Original Research Paper

Volume -10 | Issue - 4 | April - 2020 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Nephrology

A CLINICAL PROFILE OF ADULT ONSET NEPHROTIC SYNDROME WITH SPECIAL REFERANCE TO HISTOPATHOLOGY

Dr Pavan S Wakhare	Mbbs MD (medicine) Dm (nephrology)
Dr Pramod Ghuge*	MBBS MD (medicine) Dm (nephrology) *Corresponding Author
Prof Vivek Kute	MBBS, MD, FCPS, DM Nephrology (Gold Medalist), FASN ,FISOT,FISN, FRCP London

ABSTRACT The nephrotic syndrome (NS) refers to a classic triad of proteinuria 3.5 g/day/1.73 m2 (in practice > 3-3.5 g/day), hypoalbuminemia(<3 g/dl), and edema. Most patients also presents with hypercholestrolemia.1 2012 KDIGO GN guidelines defines nephrotic syndrome as Edema, 3+ protein on urine dipstick or 24 hr urinary protein >3.5g/day for adults or >40 mg/hr/m2 for children or uPCR>2000 mg/g and hypoalbuminaemia<2.5 g/dl. Present study was undertaken to know clinical profile, underlying different etiologies with special emphasis to histopathology and IF, age and gender distribution of different etiologies of nephrotic syndrome in the Indian setup particularly in our hospital which is a tertiary referral centre, and the response and results with prevailing recommended treatment

KEYWORDS :

AIMS AND OBJECTIVES

1. To study the clinical profile of adult onset nephrotic syndrome at our centre.
2. To confirm the diagnosis and appreciate incidence of different etiologies of nephrotic syndrome by histopathological examination of renal biopsy.
3. To study the clinical and biochemical and profile of nephrotic syndrome with respect to different histopathological and immunofluoroscence reports.

MATERIALS AND METHODS

The present study was an observational analysis of all consecutive patients presenting to the Institute of Kidney Diseases & Research Centre – Institute of Transplantation Sciences (IKDRC-ITS), Ahmedabad during the period from January 2012 till December 2013. Patients were enrolled in the study on fulfillment of defined criteria and followed till March 2014.

Inclusion criteria

- Age at presentation being 18 years or more
- Clinical diagnosis of NS or presence of nephrotic range proteinuria on investigation, irrespective of renal function.

Patients who had long history of NS, but had undergone renal biopsy during the study period were also included.

Certain patients who did not have nephrotic range proteinuria by definition (> 3.5 g/24 hours) were also included if they had marked hypoalbuminemia (< 2.5 g/dL) and clinical features and other lab parameters suggestive of nephrotic syndrome.

Exclusion criteria

- Known diabetics who presented with probably diabetic nephropathy were not included, as most of such patients were not biopsied regularly and diagnosis was made on clinical grounds.
- Patients who were lost to follow up within 4 months of starting treatment were excluded.

Enrollment

A detailed history was recorded in each case including age, sex, present illness, duration of present illness, past illness, treatment taken, personal and family history along with other demographic profile. Thorough clinical examination was followed by laboratory investigations according to specially designed proforma (on page 76).

Renal biopsy

Ultrasound guided, percutaneous renal biopsy was carried out in every patient using disposable true-cut needle of 16 gauge with the help of Biopty gun. The specimen was subjected to histopathological examination (H&E, PAS, silver and Gomori'sTrichrome staining) and immunoflurosence study with anti humanIgG, IgM, IgA, C3, C1q, antifibrin, κ- and λ-light chain antisera. Special staining with Congo red was performed in cases with suspicion of renal amyloidosis. Electron microscopy was not performed due to lack of feasibility.

OBSERVATIONS & DISCUSSION

Total 148 patients were enrolled in the present study but 44 patients lost to follow up within 4 months of starting treatment so they were excluded .There were total of 104 adult patients fulfilling the study inclusion criteria, who were included in this study during the period from January 2012 till December 2013. They were evaluated for etiologies.

Demographics:

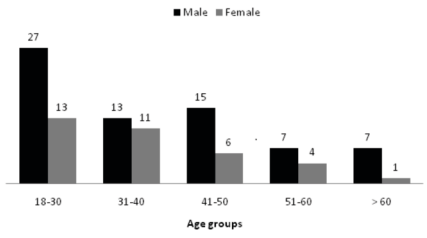

Fig 1: Age and gender distribution

Adult patients above the age of 18 years were included, and the eldest patient was 68 years old. The mean age at presentation was 37.36 ± 14.14 years.

Sixty six (66.35%) patients were males and 33.65 % were females. Male: female ratio was 1.9:1 indicating a male preponderance. In this study maximum number of patients were young and within the age group of 18 to 30 years (38.46%). Only 19 (18.26%) patients were older than 50 years. Comparison of demographics with other studies: -(Table 1)

Comparison of demographics with other studies: -(Table 1)

Age (years)	Present study (%) N=104	Cameron JS (%)64 N=506	Woo KT et al65 (%) N=25	AnuradhaS et al66 (%) N=30
< 30	40	30.8	60	60
31-40	24	15.6	20	33.3
41-50	21	16.4	12	6.7
51-60	11	18.6	4	0
> 60	8	18.6	4	0

A similar age distribution trend was also found in studies reported by Cameron JS64 however Woo KT et al and AnuradhaS et al66 reported higher incidence in 2nd and 3rd decade of life as compared to our study.

Presenting features:

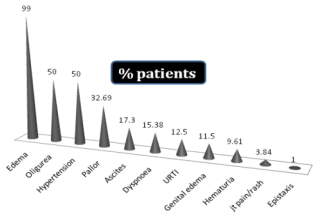

Fig 2: Common presenting features (%)

Nearly all patients (99%) presented with edema, while almost half had hypertension. Pallor was present in a 32.69% of our patients. Other common presenting features included ascites (17.30%), oliguria (50%), fever (12.5%), gross hematuria (9.6%), genital swelling (11.5%), and dyspnea (15.38%). Four patients of lupus nephritis had skin rash and joint pains; one patient of paucimmunecrescentic GN had epistaxis. History of URTI, diarrhea and fever was more common in patients with MCD and IgA nephropathy.

Past History:

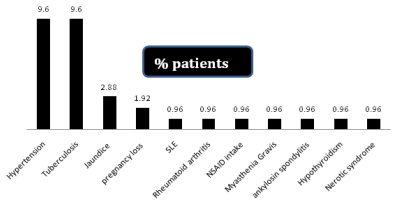

Fig 3: Past history (%)

Ten patients (9.6%) had past history of hypertension. These patients were older than 40 yrs. Ten patients (9.6%) had past history of tuberculosis out of them eight patients were of AA amyloidosis and one was of MGN. One patient of membranous nephropathy had history of ankylosing spondylitis. One patient had history of systemic lupus erythematosus since 2007 and had defaulted treatment. One pt of MePGN had history of Myasthenia Gravis since 2010 and had undergone thymectomy in 2011. This patient had renal dysfunction on presentation and improved after steroid treatment. Two pts of Lupus nephritis had history of recurrent abortions, one of ATIN had history of NSAID intake for ankle sprain, 3 pts had history of jaundice and on further investigations one of them had HBV seropositivite and another one was HCV seropositive. One pt. of cellular FSGS had history of hypothyroidism.

Biochemical parameters:

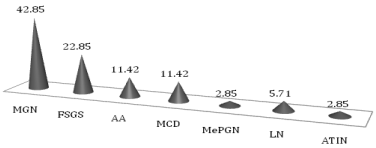

Fig 4: Massive proteinuria in different etiologies

The maximum value of proteinuria of 17.8 g/day was observed in a patient of AA amyloidosis. It is apparent that massive proteinuria was most frequently observed in patients with MGN.

Etiologies of Nephrotic syndrome: (Table 2)

Diagnosis	No. of patients (%)
MGN	29 (27.88%)
FSGS	17 (16.34%)
MCD	12 (11.53%)
MePGN	11 (10.57%)
Amyloidosis	11 (10.57%)
Lupus Nephritis	9 (8.65%)
MPGN	5 (4.80%)
PIGN	3 (2.88%)
IgA	3 (2.88%)
IgM	2 (1.92%)
PaucimmuneCrscentic GN	1 (0.96%)
ATIN	1 (0.96%)
FSGS Types	No. of pts
NOS	6
Perihilar	2
Cellular	5
Tip	1
collapsing	3
LN type	No. of pts
IV	7
V	1
VI	1
Amyloidosis type	No. of pts
AA	9
AL	2

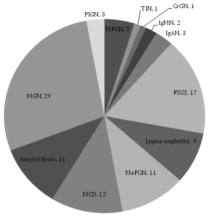

Fig5 : Histopathological diagnosis (no. of pts)

Most common cause of adult onset nephrotic syndrome in our study was Membranous nephropathy 27.88%, followed by FSGS 16.34%, followed by MCD 11.53%. Other common causes were MePGN 10.57%, Amyloidosis 10.57%, Lupus Nephritis 8.65%. Other less common causes were MPGN 4.80%, PIGN 2.88%, IgA 2.88%, IgM 1.92%, PaucimmuneCrescentic GN 0.96% and Acutetubulointerestitial nephritis 0.96%. In present study out of 38 females 8 (21%) females had Lupus nephritis as cause of Nephrotic syndrome.

Comparison of etiologies with other studies –(Table 3)

HPE	Present study (%) N=104	Cameron JS64 (%) N=506 Yr 1985	Shanbhag et al68 (%) N=67 Yr 1973	Orth et al71 (%) Yr 1998	Haas et al46 (%) N=233 Yr 1997	Medawar et al72 (%) Yr 1990	Singh RG et al73 (%) N=30 Yr 1983
MCD	11.53	22	5.97	20	15	12	36.7
FSGS	16.34	11.8	7.5	15	35	16	16.7
MGN	27.88	19.7	47.76	40	33	28	3.3
MePGN	10.57	16	19.4	-	-	-	6.7
MPGN	4.80	9.8	8.95	7	2	17	6.7
IgAN	2.88	-	-	-	9	-	-
IgMN	1.92	-	-	-	-	-	-
Lupus	8.65	10.8	-	-	-	-	-
Amyloid	10.57	5.9	10.45	-	4	13	10
Others	4.80	3.2	-	18	3	14	19.9

Most common cause of adult onset NS in our study was MGN (27.88%) followed by FSGS (16.34%).Shanbhaget al68, Orth et al71, Haas et al46 and Medawar et al72 also report membranous nephropathy as the commonest morphological variety of adult nephrotic syndrome. Present study findings are similar to as reported by Medawar et al72 except that Medawar et al reported more cases of

MPGN and no cases MePGN as compared to our study. These studies also suggest rising incidence of FSGS (7.5% Shanbhag et al Yr 1973, 35 % Haas et al Yr 1997).

Comparison of etiologies with Indian studies- (Table 4)

Reference	Date et al	Agarwal et al	Aggarwal at al	Das et al	Goyal et al	M. Rathi et al	Present study
year	1971-85	1987-95	2000	1990-2008	2010-12	2002-07	Jan 2012-dec.2013
Place	vellore	Delhi	Rohtak	Hydrab-ad	Kolkata	chandigarh	Ahmedabad IKDRC
No of Pts	1532	2250	404	1615	410	364	104
FSGS	18.6	20	17.6	15.2	27.4	30.6	16.34
MGN	13.6	20	16.9	10.1	24.6	24.4	27.88
MPGN	13.9	11.6	18.2	5.7	6.6	17.9	4.80
MCD	35.8	37	33.3	21.8	27.1	14.8	11.53
DPGN/ PIGN	2.5			14.9	1.6	2.8	2.88
IgA/MePGN	4.5	11.2	10	13.8	8.1	1.8	13.45
CSGN	2.8			9.7	0.8	3.7	0.96
Sec. glomerular diseases	16.7	41.5	21.3	20.9	11.9	11	19.22

Incidence of FSGS is increased in recent studies from different parts of India as compared to previous studies. In studies done by Goyal et al and M. Rathi et al FSGS was the commonest cause and MGN was second most common cause of adult NS. Agarwal et al and Das et al have reported secondary glomerular diseases (LN/ Amyloidosis) as most common cause of adult NS. The marginal difference in prevalence of histopathological pattern in different studies could be attributed to different study selection criteria and the different populations from different geographic areas under study.

Clinical parameters in different subgroups: (Table 5)

HPE	Hyper-tension (%)	Hematuria (%)	Anemia (%)	Renal insufficiency (%)	
				on presentation	on last FU
MCD	3/12(25)	3/12 (25)	5/12(33.33)	5/12 (33.33)	0/12 (0)
FSGS	9/17 (52.9)	8/17(47)	10/17 (58.8)	9/17(52.9)	3/17(17.6)
MGN	8/29 (27.58)	7/29 (24.13)	9/29 (31.03)	11/29 (37.93)	3/29(10.34)
MePGN	5/11 (45.45)	7/11 (63.63)	3/11 (27.2)	5/11 (45.45)	2/11 (18.18)
MPGN	3/5 (60)	4/5 (80)	2/5 (40)	3/5 (60)	2/5 (540)
Lupus	7/9 (77.7)	9/9 (100)	8/9 (88.8)	9/9 (100)	3/9 (33.33)
Amyloid	2/11 (18.8)	2/11 (18.8)	8/11 (72.7)	7/11 (63.63)	8/11(72.72)
IgAN	2/3 (66.66)	3/3 (100)	0/3 (0)	1/3 (33.33)	0/3(0)
IgMN	0/2 (0)	1/2 (50)	0/2 (0)	0/2(0)	0/2(0)
CrGN	1/1 (100)	1/1 (100)	0/1 (0)	1/1 (100)	0/1 (0)
PIGN	3/3 (100)	3/3 (100)	2/3 (66.6)	2/3 (66.6)	0/3 (0)
ALL	44/104 (42.3)	46/104(44.23)	47/104(45.19)	54/104(51.92)	21/104(20.19)

Hypertension was least common in amyloidosis patients (18.8%), while in MePGN and MCD its incidence was 45.4% and 25% respectively. In membranous nephropathy hypertention was present in 8/29 (27.58 %), in FSGS 9/17 (52.9%), in MPGN 3/5 (60%) and in PIGN 3/3 100% of patients. Most of the patients of MCD, MePGN and PIGN required antihypertensives only for short duration whereas most patients with FSGS, LN & MPGN required antihypertensives for longer duration.

Microscopic hematuria was present in all patients with IgAN, IgMN and crescentic GN. All patients with lupus nephritis (100%) had either microscopic hematuria (77.8%) or macroscopic hematuria (22.2%). Majority of patients with MPGN (80%), MePGN (63.6%) and FSGS (47%) had presence of hematuria on urine examination; incidence amongst amyloidosis, MCN and membranous nephropathy was 18%, 25% and 27.5% respectively.

Macroscopic hematuria was reported in 10 patients (9.6%) in this series, with it being most in IgAN (3 of 3 pts, 100%), PIGN (3 of 3 pts, 100%) and LN (2 of 9 pts, 22.2%). One patient (100%) of ANCA associated crescentic GN also presented with macroscopic hematuria. On follow up it has been observed that with treatment in all the etiologies decreasing hematuria was also important predictor of preservation of renal function along with improvement in clinical status and reduction in severity of proteinuria.

Renal insufficiency in the form of serum creatinine > 1.4 mg/dL on presentation was seen in all patients with LN and crescentic GN ; while it was also more common in Amyloidosis (63.6%) followed by MPGN (60%), FSGS (52.9%), MePGN (45.45%), MGN (37.93%), IgAN (33.33%), and MCD (33.3%). Renal function improved in all the subgroups except in patients with renal amyloidosis. Follow up outcome of important individual categories is discussed later on.

Complications of nephrotic syndrome:

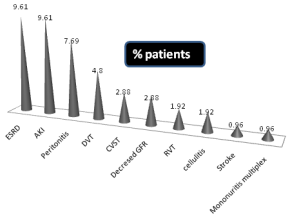

Fig. 6 Complications of nephrotic syndrome (%)

Of the total 104 patients Complications occurred in 53.84% patients, with lower limb deep vein thrombosis in 5 (4.8%), renal vein thrombosis in 2 (1.92%), peritonitis in 8 (7.69%), cellulitis in 2 (2%), massive pleural effusion in 5 (4.8%) and AKI in 10 (9.6%) cases. Other complications included perinephric hematoma as a complication of renal biopsy in 2 patients (1 with amyloidosis, 1 with lupus nephritis) which were managed conservatively.

Progression of renal dysfunction was encountered in total 14 (13.46 %) patients which included 3 pts of MGN (3of 29, 10.34%), 7 pts of amyloidosis (7 of 11, 63.63%), 2 pts of FSGS (2of 17, 11.76%), 1 pt Of MePGN (1of 11, 9.09%) and 1 pt of LN (1 of 9, 11.11%). Out of these 14 pts 10 pts developed ESRD and became dialysis depedent during follow up period. Five patients of Amyloidosis, 2 pts of MGN, 2 pts of FSGS collapsing variant and one pt. of lupus nephritis progressed to ESRD and became dialysis dependent. Two pts of Amyloidosis, one pt of MePGN and one pt of MGN not responded to any form of treatment and had gradual worsening of renal function but not required dialysis during follow up period. Two patients of in this study died during the follow up period. Both were suffering from advanced renal amyloidosis with vascular involvement.

SUMMARY AND CONCLUSIONS

Total 104 patients of adult onset nephrotic syndrome were included in the present study to evaluate clinical features, incidence of different histopathological lesions and response to various treatment protocols. All patients were subjected to renal biopsy with histopathological and immunofluorescence examinations. Diabetics and patients who lost to follow up within four months of starting treatment were excluded from the study.

1. Clinical features:

The commonest age-group of patients with adult onset nephrotic syndrome was 18 to 30 years. Most patients were under 50 years of age, and male to female ratio was 1.9:1. Edema (pedal/facial) was the cardinal symptom of presentation, seen in 99.03% patients. Hypertension was detected in 50% patients. Frank hematuria was seen in 10 (9.68%) cases which included 3 patients with IgA nephropathy, 3 patients PIGN, 2 patients with LN, 1 patient with MPGN and one patient with ANCA associated crescentic GN. Hypertension was uncommon in patients with amyloidosis (1.92%) MGN (27.58%) and MCD (25%). Nearly half of the patients with MPGN (60%), FSGS

(52.94%), and MePGN (45.45%) had hypertension at presentation. Most patients with lupus nephritis (77.77%) and IgAN (66.66%) had hypertension.

2. Laboratory parameters:

Mean 24 hour urinary protein excretion was 6.46 ± 3.14 g per day. More patients with FSGS, membranous nephropathy and amyloidosis presented with massive protienuria.

Serum cholesterol levels was near normal in nephrotic presentation of pauci-immune crescentic GN and amyloidosis, while highest group mean was observed in patients with MCN.

Microscopic hematuria was present in near to half of adult nephrotics (44.23%). The incidence was low in MCD (25%) and MGN (27.7%). Hematuria was Particularly high in FSGS (47%), MPGN (60%), MePGN (63.6%), lupus nephritis (100%) and IgAN (100%).

3. Histopathological diagnosis:

When taken together, MCN-FSGS complex was the overall leading cause of adult onset nephrotic syndrome, present in 28.2% patients. Membranous nephropathy was the single most common etiology (27.88%), followed by FSGS (16.34%), MCD (11.53%), idiopathic mesangial proliferative GN (10.57%), Amyloidosis (10.57%), Lupus Nephritis (8.65%), MPGN (4.8%), PIGN (2.88%). IgA nephropathy (2.88%) IgM nephropathy (1.92%), ATIN (0.92%) and pauci-immune crescentic GN (o.92%) were other uncommon casues. Similarly a higher incidence of amyloidosis could be explained on the basis of high prevalence of tuberculosis in the community, which was the commonest cause of secondary amyloidosis.

4. Renal function at presentation:

Overall renal insufficiency (s.creatinine>1.4 mg/dl) at the time of presentation was present in 47 patients (45.19%) of nephotic syndrome but majority of them responded to treatment so renal insufficiency at last follow up was present in only 20(19.23%) patients. Renal insufficiency at the time of presentation was found in 37.9% patients with membranous nephropathy, 33.3% patients with MCD and 18.18% patients of MePGN. It was seen in higher proportions in cases with FSGS (52.9%), MPGN (60%), amyloidosis (63.6%), lupus nephritis (100%) and crescentic GN (100%).

Most of the patients of SLE, FSGS, Crescentic GN improved after treatment but most of the patients of amyloidosis had relentless progression of renal dysfunction.

5. Age and gender distribution of different diseases:

Majority of the patients of MCD, FSGS, MePGN and LN nephritis were younger (<40 yrs) as compared to Membranous nephropathy in which majority of the patients were above the age of 40 yrs. Overall nephrotic syndrome was more common in males as compared to females.

REFERENCES

1. Donckerwolke RAMG, Cameron JS. The nephrotic syndrome: management, complications and pathophysiology. In: Davison AM, Cameron JS, et al eds. Oxford Textbook of Clinical Nephrology, Vol 1, 3rdedn. Oxford: Oxford University Press: 2005; 415-438
2. Cameron JS. Five hundred years of the nephrotic syndrome: 1484-1984. Ultser Med J 1985; 54 (Suppl): S5-S19
3. Schnaper HW, Robson AM, Kopp JB. Nephrotic syndrome: minimal change nephropathy, focal segmental glomerulosclerosis, and collapsing glomerulopathy. In: Schrier RW ed. Diseases of the Kidney and Urinary Tract,Vol 2, 8thedn. Philadelphia: Lippincott Williams & Wilkins; 2007: 1585-1672
4. International Study of Kidney Disease in Children. A controlled therapeutic trial of cyclophosphamide plus prednisone vs. prednisone alone in children with focal segmental glomerulonephritis. Pediatr Res 1980; 14: 1006
5. Glassock RJ. The nephrotic syndrome. HospPract 1979; 14: 105
6. M Rathi,V. Sakhuja et al:changing histologic spectrum of adult nephrotic syndrome over five decades in north India. IJN, 2014:14:86-11.
7. Kriz W and Elger M. Renal anatomy. In: Feehally J, Floege J and Johnson RJ eds. Comprehensive Clinical Nephrology,Vol 1, 3rdedn. Philadelphia: Mosby; 2007: 1-11
8. Rostgaard J, Qvortrup K. Electron microscopic demonstrations of filamentous molecular sieve plugs in capillary fenestrae. Microvasc Res 1997; 53: 1-13
9. Inoue S. Ultrastructural architecture of basement membranes. ContribNephrol 1994; 107: 21-28
10. Pavenstadt H, Kriz W, Kretsler M. Cell biology of the glomerular podocyte. Phsiol Rev 2003; 83: 253-307
11. Bernard DB. Extrarenal complications of nephrotic syndrome. Kidney Int 1988; 33(6): 1184-1202
12. VandeWalle JG, Donckerwolcke RA, van Isselt JW, et al. Volume regulation in children with early relapse of minimal-change nephrosis with or without hypovolaemic symptoms. Lancet 1995; 346: 148-152
13. Noddeland H, Riisnes SM, Fadnes HO. Interstitial fluid colloid osmotic and hydrostatic pressures in subcutaneous tissue of patients with nephrotic syndrome. Scand J Clin Lab Invest 1982; 42: 139-146
14. Joles JA, Rabelink TJ, Braam B, Koomans HA. Plasma volume regulation: Defences against edema formation (with special emphasis on hypoproteinemia). Am J Nephrol 1993; 13: 399-412
15. Geers AB, Koomans HA, Roos JC, et al. Functional relationships in the nephrotic syndrome. Kidney Int 1984; 26: 324-330
16. Kuster S, Mehls O, Seidel C, Ritz E. Blood pressure in minimal change and other types of nephrotic syndrome. Am J Nephrol 1990; 10(Suppl 1): 76-80
17. Brown EA, Markandu ND, Sagnella GA, et al. Lack of effect of captopril on the sodium retention of the nephrotic syndrome. Nephron 1984; 37: 43-48
18. Brown EA, Markandu ND, Roulston JE, et al. Is the renin-angiotensin-aldosterone system involved in the sodium retention in the nephrotic syndrome? Nephron 1982; 32: 102-107
19. Brown EA, Markandu ND, Sagnella GA, et al. Evidence that some mechanism other than the renin system causes sodium retention in nephrotic syndrome. Lancet 1982; 2: 1237-1240
20. Dusing R, Vetter H, Kramer HJ. The renin-angiotensin-aldosterone system in patients with nephrotic syndrome: Effects of 1-sar-8-ala-angiotensin II. Nephron 1980; 25: 187-192
21. Crew RJ, Radhakrishnan J, Appel G. Complications of the nephrotic syndrome and their treatment. ClinNephrol 2004; 62: 245-259
22. Joven J, Villabona C, Vilella E, et al. Abnormalities of lipoprotein metabolism in patients with the nephrotic syndrome. N Engl J Med 1990; 323: 579-584
23. Appel GB. Lipid abnormalities in renal disease. Kidney Int 1991; 39: 169-183
24. Shearer GC et al. Hypoalbuminemia and proteinuria contribute separately to reduced lipoprotein catabolism in the nephrotic syndrome. Kidney Int2001;59: 179–189
25. Nikkilä EA, Pykäpistö O. Regulation of adipose tissue lipoprotein lipase synthesis by intracellular free fatty acid. Life Sciences 1968; 7: 1303–1309
26. Cohen SL et al. The mechanism of hyperlipidemia in nephrotic syndrome—role of low albumin and the LCAT reaction. ClinicaChimicaActa1980;104: 393–400
27. Cameron JS. Thromboembolic complications of the nephrotic syndrome. Advances in Nephrol1984;13: 75–114
28. Cameron JS. Platelets in renal disease. In: Page CP ed. Platelets in Health and Disease Oxford: Blackwell; 1991; 228-260
29. Andrew M, Brooker LA. Hemostatic complications in renal disorders of the young. PediatrNephrol1996; 10: 88–99
30. Lilova MI, Velkovski IG, Topalov IB. Thromboembolic complications in children with nephrotic syndrome in Bulgaria. PediatrNephrol2000;15: 74–78
31. Hoyer PF et al. Thromboembolic complications in children with nephrotic syndrome. ActaPaediatrScand1986; 75: 804–810
32. Nachman PH, Jennette JC, Falk RJ. Primary glomerular disease. In: Brenner BM ed. Brenner and Rector's The Kidney,Vol 1, 8thedn. Philadelphia: Saunders Elsevier; 2007; 987-1066
33. Gulati S et al. Tuberculosis in childhood nephrotic syndrome in India. PediatrNephrol1997; 11: 695–698
34. Elidrissy ATH. Primary peritonitis and meningitis in nephrotic syndrome in Riyadh. Int J PediatrNephrol1982;3: 9–12
35. Chuang TF et al. Spontaneous bacterial peritonitis as the presenting feature in an adult with nephrotic syndrome. Nephrol Dial Transplant 1999; 14: 181–182
36. Speck WT, Dresdale SS, McMillan RW. Primary peritonitis and the nephrotic syndrome. Am J Surg1974;127: 267–269
37. Tain Y-L, Lin G-J, Cher T-W. Microbiological spectrum of septicemia and peritonitis in nephrotic children. PediatrNephrol1999;13: 835–837
38. Anderson DC et al. Assessment of factor B, serum opsonins, granulocyte chemotaxis and infection in nephrotic syndrome of children. J Infect Dis 1979; 140: 1–11
39. Brown EA, Sampson B, Muller BR, Curtis JR. Urinary iron loss in the nephrotic syndrome—an unusual case of iron deficiency with a note on the excretion of copper. Postgrad Med J 1984; 160: 125–128
40. Vaziri ND, Kaupke CJ, Barton CH, Gonzales E. Plasma concentration and urinary excretion of erythropoietin in adult nephrotic syndrome. Am J Med 1992; 92: 35–40
41. Tessitore N, Bonucci E, D'Angelo A, et al. Bone histology and calcium metabolism in patients with nephrotic syndrome and normal or reduced renal function. Nephron 1984; 37: 153–159
42. Wyatt RJ. Current estimates of the incidence of steroid responsive idiopathic nephrosis in Kentucky children of 1-9 years of age. Int J PediatrNephrol 1982; 3: 63-65
43. Grimbert P et al. Recent approaches to the pathogenesis of minimal change Nephrotic Syndrome. Nephrol Dial Transplant 2003; 18: 245-248
44. British Association for Paediatric Nephrology. Levamisole for corticosteroid-dependent nephrotic syndrome in childhood. Lancet 1991; 337: 1555-1557
45. Francois H, Daugas E, et al. Unexpected efficacy of rituximab in multirelapsing minimal change nephrotic syndrome in the adult: first case report and pathophysiological considerations. Am J Kid Dis 2006; 49: 158-161
46. Haas M, Meehan SM, Karrison TG, et al. Changing etiologies of unexplained adult nephrotic syndrome: a comparison of renal biopsy findings from 1976-1979 and 1995-1997. Am J Kidney Dis 1997; 30: 621
47. Cho ME, Kopp JB. Focal segmental glomerulosclerosis and collapsing glomerulopathy. In: Wilcox CS ed. Therapy in Nephrology & Hypertension: A Companion to Brenner & Rector's The Kidney, 3rdedn. Philadelphia: Saunders Elsevier; 2008; 220-238
48. Bargman JM. Management of minimal lesion glomerulonephritis: evidence based recommendations. Kidney Int 1999; 55 (Suppl 70s): S3-S16
49. Reich H, Cattran D. Membranous nephropathy. In: Davison AM, Cameron JS, et al eds. Oxford Textbook of Clinical Nephrology, Vol 1, 3rdedn. Oxford: Oxford University Press: 2005; 503-522
50. Rosner M, Bolton WK. Membranous nephropathy. In: Schrier RW ed. Diseases of the Kidney and Urinary Tract,Vol 2, 8thedn. Philadelphia: Lippincott Williams & Wilkins; 2007: 1568-1584
51. DeHeer, E Daha MR, Bhakdi S, et al. Possible involvement of terminal complement complex in active Heymann Nephritis, Kidney Int 1985; 27: 388
52. Hogan SL, Muller KE, Jennette JC, Falk RJ. A review of therapeutic studies of idiopathic membranous glomerulopathy. Am J Kidney Dis 1995; 25: 862-875
53. Ponticelli C, Zucchelli P, Passerini P, Cesana B. Methylprednisolone plus chlorambucil as compared with methylprednisolone alone for the treatment of idiopathic membranous nephropathy. The Italian Idiopathic Membranous Nephropathy Treatment Study Group. N Engl J Med 1992; 327: 599-603
54. Branten AJ, Reichert LJ, Koene RA, Wetzels JF. Oral cyclophosphamide versus chlorambucil in the treatment of patients with membranous nephropathy and renal insufficiency. Q J Med 1998; 91: 359-366
55. Imperiale TF, Goldfarb S, Berns JS. Are cytotoxic agents beneficial in idiopathic membranous nephropathy? A meta-analysis of the controlled trials. J Am SocNephrol 1995; 5: 1553-1558
56. Glassock RJ. Other glomerular disorders, including congenital nephrotic syndrome. In: Feehally J, Floege J and Johnson RJ eds. Comprehensive Clinical Nephrology,Vol 1, 3rdedn. Philadelphia: Mosby; 2007: 333-342
57. Ronco PM, Aucouturier P, Mougenot B. Monoclonal gammopathies: multiple myeloma, amyloidosis, and related disorders. In: Schrier RW ed. Diseases of the Kidney and Urinary Tract,Vol 3, 8thedn. Philadelphia: Lippincott Williams & Wilkins; 2007:

1941-1985
58. Bamelou A, Legrain M. Medical nephrectomy with anti-inflammatory non-steroidal drugs. Br Med J 1982;284: 234
59. Rieu P, Faucher C, Baumelou A, et al. Medical nephrectomy with CsA and angiotensin II in a case of life-threatening membranous glomerulonephritis. Nephrol Dial Transplant 1994; 9: 83–84
60. Olivero JJ, Frommer JP, Gonzalez JM. Medical nephrectomy: the last resort for intractable complications of the nephrotic syndrome. Am J Kidney Dis 1993; 21: 260–263
61. Bellomo R, Atkins RC. Membranous nephropathy and thromboembolism: is prophylactic anticoagulation warranted? Nephron 1993;63: 249–254
62. Sarasin FP, Schifferli JA. Prophylactic oral anticoagulation in nephrotic patients with idiopathic membranous nephropathy. Kidney Int1994;45: 578–585
63. Parikh CR, Gibney E, Thurman JM. The long-term outcome of glomerular diseases. In: Schrier RW ed. Diseases of the Kidney and Urinary Tract,Vol 2, 8thedn. Philadelphia: Lippincott Williams & Wilkins; 2007: 1811-1859
64. Cameron JS. The nephrotic syndrome and its complications. Am J Kidney Dis 1987; 10: 157-171
65. Woo KT et al. Iso electric focusing and selectivity Index in IgA nephrotic syndrome. Nephron 1994; 67: 408-413
66. Anuradha S, et al. Ultrastructural study of glomerular lesions in adult idiopathic nephrotic syndrome. Indian J Nephrol 7: 1-5
67. George AK, John G et al. Albumin synthesis, albuminuria and hyperlipemia in nephrotic patients: Kidney Int 1987; 31: 1308-1376
68. Shanbhag VV et al. Nephrotic Syndrome in adults. J Assoc Physicians India 1973; 21 : 923-930
69. Gherardi E, Rota E Calandra S, et al. Relationship among the concentrations of serum lipoproteins and changes in their chemical composition in patients with nephrotic syndrome. Eur J Clin Invest 1977; 7: 563-570
70. Khanna UB, Nerurkar SV, Almeida AF, et al. Study of hyperlipidemia in adults with nephrotic syndrome. J Postgrad Med 1985; 31: 140
71. Orth SR, Ritz E. The nephrotic syndrome. N Engl J Med 1998; 338(17): 1202-1210
72. Medawar W, Green A, Campbell E et al. Clinical and histopathologic findings in adults with the nephrotic syndrome. Irish J Med Sci 1990; 159: 137-140
73. Singh R.G. Usha et al: Morphological spectrum of glomerulonephritis. Indian Med Gaz 1983; 37: 361-365
74. Donadio JV Jr, Holley KE et al. Controlled trial of cyclophosphamide in idiopathic membranous nephropathy. Kidney Int 1974; 6: 431-439
75. Burns FJ, Adler S, Fraley DS, Segel DP. Sustained remission of membranous glomerulonephritis after cyclophosphamide and prednisone. Ann Intern Med 1991; 114: 725-730
76. Agarwal SK, Wani M, Kalra V, et al. Ponticelli regime in idiopathic membranous nephropathy: AIIMS experience. Abstract Book. ISNCON 2002; 65
77. Kandasamy S, Edwin F, Venkatraman R et al. Profile of patients with membranous nephropathy. Abstract book. ISNCON 2003; 60
78. Cattran D, Cardella C, Charron R et al. Results of alternate day prednisolone (ADS) in idiopathic membranous glomerulonephritis (IMG) [Abstract]. Proceedings of the 9th International Congress of Nephrology, Los Angles, 1984; 74A
79. Pascoe MD, Swanepoel CR, van Zyl-Smit R. Renal amyloidosis: a renal biopsy study [Abstract]. In: South African Society of Nephrology Renal Congress. Kidney Int 1993; 43: 1179-1190
80. Couser WG. Membranous nehpropathy. In: Feehally J, Floege J and Johnson RJ eds. Comprehensive Clinical Nephrology,Vol 1, 3rdedn. Philadelphia: Mosby; 2007: 231-242
81. Black DA, Rose G, Brewer DB. Controlled trial of prednisone in adult patients with nephrotic syndrome. Br Med J 1970; 3: 421