Original Research Article

Histopathological study in glomerular disease in patient with significant proteinuria in Government Dharmapuri Medical College, Dharmapuri

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Abstract

Introduction: Injury to glomeruli results in a variety of signs and symptoms of disease, including proteinuria, hematuria, azotemia, oliguria, edema and hypertension. Specific glomerular diseases tend to produce particular syndromes of renal dysfunction; although multiple glomerular diseases can produce the same syndrome. Evaluation of pathogenic features identified in a renal biopsy specimen may be required for definitive diagnosis. In patients with glomerular disease, renal biopsy provides tissue that can be used to determine the cause, predict the prognosis, and direct the treatment**.**

Aim of the Study: To evaluate the renal histopathology of patients with glomerular disease (with Significant Proteinuria > 1 gms/ 24 hours).

Materials and methods: The amount of proteinuria, renal insufficiency, hypertension, and microscopic hematuria differ in different histopathological types and in different age groups .Hence all these parameters and the histopathological type of glomerular disease have prognostic implications in patients with glomerular disease Renal biopsy was performed in patients with glomerular disease (proteinuria <1 gms/24 hrs.) attending the nephrology clinic.

Results: Among the 50 patients studied Focal segmental glomerulosclerosis (FSGS) was found in 11, IgA nephropathy and minimal change disease (MCD) in 8; Mesangi proliferative glomerulonephritis in 7, Membranous nephropathy and Lupus nephritis in 6, Membrano proliferative glomerulonephritis (MPGN) in 3 and Amyloidosis in 1 patient. The incidence of renal insufficiency was common in patients with MPGN (100%) and amyloidosis (100%) , followed closely by FSGS (87.5%), lupus

nephritis (66.66%), mesangio proliferative glomerulonephritis (57.14%), FSGS (27.27%) and membranous nephropathy (16.66%).

Conclusion: 50 patients with proteinuria more than 1 gram per 24 hours above the age of 12 years were biopsied for renal histopathological examination. There were 32 (65%) females and 18 (36%) males, with a mean age of 27.54 years. The commonest histopathological type found was FSGS in 11 (22%) patients followed by, IgAN in 8 (16%), MCD in 8 (16%), mesangio proliferative in 7 (14%), membranous nephropathy in 6 (12%), lupus nephritis in 6 (12%), MPGN in 3 (6%) and amyloidosis in 1 (2%). MCD was commonest histopathological type in age group of less than 20 years of age, FSGS in 21 to 40 years and mesangio proliferative glomerulonephritis above 40 years of age group. 23 (46%) of the 50 patients had renal insufficiency and is common in patients with MPGN (100%), amyloidosis (100%), IgAN (87.5%) and lupus nephritis (66.66%). None of the patients with MCD had renal insufficiency. 5.20 (40%) of the total patients studied had microscopic hematuria

Key words

Proteinuria, Membranous nephropathy, Mesangi proliferative glomerulonephritis, Amyloidosis.

Introduction

The major inflammatory glomerulopathies are focal proliferative glomerulonephritis (termed mesangial proliferative glomerulonephritis if the proliferating cells are predominantly mesangial cells); diffuse proliferative glomerulonephritis, and cresentic glomerulonephritis [1]. These diseases typically present with a nephritic- type active urine sediment characterized by the presence of red blood cells, red blood cast, leukocytes, and sub nephrotic proteinuria .The severity of renal insufficiency varies in proportion to the degree of glomerular inflammation. The glomerulus is a modified capillary network that derives an ultra-filtrate to Bowman's space, the most proximal portion the renal tubule [2]. Approximately 1.6 million glomeruli are present in two mature kidneys and collectively they produce 120 to 180 L of ultra-filtrate daily. Glomerular filtration rate is dependent on glomerular blood flow, ultrafiltration pressure, and the area and composition of the filtration barrier [3]. These parameters are tightly regulated through changes in afferent and efferent arteriolar tone and mesangial cell contractility. Arteriolar tone and mesangial cell contractility are in turn, modulated by neurohumoral factors, local myenteric reflexes, and endothelium-derived vasoactive substances [4]. In health, the glomerular endothelium is also antithrombotic and antiadhesive for leukocytes and platelets, thereby preventing inappropriate vascular thrombosis and inflammation during the filtration process. Filtration of plasma proteins and all blood cells is normally prevented as a consequence of fenestrated glomerular endothelium, basement membrane, and foot processes and slit diaphragms of visceral epithelial cells. In keeping the physiological function of glomerulus, virtually all glomerular injury results in impairment of glomerular filtration and/or the inappropriate appearance of plasma proteins and red blood cells in the urine [5]. The major morphologic patterns affecting the glomerular filtration barrier of proteins, namely the glomerular basement membrane and visceral epithelial cells, are membranous glomerulopathy, minimal change disease and focal and segmental glomerulosclerosis (FSGS). These entities typically present with nephritic – range proteinuria and the presence of relatively few red blood cells, leukocytes, or cellular casts [6]. As a consequence of the heavy proteinuria, nephrotic syndrome was associated with hypoalbuminemia, edema, hyperlipidemia and lipiduria and a prothrombotic state. Membranoproliferative glomerulonephritis, as the name suggests, is a hybrid lesion that presents with a combination of nephrotic and nephritic features [7].

Materials and methods

This was a prospective study of fifty consecutive patients attending the nephrology clinic from March 2016 to May 2017 in Government Dharmapuri Medical College, Dharmapuri in whom ultra-sonogram guided renal biopsy were done in patients with the following criteria.

Inclusion criteria

- Patients aged more than twelve years
- Proteinuria more than 1 gms / 24 hours

Exclusion criteria

- All known cases of diabetes mellitus.
- All known cases of systemic hypertension.
- All known cases with contracted kidneys proved by ultrasonogram.
- Post-transplant patients.5.Cases of nephritic syndrome responding to immunosuppressive therapy.

Renal biopsy helps in establishing accurate diagnosis, identifying any reversible pathology, helps in devising appropriate management plan for the patients and is very useful in understanding the histological nature of the disease The incidence of glomerular disease had increased dramatically in last decade and the pattern of glomerular pathology is changing dynamically with time .The type of glomerular disease varies in different geographies and among different age group of patients The amount of proteinuria, renal insufficiency, hypertension, and microscopic hematuria differ in different histopathological types and in different age groups .Hence all these parameters and the histopathological type of glomerular disease have prognostic implications in patients with glomerular disease Renal biopsy was performed in patients with glomerular disease (proteinuria <1 gms/24 hrs.) attending the nephrology clinic from august 2004 to august 2006 All the biopsy specimen were evaluated by light microscopy and immunofluorescent staining. Laboratory investigations including twenty four hour urinary proteinuria, serum creatinine, hemoglobin, total leukocyte count, differential count, erythrocyte sedimentation rate, serum proteins, serum calcium, serum cholesterol, ultra sonogram of kidneys were done along with the histopathological analysis of kidney biopsy.

Results

Among the 50 patients studied Focal segmental glomerulosclerosis (FSGS) was found in 11, IgA nephropathy and minimal change disease (MCD) in 8; Mesangiproliferative glomerulonephritis in 7, Membranous nephropathy and Lupus nephritis in 6, Membranoproliferative glomerulonephritis (MPGN) in 3 and Amyloidosis in 1 patient (**Table – 1**).

Table – 1: Frequency of the histopathological types.

Histopathological type	n	%
Focal segmental glomerulosclerosis	11	22
IgA nephropathy	8	16
Minimal change disease	8	16
Mesangioproliferative glomerulonephritis	7	14
Membranous nephropathy	6	12
Lupus nephritis	6	12
Membranoproliferative glomerulonephritis	3	6
Amyloidosis	1	2

Of the 23 patients with renal insufficiency, number of patients with Serum Creatinine 1.5 to 2.9 mg/dl – 14 Serum Creatinine 3.0 to 4.9 mg/dl – 6 Serum Creatinine > 5 mg/dl – 3 (**Table – 2**).

The amount of proteinuria was quantified and the patients were divided in toe groups as follows.Nephrotic range (>3.5 gms/24 hours) – 32 (64%) patients. Subnephrotic range (1 – 3.4 gms / dl) – 18 (36%) patients (**Table – 3**).

Table – 2: Severity of renal insufficiency in various histopathological types.

HISTOPATH TYPE	S.CREATININE 1.5 – 2.9 mg/dl	S.CREATININE 3- 4.9 mg/dl	S.CREATININE >5.0 mg / dl	TOTAL
AMYLOIDOSIS	0	1	O	1
FSGS	2	1	0	3
IgAN	3	3	1	7
LUPUS NEPHRITIS	4	0	0	4
MCD	0	0	0	0
MEMBRANOUS NEPHROPATHY	1	0	0	1
MPGN	0	1	2	3
MESANGIO PROLIFERATIVE	4	0	0	4
TOTAL	14	6	3	23

Table – 3: Prevalence of nephrotic range of proteinuria.

HISTOPATH TYPE	SUBNEPHROTIC RANGE (<3.5gms/dl)	NEPHROTIC RANGE (>3.5gms/dl)	TOTAL
AMYLOIDOSIS	1	0	1
FSGS	5	6	11
IgAN	3	5	8
LUPUS NEPHRITIS	2	4	6
MCD	2	6	8
MEMBRANOUS NEPHROPATHY	1	5	6
MPGN	1	2	3
MESANGIO PROLIFERATIVE	3	4	7
TOTAL	18	32	50

Discussion

All the fifty patients included in the study were in the age group of twelve to sixty years with a mean age of 27.54 years. All the fifty patients were divided in to three groups based on the age I – 12 to 20 years of age [8]. There were 14 (28%) patients in this group with a mean age of 14.85 years II – 21 to 40 years of age. There were 30 (60%) patients in this group with a mean age of 30.6 years III – 41 to 60 years of age. There were 6 (12%) patients in this group with a mean age of 44.5 years. None of the patients were above 60 years of age [9]. Of the 50 patients included in the study 32(64%) were females and 18 (36%) were males. The histopathological examination of the kidney biopsy revealed eight histopathological types [10]. Focal segmental glomerulosclerosis (FSGS) was the commonest type found in 11 (22%) patients followed by IgA nephropathy (IgAN) and minimal change disease (MCD) in 8 (16%) patients each. Mesangioproliferative glomerulonephritis was found in 7 (14%) patients, membranous nephropathy and lupus nephritis was found in 6 (12%) patients each, 3 (6%) patients had membranoproliferative glomerulonephritis (MPGN) and 1 (2%) had amyloidosis. Except FSGS and mesangioproliferative glomerulonephritis which are common in males all other types are common

in females in our study which is in contrast to the study conducted in Vellore where males dominated in all histopathological types barring lupus nephritis [11]. MCD was the commonest histopathological type in the age group of less than twenty years of age. FSGS is the commonest type in 21 to 40 years of age group and mesangioproliferative glomerulonephritis above 40 years of age. Where as in the study in Vellore MCD was the commonest histopathological type in the age group of less than 15 years and FSGS, the commonest type in all other age groups Of the total fifty patients studied 11 (22%) had FSGS on histopathological examination and this happened to be the commonest type found. Of the 11 patients with FSGS hypertension was found in only 2 (18.18%) against 13.3% in the study by Jayakumar, et al. in madras medical college, Chennai [8], renal insufficiency in 3 (27.27%) against 23.3% in the study by Jayakumar, et al. and 8.4 (36.36%) against 46.67% in the study by Jayakumar, et al. [12] of the patients with FSGS had microscopic hematuria. Of the 11 patients with FSGS nephrotic range proteinuria was present in 6 (54.54%) and subnephrotic range of proteinuria in 5 (45.45%) patients of the 11 patients with FSGS 2 (18.18%) were in the age group of 12 to 20 years, 8 (72.72%) in the age group of 21 to 40 years and 1 (9.09%) above 40 years of age. none of the patients with FSGS had hypocalcaemia (serum calcium < 8gms/ dl) or hyperlipidemia(serum cholesterol >200 mg /dl) but 2 (18.18%) patients had elevated ESR (>25 mm @ 1 hour) [13]. Of the 50 patients studied 8 (16%) patients had IgA nephropathy. All the 8 patients with IgAN were females.Among the eight patients with IgAN 3 (37.5%) patients were in the age group of 12 to 20 years, 5 (62.50%) in 21 to 40 years age group and none were above 40 years of age. In patients with IgAN, 7 (87.50%) patients had renal insufficiency against 68.7% in study of A Bakshi, et al. [9]. Of the 8 patients with IgAN 6 (75%) had hypertension against 53.1 in the study of A Bakshi, et al. [9]. 2 (25%) patients with stage 1 and 4 (50%) with stage 2 hypertension. Microscopic hematuria was found in 7 (87.50%) patients against 81.2% in the study of A Bakshi, et al. [9]. Nephrotic range of proteinuria was found in 5 (62.50%) of patients with IgAN and 3(37.50%) had non-nephrotic range of proteinuria. Anemia was found in 4 (50%) of patients with IgAN. Elevated ESR in 7 (87.50%), hyperlipidemia in 7 (87.50%) and hypocalcaemia in 3(37.50%) were found in patients with IgAN [14]. 6 (12%) of the 50 patients studied had membranous nephropathy. This type was more prevalent in the age group of 21 to 40 years, 4 (66.66%) patients were in this age group and 1 (16.66%) patients were in the age group of less than 20 years and more than 40 years each. Renal failure was prevalent in only 1 (16.66%) patient with membranous nephropathy against < 10% in the study of Noel LH, et al., 32% in the study of AD Parekh, et al. [11] and Hypertension was prevalent in 3(50%) of the 6 patients with membranous nephropathy (40%) in the study of AD Parekh et al. [11] and all the 3 had stage 2 hypertension. Hematuria was prevalent in 2 (33.33%) patients (30-50% in the study of Noel LH, et al. [16] and 44% in the study of AD Parekh, et al. [15]. Nephrotic range of proteinuria was prevalent in 5 (83.33%) of patients with membranous nephropathy and only 1 (16.66%) had subnephrotic range of proteinuria. Anemia and elevated ESR was found in 3 (50%) of patients with membranous nephropathy and hyperlipidemia was prevalent in 5 (83.33%) of the patients. Among the various parameters taken for the study renal insufficiency was found in 23 (46%) patients, against 47.16% in the study conducted in Visakhapatnam 13, 45% in the study in Bangalore among the 23 patients with renal insufficiency 17 were females and 6 were males [16]. None of the 8 (100%) with MCD had renal insufficiency, whereas all the 3 (100%) patients with MPGN, 1 (100%) patient with amyloidosis, 7 (87.5%) of patients with IgAN (68.7% in the study of A Bashir, et al. [9], 3 (27.27%) of 11 patients with FSGS (23.3% in the study of A Bashir, et al. [9], 4 (66.6%) of 6 patients with lupus nephritis (72% in the study of A Bashir, et al. [9]. 1 (16.6%) of 6 patients with membranous nephropathy (<10% in the study of Noel LH, et al. [16] and 32% in the study of AD Parekh, et al. 4 (57.14%) of 7 patients with

mesangioproliferative GN (18.33% in the study of Usha, et al. [10], had renal insufficiency [17]. All the patients with renal insufficiency were divided into three groups depending on the serum creatinine value as follows. I – Serum creatinine 1.5 to 2.9 mgs/dl. II– Serum creatinine 3.0 to 4.9 mgs/dl III – Serum creatinine > 5.0 mgs / dl [18]. Among the 23 patients with renal insufficiency 14 patients fell in-group I, 6 in-group II, 3 in-group III. 15 (50%) of the 30 patients in the age group of 21 to 40 years, 3 (50%) of the 6 patients in the age group above 40 years of age had renal insufficiency. whereas only 5 (35.71%) of the 14 patients in the younger age group of 12 to 20 years had renal insufficiency [19].

Conclusion

The most common histopathological type was Focal segmental glomerulosclerosis (FSGS). Renal insufficiency was common in patients with Membranoproliferative glomerulonephritis (MPGN). Hypertension was common in patients with IgA nephropathy (IgAN). Nephrotic range proteinuria was common in patients with Minimal change disease (MCD). Microscopic hematuria was common in patients with IgA nephropathy (IgAN) [20].

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