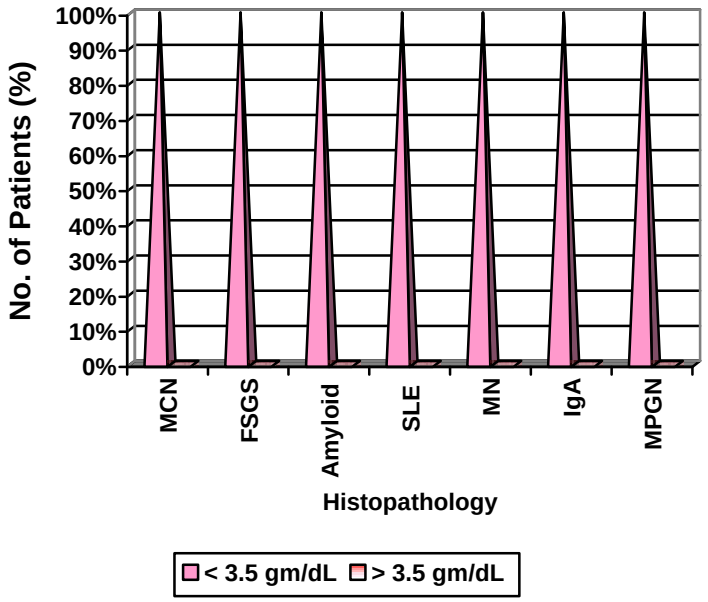


Out of 30 patients, 10 (33.33%) had hypertension. 23% of males and 45% of females were found to have hypertension. 36% of MCN patients, 66% of SLE and 25% of FSGS patients had hypertension.

Table No. 10: Comparison of serum albumin and histopathology

Histopathology	< 3.5 gm/dL		> 3.5 gm/dL	
	Number	Percentage	Number	Percentage
MCN	14	100.00%	00	0.00%
FSGS	04	100.00%	00	0.00%
AMYLOID	04	100.00%	00	0.00%
SLE	03	100.00%	00	0.00%
MN	03	100.00%	00	0.00%
IgA	01	100.00%	00	0.00%
MPGN	01	100.00%	00	0.00%

Graph No. 6: Comparison of serum albumin and histopathology



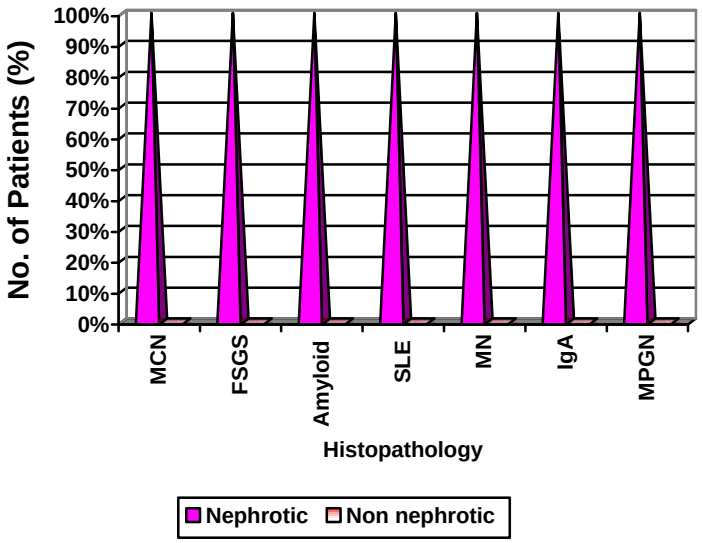
In the present study all the patients had decreased serum albumin. The mean serum albumin was 1.4 gm/dL. The mean serum albumin in different histopathological patients was similar. No much difference is seen between different histopathological variants.

Table No. 11: Comparison of proteinuria and histopathology

Histopathology	Nephrotic range*		Non nephrotic range	
	Number	Percentage	Number	Percentage
MCN	14	100.0%	00	0.00%
FSGS	04	100.0%	00	0.00%
AMYLOID	04	100.0%	00	0.00%
SLE	03	100.0%	00	0.00%
MN	03	100.0%	00	0.00%
IgA	01	100.0%	00	0.00%
MPGN	01	100.0%	00	0.00%

*Proteinuria more than 3.5 gm/1.73m^2/day or 50 mg/kg/day

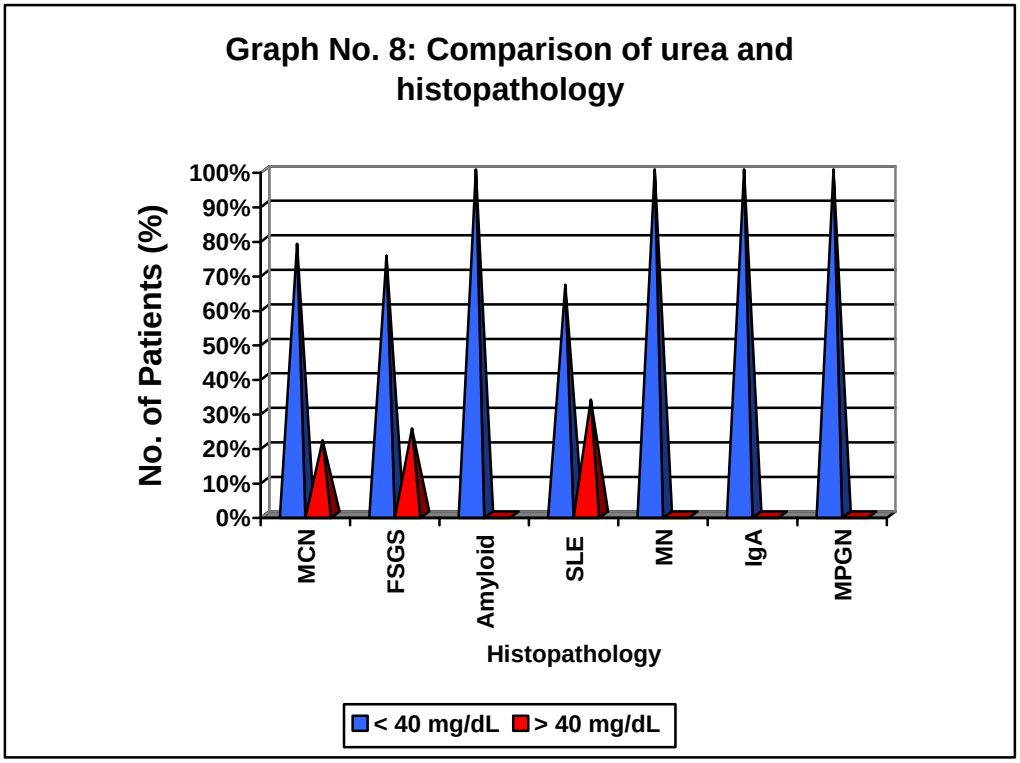
Graph No. 7: Comparison of proteinuria and histopathology



In the present study all 30 patients (100%) had urinary protein excretion in nephrotic range.

Table No. 12: Comparison of urea and histopathology

Histopathology	< 40 mg/dL		> 40 mg/dL	
	Number	Percentage	Number	Percentage
MCN	11	78.5%	03	21.5%
FSGS	03	75.0%	01	25.0%
AMYLOID	04	100.0%	00	0.0%
SLE	02	66.6%	01	33.3%
MN	03	100.0%	00	0.0%
IgA	01	100.0%	00	0.0%
MPGN	01	100.0%	00	0.0%

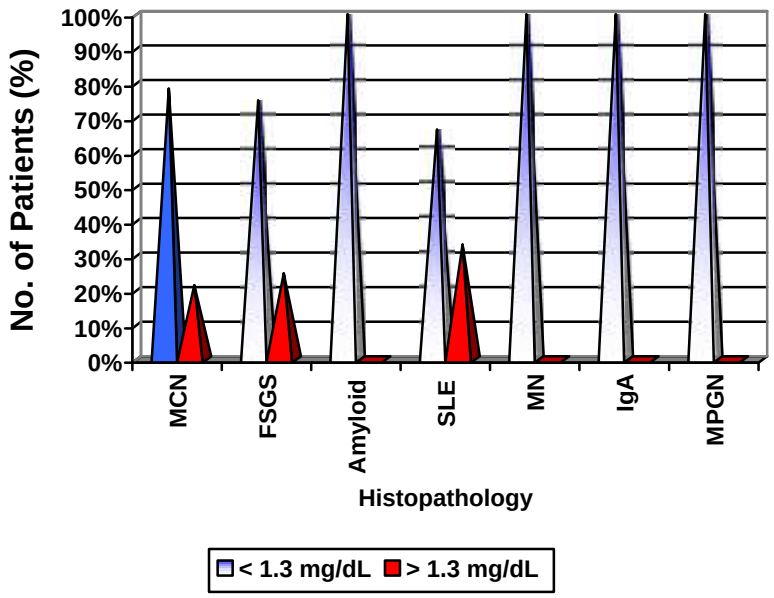


Out of 30 patients five (16.6%) patients had elevated urea levels. 21.5% of MCN, 33% of SLE and 25% of FSGS patients had elevated urea levels.

Table No. 13: Comparison of serum creatinine and histopathology

Histopathology	< 1.3 mg/dL		> 1.3 mg/dL	
	Number	Percentage	Number	Percentage
MCN	11	78.5%	03	21.5%
FSGS	03	75.0%	01	25%
AMYLOID	04	100%	00	0.0%
SLE	02	66.6%	01	33.3%
MN	03	100.0%	00	0.0%
IgA	01	100.0%	00	0.0%
MPGN	01	100.0%	00	0.0%

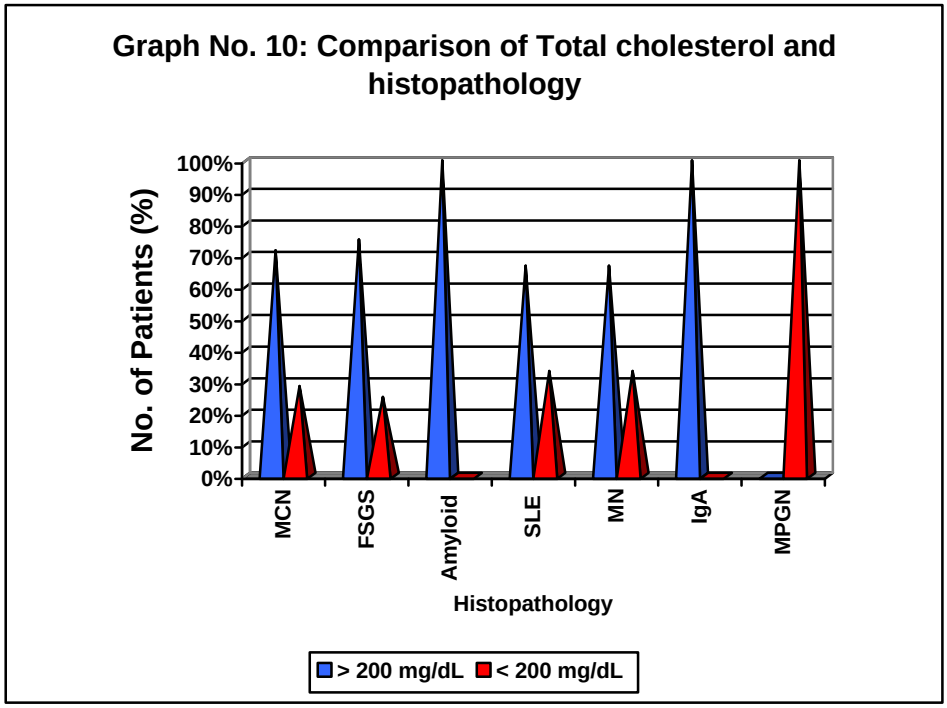
Graph No. 9: Comparison of serum creatinine and histopathology



In the present study out of 30 patients five (16.6%) had elevated creatinine levels. 21.5% MCN, 33% of SLE and 25% of FSGS patients had elevated creatinine levels.

Table No. 14: Comparison of total cholesterol and histopathology

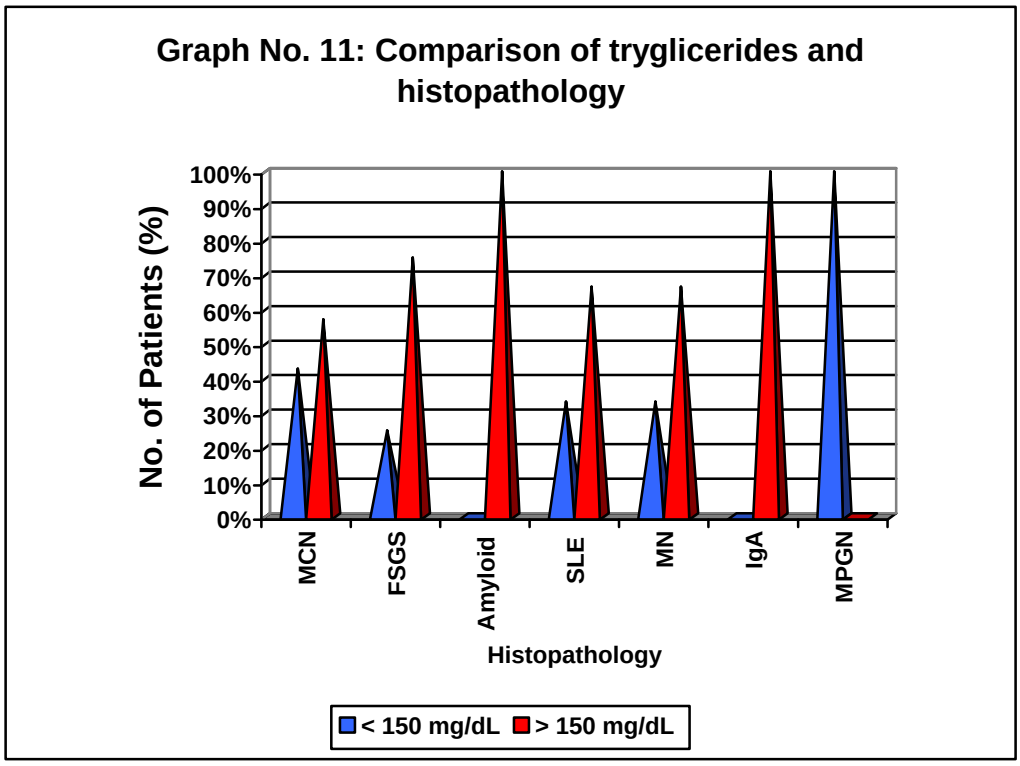
Histopathology	> 200 mg/dL		< 200 mg/dL	
	Number	**Percentage**	**Number**	**Percentage**
MCN	10	71.48%	04	28.5%
FSGS	03	75.0%	01	25.0%
AMYLOID	04	100.0%	00	0.0%
SLE	02	66.6%	01	33.3%
MN	02	66.6%	01	33.3%
IgA	01	100.0%	00	0.0%
MPGN	00	0.00%	01	100.0%



A total of 22 (75%) patients had high cholesterol levels. 100% of amyloid, 75% of FSGS, 71.48% of MCN, 66.6% of SLE and 66% of MCN subjects had high cholesterol levels.

Table No. 15: Comparison of triglycerides and histopathology

Histopathology	< 150 mg/dL		> 150 mg/dL	
	Number	Percentage	Number	Percentage
MCN	06	42.85%	08	57.1%
FSGS	01	25.0%	03	75.0%
AMYLOID	00	0.00%	04	100.0%
SLE	01	33.3%	02	66.6%
MN	01	33.3%	02	66.6%
IgA	00	0.00%	01	100.0%
MPGN	01	100.0%	00	0.00%

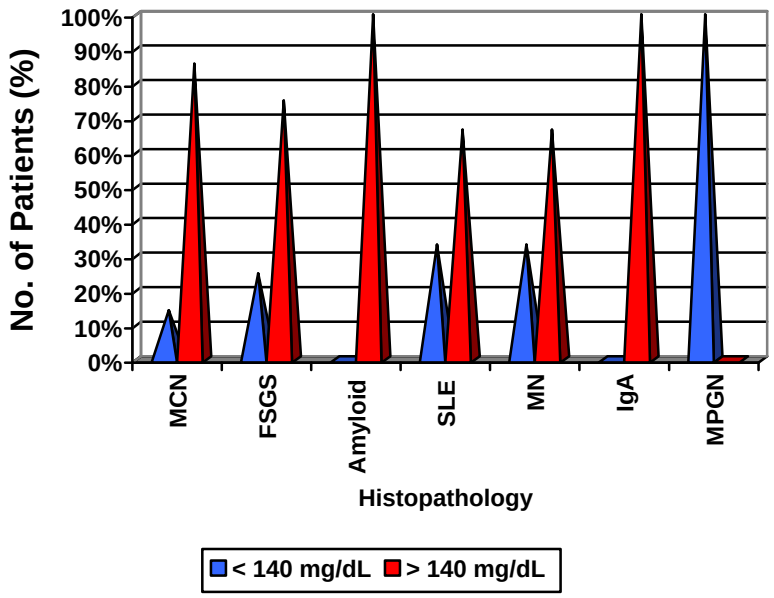


A total 20 (66.7%) patients had high triglyceride levels. 100% of amyloid, 75% of FSGS, 57% of MCN, 66.6% of SLE and 66% MN patients had elevated TG levels.

Table No. 16: Comparison of LDL cholesterol and histopathology

Histopathology	< 140 mg/dL		> 140 mg/dL	
	Number	**Percentage**	**Number**	**Percentage**
MCN	02	14.28%	12	85.70%
FSGS	01	25.00%	03	75.00%
AMYLOID	00	0.00%	04	100.00%
SLE	01	33.30%	02	66.60%
MN	01	33.30%	02	66.60%
IgA	00	0.00%	01	100.00%
MPGN	01	100.00%	00	0.00%

Graph No. 12: Comparison of LDL cholesterol and histopathology



Out of 30 patients, 24 patients had high LDL cholesterol levels. 100% of amyloid, 75% of FSGS, 85.7% of MCN, 66.6% of SLE and 66% of MN patients had elevated LDL levels.

Table No. 17: Comparison of HDL cholesterol and histopathology

Histopathology	< 40 mg/dL		> 40 mg/dL	
	Number	**Percentage**	**Number**	**Percentage**
MCN	14	100.00%	00	0.00%
FSGS	04	100.00%	00	0.00%
AMYLOID	04	100.00%	00	0.00%
SLE	03	100.00%	00	0.00%
MN	03	100.00%	00	0.00%
IgA	01	100.00%	00	0.00%
MPGN	01	100.00%	00	0.00%

In the present study all 30 patients had low HDL levels.

Table No. 18: Comparison of urine white blood cells and histopathology

Histopathology	< 5 cells/hpf		> 5 cells/hpf	
	Number	**Percentage**	**Number**	**Percentage**
MCN	05	35.72%	09	64.28%
FSGS	00	0.00%	05	100.0%
AMYLOID	03	75.0%	01	25.00%
SLE	00	0.00%	03	100.00%
MN	01	33.3%	02	66.66%
IgA	01	100.0%	00	0.00%
MPGN	00	0.00%	01	100.0%

In the present study, out of 30 patients, 20 (66.6%) had pyuria. Among them 100% of FSGS and SLE, 71% of MCN and 66.7% of MN subjects had pyuria.

Table No. 19: Comparison of urine Red blood cells and histopathology

Histopathology	< 5 cells/hpf		> 5 cells/hpf	
	Number	**Percentage**	**Number**	**Percentage**
MCN	10	71.40%	04	28.60%
FSGS	02	50.00%	02	50.00%
AMYLOID	03	75.00%	01	25.00%
SLE	02	66.66%	01	33.33%
MN	01	33.33%	02	66.66%
IgA	01	100.00%	00	00.00%
MPGN	01	100.00%	00	00.00%

Ten (33.3%) patients had microscopic hematuria. Among them 29% of MCN, 50% of FSGS and 66.6% of MN subjects were found to have microscopic hematuria.

DISCUSSION

Adult nephrotic syndrome is a clinical syndrome secondary to different glomerular disorder. Different studies from India and other countries show differences in prevalence of histopathology. The present study helps to evaluate various histopathological variety causing nephrotic syndrome in adults in south India.

A total of 30 subjects were studied and were divided into different groups as per their histological diagnosis. The seven groups with the histopathological diagnosis were MCN (46.66%), FSGS (13.33%), Amyloid (13.33%), MN (10%), SLE (10%), MPGN (3.33%) and IgA (3.33%).

The majority (63.33%) of the subjects were males. The male to female ratio is 1.72:1. This was almost similar to the studies done by Reshi AR et al (2:1),[15] Kazi JI et al (1.7:1),[64] and Panichvi et al (1.5:1).[65] The probable reason for male preponderance is that male patients are more frequently affected by nephrotic syndrome as reported in literature[1] and also males are more frequent visitors to hospital than females due to socio-economic reason.

In the present study population the mean age was 31.1 years, there was no significant statistical difference in the mean age among the different histopathological variants making them comparable. This is comparable to that of other studies as Sharma BK et al[66] in their study found the mean age to be 33.4 years, Kazi JI et al (29 years)[64] and Malafronate et al (34 years).[67]

The commonest presentation among these groups was pedal edema, puffiness of face and oliguria, and the average duration of symptoms were three months (range one to five months). All study subjects had proteinuria in nephrotic range and serum albumin less than 3.5 gms/dl. The mean proteinuria was 4.7 gms/day and mean serum albumin was 1.4 gms/dl. All 30 (100%) subjects had urine albumin more than or equal to 2+. This is similar to the studies done by Prakash C et al.[68] The mean proteinuria and mean serum albumin in different histological variants were similar and no correlation was found among the various histopathological variants. However one subject in the MCN group had more protienuria (15 grams/day) which has been documented in other studies also.

The Total cholesterol, Triglycerides, LDL cholesterol and HDL cholesterol were 240 mg/dl, 170 mg/dl, 176 mg/dl and 30 mg/dl respectively. These results are consistent with the study done by Khanna UB et al.[69] Majority of subjects in all histopathological variants had high TC, TG, LDL levels and all subjects had low HDL levels, being consistent with the diagnosis of nephrotic syndrome.

The mean blood urea and creatinine were 27.63 mg/dl and 1.1 mg/dl. Only five of the study subjects had raised renal functions. The probable reason for most patients having normal creatinine is that majority of our study subjects were histopathologically having MCN which usually has normal renal functions. One patient (25.0%) of FSGS and one patient (33.3%) of SLE had high renal functions, however the number of subjects in each these groups were limited, hence it is difficult to draw conclusions.

There were 10 (33.33%) subjects who had microscopic haematuria of which majority were MCN (40%) followed by FSGS (20%) and MN (20%). This was in consistent with results as published by K. Sud et al,[70] in their study they found 37% of the subjects having microscopic haematuria. Even though microscopic haematuria is more common in MPGN, FSGS and Lupus Nephritis, since our study had more MCNS subjects, it is difficult to draw the incidence of microscopic haematuria in above mentioned groups.

There were 10 (33.33%) subjects who had hypertension of which 50% were MCN, 20% were SLE and 10% were FSGS. This is similar to the studies done by K. Sud et al,[70] in their study found 32.4% of the subjects having hypertension. Even though hypertension is more common in MPGN, FSGS and Lupus Nephritis, since our study had more MCNS subjects, it is difficult to draw the incidence of hypertension in above mentioned groups.

In this study, primary glomerular disease was the predominant cause of nephrotic syndrome and accounted for 76.6% of all biopsies. This is similar to studies done by Narasimhan et al (71%),[14] Panichvi V et al (70%)[65] and Kazi JI et al (80%).[64] Among primary glomerular disease minimal change disease was the most common histological lesion, accounted for 46.6% of all biopsies and 60% of primary glomerular disease, followed by FSGS accounted for 13% of all biopsies and 18% of primary glomerular disease. This is almost similar to the studies done by Reshi AR et al (MCN- 44% and FSGS- 17%),[15] Sud K et al (MCN-36% and FSGS- 25%)[70] and Agarval SK et al (MCN-38%).[71]

The prevalence of MCN varies within India, being less than 12% in Vellore[14] (southern part of India) to 33% in Haryana[72] and 44% in Kashmir.[15] The reported prevalence of MCN in other countries are less than 14% in Thailand[74] and Pakistan[64] and less than 17% in Iraq.[9] When compared to studies in south India the prevalence of primary glomerular disease varies. The prevalence of MCN was less than 12% in Vellore [14] and 70% in Kerala.[73] In our study the prevalence of MCN was 60%, which was comparable to study in Kerala.[73] However in study from Vellore,[14] mesangio proliferative glomerulo nephritis was the most common cause of primary glomerular disease.

In this study Secondary glomerular disease accounted for 23.4% which was comparable to studies done by Carvalho E et al (29%)[75] and Panichvi V et al (25%).[65] Amongst Secondary glomerular disease amyloid was the most common histological lesion which accounted for 57% followed by lupus nephritis (42%). This was comparable to the studies done by Sud K et al (Amyloid 53% and Lupus Nephritis 35%).[70] Out of four Amyloid subjects, pulmonary tuberculosis was the cause of amyloid in one subject. In the rest of the subjects the diagnosis of Amyloidosis was revealed only on histopathological examination; the clinical examination being non-suggestive of any predisposing illness in these subjects and further investigations could not be performed due to lack of consent from patient's side. This shows the paramount importance of renal biopsy in diagnosing underlying histopathology of all adult nephrotic syndrome.

The prevalence of secondary glomerular disease varies within India, diabetes mellitus was the most prevalent Secondary glomerular disease in New Delhi,[72] Amyloidosis was more prevalent in Chandigarh,[70] lupus nephritis was

more prevalent in Vellore.[14] In our study the prevalence of amyloid was 57% followed by lupus nephritis 42%, which was comparable to the study in Chandigarh.[70] However it was different from the study done in New Delhi,[71] where diabetes mellitus was the most common cause of secondary glomerular disease.

CONCLUSION

In this study, primary glomerular disease was the predominant cause of nephrotic syndrome and accounted for 76.6%. Among primary glomerular disease minimal change disease was the most common histological lesion (60%), followed by FSGS (17%). Among Secondary glomerular disease amyloid was the most common histological lesion (57%), followed by lupus nephritis (42%).

Out of 30 subjects studied, majority were MCN followed by FSGS and amyloid. Majority (70%) of the subjects presenting to the hospital with nephrotic syndrome were male.

The commonest presentation among these groups was pedal edema, puffiness of face and oliguria. The average duration of these symptoms was three months.

All histopathological variants had proteinuria in nephrotic range, high TC, TG and LDL levels with low HDL levels without any difference among the histological variants.

Most patients had normal renal functions, as our study had more patients having MCN.

Hypertension was more prevalent among the MCN and FSGS type of histological variants.

Renal biopsy is of paramount importance in diagnosing underlying histopathology of adult nephrotic syndrome.

SUMMARY

Nephrotic syndrome refers to a classic tetrad of proteinuria, hypoproteinemia, edema and hyperlipidemia. The objectives of the present study were to study the clinical features, biochemical and histopathological spectrum in the adult onset nephrotic syndrome and to correlate the clinical and biochemical parameters with histopathological diagnosis.

The present one year cross sectional study was conducted in the Department of Nephrology and Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum, on patients clinically diagnosed to have adult onset nephrotic syndrome during the period of January 2007 to December 2007.

In this study, primary glomerular disease was the predominant cause of nephrotic syndrome and accounted for 76.6%. Among primary glomerular disease minimal change disease was the most common histological lesion (60%), followed by FSGS (17%). Among Secondary glomerular disease AMYLOID was the most common histological lesion (57%), followed by lupus nephritis (42%). The commonest presentation among these groups was pedal edema, puffiness of face and oliguria. The average duration of these symptoms was three months. Most patients had normal renal functions, probably because most of them were histopathologically having MCN.

All histopathological variants had high Lipid profile levels with low HDL without any difference among the histological variants. Hypertension and

microscopic hematuria was more prevalent among the MCN and FSGS type of histological variants.

In view of common clinical presentation and similar biochemical abnormalities, it is difficult to predict the underlying histopathology in majority of the patients. Histopathological variety is paramount important for treatment and prediction of prognosis. Present study showed four patients having amyloidosis, wherein amyloidosis was not considered in three patients before surgery, but biopsy revealed amyloidosis. Hence kidney biopsy in adult nephrotic syndrome is must.

BIBLIOGRAPHY

1. Schrier RW. Diseases of the Kidney and Urinary Tract. 8th Ed. Philadelphia: Lippincott Williams & Wilkins; 2007.

2. Jamison DT, Breman JG, Measham AR, Alleyne G, Cleason M, Evans DB, et al. Disease control priorities in developing countries. 2nd Ed. Washington DC: Oxford University Press; 2006.

3. Levy M, Berger J. Worldwide perspective of IgA nephropathy. Am J Kidney Dis 1988; 12: 340-7.

4. Schena FP. A retrospective analysis of the natural history of primary IgA nephropathy world-wide. Am J Med 1990; 89: 209-15.

5. Korbet SM, Genchi RM, Borok RZ, Schwartz MM. The racial prevalence of glomerular lesions in nephrotic adults. Am J Kidney Dis 1996; 27: 647-51.

6. Mitwalli AH, Al-Wakeel JS, Al Mohaya SS, Malik HG, Abu-Aisha H, Hassan OS, et al. Pattern of glomerular disease in Saudi Arabia. Am J Kidney Dis 1996; 27: 797-802.

7. Chiang GS, Woo KT, Edmondson RP. Pattern of glomerulonephritis in Singapore. Proc 3rd Asian Pacific Congr Nephrol: Singapore; 1986.

8. Lim GJ. Hepatitis B virus associated membranous glomerulonephritis in children in Taiwan. Proc 7th Asian Colloquium Nephrol: Taipei; 1987.

9. Shaker IK, Al-Saedi AJ, Al-Salam S, Saleem MS, Al-Shamma IA. Spectrum of glomerular disease in Iraqi patients from a single center. Saudi J Kidney Dis Transpl 2002; 13: 515-9.

10. Sitprija V. Nephrology in South East Asia: Fact and concept. Kidney Int Suppl 2003; 83: S128-30.

11. Morgan AG, Shah DJ, Williams W, Forrester TE. Proteinuria and glomerular disease in Jamaica. Clin Nephrol 1984; 21: 205-9.

12. Seggie J, Nathoo K, Davies PG. Association of hepatitis B antigenaemia and membranous glomerulonephritis in Zimbabwean children. Nephron 1984; 38: 115-9.

13. Frank AO. Apparent predisposition to systemic lupus erythematosus in Chinese patients in West Malaysia. Ann Rheum Dis 1980; 39: 266-9.

14. Narasimhan B Chacko B, John GT, Korula A, Kirubakaran MG, Jacob CK. Characterization of kidney lesions in Indian adults: towards a renal biopsy registry. J Nephrol 2006; 19(2): 205-10.

15. Reshi AR, Bhat MA, Najar MS, Banday KA, Naik MA, Singh DP, Wani F. The etiological profile of nephritic syndrome in Kashmir. Indian Journal of nephrology 2008; 18 (1); 9-12.

16. Date A, Raghavan R, John JT, Richard J, Kirubakaran MG, Shastry JCM. Renal disease in adult Indians: A Clinicopathological study of 2,827 patients. Q J Med 1987; 64: 729-37.

17. Vanikar AV, Kanodia KV, Patel RV, Trivedi HL. Primary IgA Nephropathy in western India. Indian J Nephrol 2005; 15: 227-31.

18. Brenner BM. Brenner and Rector's The Kidney. 8th Ed. Philadelphia: Saunders Elsevier; 2007.

19. Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, et al. Harrison's Principles of Internal Medicine. 17th Ed. New York: McGraw Hill; 2008.

20. Akhtar M, Al Mana H. Molecular Basis of Proteinuria, Adv Anat Pathol 2004; 11: 304-9.

21. Chopra JS, Mallick NP. Hyperlipoproteinemias in the nephrotic syndrome. Lancet 1971; 1: 317.

22. Marsh JB, Sparks CE. Hepatic secretion of lipoproteins in the rat and the effect of experimental nephrosis. J Clin Invest 1979; 64: 1229.

23. De Sain Van Der Velden MG, Kaysen GA, Barrett HA, Stellard F, Gaoellaa MM, Voorbij HA et al. Increased VLDL in nephrotic patients results from decreased catabolism while increased LDL results from increased synthesis. Kidney Int 1998; 53: 994.

24. Appel GB, Blum CB, Chien S, Kunis CL, Appel AS. The hyperlipidemia of the nephrotic syndrome. Relation to plasm albumin concentration, oncotic pressure and viscosity. N Engl JMed 1985; 312: 1544.

25. Grundy SM. Management of hyperlipidemia of kidney disease. Kidney Int 1990; 37: 847.

26. Joven J, Villabona C, Vilella E, Masana L, Alberti R, Valles M. Abnormalities of lipoprotein metabolism in patients with the nephritic syndrome. N Engl J Med 1990; 323: 579.

27. Cohen L, Cramp DG, Lewis AD, Tickner TR. The mechanism of hyperlipidemia in nephrotic syndrome -Role of low albumin and the LCAT reaction. Clin Chim Acta 1980; 104: 393.

28. Gitlin D, Cornwell DG, Nakasato D, Oncley JL, Hughes WL, Janeway CA. Studies on the metabolism of plasma proteins in the nephrotic syndrome. II. The lipoproteins. J Clin Invest 1958; 37: 172.

29. Fielding CJ, Shore VG, Fielding PE. Lecithin: cholesterol acyltransferase: Effects of substrate upon enzyme activity. Biochim Biophys Acta 1972; 270: 513.

30. Kallen RJ, Brynes RK, Aronson AJ, Lichtig C, Spargo BH. Premature coronary atherosclerosis in a 5 year-old with corticosteroid-refractory nephrotic syndrome. Am J Dis Child 1977; 131: 976.

31. Berlyne GM, Mallick NP. Ischaemic heart disease as a complication of nephritic syndrome. Lancet 1969; ii: 399.

32. Wass VJ, Jarrett RJ, Chilvers C, Cameron JS. Does the nephrotic syndrome increase the risk of cardiovascular disease? Lancet 1979; ii: 664.

33. Watts GF, Herrmann S, Dogra GK, Playford DA, Best JD, Thomas MA, et al: Vascular function of the peripheral circulation in patients with nephrosis. Kidney Int 2001; 60: 182-9.

34. Christoph J, Olbricht, Christoph W, Joachim T, Achim B. Simvastatin in Nephrotic Syndrome. Kidney Int 1999; 56:113-6.

35. Egli F, Eiminger P, Stalder G. Thromboembolism in the nephrotic syndrome. Pediatr Res 1974; 8: 903.

36. Llach FH. Hypercoagulability, renal vein thrombosis, and thrombotic complications of nephrotic syndrome. Kidney Int 1985; 28: 429.

37. Vaziri ND, Gonzales EC, Shayestehfar B, Barton CH. Plasma levels and urinary excretion of fibrinolytic and protease inhibitory proteins in nephrotic syndrome. J Lab Clin Med 1994; 124: 118.

38. Alkjaersig N, Fletcher AP, Narayanan M, Robson AM. Course and resolution of the coagulopathy in nephrotic children. Kidney Int 1987; 31: 772.

39. Kauffman RH, Veltkamp JJ, Van Tilburg N, Van Es LA. Acquired antithrombin III deficiency and thrombosis in the nephrotic syndrome. Am J Med 1978; 65: 607.

40. Feinstein EI, Chesney RW, Zelikovic I. Peritonitis in childhood renal disease. Am J Nephrol 1988; 8: 147-65.

41. Ballmer PE, Weber BK, Roy C, McNurlan MA, Watson H, Power DA, et al: Elevation of albumin synthesis rates in nephrotic patients measured with [1-13C] leucine. Kidney Int 1992; 41: 132-8.

42. Edelmann CM. Pediatric Kidney Disease. Boston: Little Brown and Co.; 1978.

43. Cameron JS. Nephrotic syndrome in the elderly. Semin Nephrol 1996; 16: 319.

44. Cameron JS, Chantler C, Ogg CS, White RS. Long-term remission in nephrotic syndrome after treatment with cyclophosphamide. Br Med J 1974; 4: 7.

45. Yeung CK, Wong KL, Ng WL. Intravenous methylprednisolone pulse therapy in minimal change nephrotic syndrome. Aust NZ J Med 1983; 13: 349.

46. Thomas DB, Franceschini N, Hogan SL, et al: Clinical and pathologic characteristics of focal segmental glomerulosclerosis pathologic variants. Kidney Int 2006; 69: 920-6.

47. Korbet SM. Primary focal segmental glomerulosclerosis. J Am Soc Nephrol 1998; 9:1333-40.

48. Beaman M, Howie AJ, Hardwicke J, Michael J, Adu D. The glomerular tip lesion: A steroid responsive nephrotic syndrome. Clin Nephrol 1987; 27: 217-21.

49. Howie AJ. Changes at the glomerular tip: A feature of membranous nephropathy and other disorders associated with proteinuria. J Pathol 1986; 150: 13-20.

50. Howie AJ, Brewer DB. The glomerular tip lesion: A previously undescribed type of segmental glomerular abnormality. J Pathol 1984; 142: 205-20.

51. Takekoshi Y, Tanaka M, Shida N, Satake Y, Saheki Y, Matsumoto S. et al: Strong association between membranous nephropathy and hepatitis-B surface antigenaemia in Japanese children. Lancet 1978; 2:1065-8.

52. Glassock RJ. Secondary membranous glomerulonephritis. Nephrol Dial Transplant 1992; 7(Suppl 1): 64-71

53. Forland M, Spargo BH. Clinicopathological correlations in idiopathic nephritic syndrome with membranous nephropathy. Nephron 1969; 6: 498-525.

54. Cameron JS, Glasgow EF, Ogg CS, White RHR. Membranoproliferative glomerulonephritis and persistent hypocomplementemia. BMJ 1970; 4: 7.

55. Habib R, Kleinknecht C, Gubler MC, Levy M. Idiopathic membranoproliferative glomerulonephritis in children: report of 105 cases. Clin Nephrol 1973; 1: 194.

56. D'Amico G. The commonest glomerulonephritis in the world: IgA nephropathy. Q J Med 1987; 64: 709-27.

57. Jennette JC. The immunohistology of IgA nephropathy. Am J Kidney Dis 1988; 12: 348-52.

58. Wallace DJ, Dubois EL. Lupus Erythematosus. 3rd Ed. Philadelphia: Lea and Febiger; 1987.

59. Johnson RJ, Feehaly J, Floege J. Comprehensive Clinical Nephrology. 3rd Ed St. Louis: Mosby; 2007.

60. Kunis CL, Teng SN. Treatment of glomerulonephritis in the elderly. Semin Nephrol 2000; 20:256-64.

61. Singh RGU, Parkash J, Kapoor R, Rai S, Sinha DK. A clinico-pathological study of renal amyloidosis in northern India. J Assoc Physicians India. 1969; 17(11): 641-50.

62. Falk R, Skinner M: The systemic amyloidosis: an overview. Adv Intern Med 2000; 45:107-31.

63. Gertz MA, Lacy MQ, Dispenzieri A: Myeloablative chemotherapy with stem cell rescue for the treatment of primary systemic amyloidosis: A status report. Bone Marrow Transplant 2000; 25:465-70.

64. Kazi JI, Mubarak M, Ahmed E, Akhter F, Naqvi SA, Rizvi SA. Spectrum of glomerulonephritides in adults with nephrotic syndrome in Pakistan. Clin Exp Nephrol 2008 Aug 7. [Epub ahead of print].

65. Panichi V, Pasquariello A, Innocenti M, Meola M, Mantuano E, Beati S. The Pisa experience of renal biopsies, 1977-2005. J Nephrol 2007; 20(3): 329-35.

66. BK Sharma, OP Karla, BN Datta, S Sagar, Spectrum of nephrotic syndrome in adults in North India- A Clinicopathologic study. JAPI 1988, 36: 12.

67. Malafronte P, Mastroianni-Kirsztajn G, Betônico GN, Romão JE, Alves MA, Carvalho MF. Paulista registry of glomerulonephritis: 5-year data report. Nephrol Dial Transplant 2006; 21(11): 3098-105.

68. Prakash C, Khanna SD, Soni N and Puri D. Nephrotic Syndrome in adults. J Assoc Phys Ind 1965, 13: 761-66.

69. Khanna UB, Nerurkar SV, Almeida AF, Taskar SP, Acharya VN. Study of Hyperlipidemia in adults with Nephrotic Syndrome. J Postgrad Med 1985; 31:140-5.

70. Sajith N, Sud K, Kohli HD, Gupta KL, Joshi K, Sakhuja V. Adolescent onset Nephrotic Syndrome in India: clinical features and Histopathological spectrum Indian J Nephrol 2000; 10: 101-44

71. SK Agarrwal, SC Dash; spectrum of renal diseases in Indian adults. JAPI 2000; 48: 594-600.

72. Aggarwal HK, Yashodara BM, Nand N, Sonia, Chakrabarti D, Bharti K. Spectrum of Renal Disorders in a Tertiary Care Hospital in Haryana J Assoc Physicians India. 2007; 55: 198-202.

73. Sreelatha M, Rajaratnam K, Aravindan KP, Ramdas P, Lakshminarayan K. Idiopathic Nephrotic Syndrome in adults- Predictors of histology and therapeutic response. Meerut: ISNCON-2001: 2001.

74. Kanjanabuch T, Kittikovit W, Lewsuwan S, Leelahavanichkul A, Avihingsanon Y, Praditpornsilpa K et al Etiologies of glomerular diseases in Thailand: a renal biopsy study of 506 cases. J Med Assoc Thai 2005; 88 Suppl 4: S305-11.

75. Carvalho E, do Sameiro Faria M, Nunes JP, Sampaio S, Valbuena C. Renal diseases: a 27-year renal biopsy study. J Nephrol 2006; 19(4): 500-7.

ANNEXURE I – CONSENT FORM

Objective and purpose of the study

To study the clinical, biochemical and histopathological features in adult onset nephrotic syndrome and to correlate clinical and biochemical parameters with histopathological diagnosis. The principal investigator of the study is **Dr. M. S. Khanpet** $_{\text{MD, DNB}}$ and the Co-investigator is **Dr. Vivekananda M.**

Procedure

If I agree to be a part of the study, I will be asked the relevant history and will be subjected to relevant clinical examination. I will also undergo investigations like : Complete blood count, Urine routine and microscopy, 24 hour urinary protein, Serum protein and serum albumin, Blood urea and serum creatinine, Fasting lipid profile, Anti-nuclear antibody and renal biopsy.

Risk and benefits

I have been explained by investigators, that there are no potential risks involved in this study and no benefits.

Alternatives

Taking part in this study is voluntary, I may choose not to take part in this study, or if I decide to take part I can later change my mind and withdraw from the study. My decision will not change the present or future health care or other services that I receive. The study doctor or sponsor may stop my participation in

this study anytime. If I choose not to take part in this study I will receive standard treatment for patients with my condition.

Privacy and confidentiality

All information collected about me during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify me in this research record.

Institutional / Sponsor policy

Does not apply to this research.

Financial incentives for participants

I will not be charged any amount for investigations subjected to me. I will not receive compensation or reimbursement for taking part in this study.

Authorization to publish results

Information from this study may be published but my identity will be confidential in any publication.

Consent statement

I voluntarily agree to take part in this study by signing below. I may withdraw at anytime. I am not giving up any legal rights by signing this form. My signature below indicates that I have read, or it has been read to me, this entire consent form, and have had all my questions answered.

Name of study participant or legally authorized representative :

Signature / Thumb print

In case of the queries during study or in future you may contact following person

Principal Investigator :	Dr. M. S. Khanpet $_{MD, DNB}$	Phone: 0831-2471350
Co-Investigator :	Dr. Vivekananda. M	Phone : 99800 58469
Name of the witness :		Signature :
Investigator Name :		Signature :
Date :		Place :

ANNEXURE II – PROFORMA

CLINICAL PROFILE OF ADULT NEPHROTIC SYNDROME

1. Name : D.O.A :
2. Age / Sex/ IP. No :
3. Occupation :
4. Marital Status :
5. Address :
6. Provisional diagnosis :
7. Final diagnosis :

No.	Symptoms	Yes	No
1.	Fever/Fatigue/malaise :		
2.	Cough & expectoration :		
3.	Dyspnea :		
4.	Edema		
5.	Abdominal distension :		
6.	Decreased urine output:		
7.	Joint pain :		
8.	Arthralgia / myalgia :		
9.	Skin rashes :		
10.	Haematuria :		
11.	Bleeding manifestation		

PAST HISTORY: Diabetes mellitus / Hypertension / Jaundice

DRUG HISTORY:

FAMILY HISTORY: History of renal disease in the family.

PERSONAL / HISTORY:

Diet:

Appetite:

Bower/Bladder:

Sleep:

Habits:

GPE

P - RR- BP- Temp-

Height - Weight - BMI -

Pallor, Icterus, Clubbing, cyanosis, lymphadenopathy, edema

SYSTEMIC EXAMINATION

Per abdomen –

Inspection

Palpation

Percussion

Auscultation

RESPIRATORY SYSTEM

Inspection

Palpation

Percussion

Auscultation

CARDIOVASCULAR SYSTEM :

Inspection

Palpation

Percussion

Auscultation

CENTRAL NERVOUS SYSTEM :

INVESTIGATION :

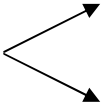
1. CBL – HB%

   TC

   DC

   ESR

   Routine

2. Urine 

   Microscopy

- ❖ 24 hours urinary protein
- ❖ Serum albumin
- ❖ Serum protein
- ❖ Blood urea
- ❖ Serum creatinine
- ❖ Fasting lipid profile
- ❖ ANA-Anti nuclear antibody (as and when required)
- ❖ Renal biopsy report

ANNEXURE III – KEY TO MASTER CHART

Abd. Dist	-	Abdominal distention
Amyloid	-	Amyloidosis
ANA	-	Anti nuclear antibody
B/D Man	-	Bleeding manifestations
BP	-	Blood Pressure
DM	-	Diabetes mellitus
F	-	Female
FSGS	-	Focal Segmental Glomerulo Sclerosis
GPE	-	General physical examination
Hb	-	Hemoglobin
HDL	-	High density lipoprotein
H/o RD	-	History or renal disease
HPF	-	High power field
hr	-	Hour
HTN	-	Hypertension
IgA	-	Immunoglobulin A
IP. No.	-	In patient Number
LDL	-	Low density lipoprotein
M	-	Male
MCN	-	Minimal Change Nephropathy
MN	-	Membranous Nephropathy
MPGN	-	Membrano Proliferative Glomerulo Nephritis
ND	-	Not done

POF	-	Puffiness of face
RBC	-	Red blood cell
SLE	-	Systemic Lupus Erythematosus
Sl. No.	-	Serial Number
Sr	-	Serum
TC	-	Total cholesterol
TG	-	Triglycerides
WBC	-	White blood cell
-	-	Absent
+	-	Present

MASTER CHART

Sl. No.	IP No.	Gender	PRESENTING COMPLAINTS											PAST HISTORY			GPE			INVESTIGATIONS															
			Fever	Cough	Dyspnoea	Oedema	POF	Oliguria	Abd Dist	Arthralgia	Skin Rash	Haematuria	Bld Man	DM	HTN	H/O RD	Pulse	BP	Lymphadenopathy	Hb	Total count	24 hr proteinuria	Sr. Albumin	Sr. Protein	Blood Urea	Sr. Creatinine	TC	TG	LDL	HDL	ANA	Urine Albumin	Urine WBC /HPF	Urine RBC /HPF	Biopsy
1	248491	M	-	+	-	+	+	-	-	-	-	-	-	-	-	-	80	120/70	-	14.1	7800	4.7	2.0	4.2	20.0	0.8	280	160	220	28	ND	3	2	0	MCN
2	210233	M	-	-	-	+	+	+	+	-	-	-	-	-	-	-	86	156/86	-	14.2	11900	7.0	0.7	4.0	52.0	3.7	447	240	360	30	ND	4	8	8	FSGS
3	218345	F	-	-	-	+	+	+	-	-	-	-	-	-	-	-	70	130/90	-	10.3	9400	2.8	1.9	4.0	54.0	2.4	384	196	309	36	N	4	20	0	MCN
4	259805	M	-	-	-	+	+	+	-	-	-	-	-	-	-	-	86	140/90	-	12.8	7900	2.6	2.2	4.3	18.0	0.8	240	150	176	34	N	4	0	6	IGA
5	237905	M	+	-	-	+	+	-	-	-	-	-	-	-	-	-	80	130/80	-	13.1	8700	2.5	2.6	4.0	36.0	1.4	140	90	92	30	N	4	6	8	FSGS
6	240546	F	+	-	-	+	+	+	-	-	-	-	-	-	-	-	100	160/96	-	13.3	10100	15.0	0.8	3.4	21.0	0.8	210	140	152	30	N	2	12	10	MCN
7	215291	M	-	-	-	+	+	+	-	-	-	-	-	-	-	-	80	120/80	-	16.3	9800	3.0	0.7	4.0	38.0	1.2	160	120	108	28	ND	2	20	0	MPGN
8	244981	M	-	-	-	+	+	-	-	-	-	-	-	-	-	-	90	130/80	-	10.4	15200	3.0	1.8	4.0	18.0	0.7	140	90	92	30	ND	3	10	0	MCN
9	217164	M	-	-	-	+	+	+	-	-	-	-	-	-	-	-	90	130/90	-	12.6	8600	3.8	1.0	3.5	38.0	1.2	160	100	115	25	N	3	3	0	MN
10	112939	M	-	+	-	+	+	-	+	-	-	-	-	-	-	-	90	130/80	-	16.1	9600	7.0	0.5	3.7	10.0	1.0	220	140	164	28	ND	4	10	3	MCN
11	198753	M	-	-	-	+	+	-	-	-	-	+	-	-	-	-	70	150/90	-	15.3	13300	3.0	0.9	5.4	12.0	0.6	180	120	126	30	ND	2	1	0	MCN
12	205464	F	-	-	-	+	+	+	-	-	-	-	-	-	-	-	84	140/80	-	14.2	10400	6.5	0.8	4.0	20.0	0.7	230	160	163	35	N	4	20	4	MCN
13	196633	M	+	+	-	+	+	+	-	-	-	-	-	-	-	-	86	130/80	-	16.7	10800	2.0	1.0	5.4	48.0	0.9	210	160	144	34	ND	4	10	15	MCN
14	208367	M	-	-	-	+	+	-	-	-	-	-	-	-	-	-	80	120/70	-	12.0	7000	3.4	2.8	5.0	17.0	0.5	190	130	134	30	ND	2	4	0	MCN
15	240866	F	+	-	-	+	+	-	-	-	-	-	-	-	-	-	88	110/70	-	13.4	15800	2.0	2.4	5.0	16.0	0.8	210	150	152	28	N	4	10	8	MN
16	234728	M	-	-	-	+	+	-	-	-	-	-	-	-	-	-	90	130/80	-	16.7	7200	2.5	2.2	4.6	28.0	1.3	230	180	160	34	ND	3	8	0	MCN
17	218565	M	-	-	+	+	+	+	+	-	-	-	-	-	-	-	80	120/80	-	12.6	7800	7.0	0.9	4.1	38.0	1.3	340	180	274	30	ND	4	8	8	MN
18	254377	M	-	-	-	+	+	-	-	-	-	-	-	-	-	-	94	110/70	-	11.2	13700	3.3	1.8	4.0	20.0	0.7	250	200	182	28	ND	2	15	1	FSGS
19	237410	F	-	-	-	+	+	-	-	-	-	-	-	-	-	-	80	140/100	-	10.4	8600	4.0	0.7	3.9	20.0	0.4	284	190	212	34	ND	3	3	0	MCN
20	232136	F	-	-	-	+	+	-	-	-	-	-	-	-	-	-	80	110/70	-	11.0	8400	7.0	1.0	3.8	23.0	0.5	260	180	194	30	ND	3	6	0	FSGS
21	221428	F	-	-	-	+	+	-	-	-	-	-	-	-	-	-	86	160/90	-	11.2	7800	4.5	1.2	3.6	24.0	0.8	220	160	164	34	ND	4	2	0	MCN
22	208285	M	-	-	-	+	+	-	-	-	-	-	-	-	-	-	86	140/90	-	12.6	7000	6.0	1.1	4.1	24.0	0.9	320	210	246	32	ND	3	0	0	Amyloid
23	241674	F	-	-	-	+	+	-	-	-	-	-	-	-	+	-	90	170/100	-	10.4	10500	2.0	1.4	4.2	30.0	1.1	210	150	152	28	+	2	15	6	SLE
24	246783	F	-	-	-	+	+	-	-	-	-	-	-	-	-	-	90	190/114	-	10.2	7000	5.0	1.4	3.8	58.0	6.0	230	180	172	26	+	3	6	2	SLE
25	201818	F	-	-	-	+	+	-	-	-	-	-	-	-	-	-	80	120/84	-	10.0	7900	4.0	0.4	3.7	13.0	0.4	289	284	202	30	N	4	10	10	Amyloid
26	262348	M	-	-	-	+	+	-	-	-	-	-	-	-	-	-	80	110/70	-	12.5	13700	5.0	1.7	4.0	17.0	0.6	270	260	192	26	ND	3	0	0	Amyloid
27	229163	F	-	-	-	+	+	-	-	-	-	-	-	-	-	-	84	112/72	-	11.0	9000	3.0	1.8	4.0	18.0	0.8	150	130	124	24	+	3	3		SLE
28	264529	M	-	-	-	+	+	+	-	-	-	-	-	-	-	-	86	130/76	-	14.6	9400	10.0	1.2	3.0	54.0	1.6	305	319	198	42	ND	3	2	1	MCN
29	268003	M	-	-	-	+	+	-	-	-	-	-	-	-	-	-	80	120/80	-	13.5	7200	6.0	2.0	4.0	24.0	1.2	260	210	190	26	ND	3	0	0	Amyloid
30	268464	M	-	-	-	+	+	-	-	-	-	-	-	-	-	-	80	160/100	-	14.0	6200	2.5	1.4	2.6	20.0	0.7	190	140	130	30	ND	4	4	0	MCN