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Title: - Renal Biopsy Profile in a Tertiary Care Referral Hospital in North Karnataka

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ABSTRACT
Background: A review of renal biopsy data gives insight into the spectrum of clinically significant renal disease and necessary epidemiological data on renal diseases. **Objectives**: to analyze the histopathological spectrum of native kidney biopsies in the north Karnataka population.
Material & Methods: A total of 772 patients who underwent kidney biopsies at Department of Nephrology KIMS Hubli from January 2000 to December 2020 were included in the study. **Results:** The mean age of patients was 36.77 ± 25.15 years. The most common histopathological diagnosis made was of primary glomerular disease (57.77%), followed by Tubulo-interstitial disease(17.61%), while the least common was the vascular disease (1.8%). Glomereular disease is the most common histopathological finding among renal biopsies. Among primary glomerular diseases Minimal change disease was the most common finding noted in 23.31% of cases followed by Focal segmental glomerulosclerosis(18.16%),IgA nephropathy (14.57%),Membranous GN(11.88%), Membrano proliferative GN(10.98%), Mesangiocapillary GN (10.76%),Complement mediated GN (5.1%), Crescentic GN21 (4.7%), IgM nephropathy (0.4%)was the least common finding among glomerular diseases.
Conclusion: a wide variation of major histological groups in the primary glomerular diseases has been observed with most common being minimal change disease. However, among most countries of tHE world, the most common secondary glomerular disease has been documented as LN.
Keywords: Histopathological diagnosis, Glomereular disease, Tubulo-interstitial disease

Introduction: Renal diseases are the major causes of morbidity and mortality. [1] Most regional hospitals treat only a limited number of patients with renal disease, especially in developing rural areas of India. KIMS Hubli hospital being the major tertiary care centre for north Karnataka.Most patients with renal diseases are referred to KIMS hospital for the same. KIMS hospital has been collecting renal disease data in the north Karnataka . Renal biopsy has been performed routinely in our hospital for last 20 years. Renal biopsy is an important tool used in evaluation of patient with renal disease. It is mainly used to reach the specific diagnosis, assessing severity of disease activity, and in decision about treatment to be made. [2] A review of renal biopsy data gives insight into the spectrum of clinically significant renal disease and necessary epidemiological data on renal diseases. [3] Renal biopsy helps in detecting pathology in intrinsic renal disease, temporal evolution of the disease and in finding specific secondary etiology causing renal disase. Reversible causes such as primary/secondary glomerulonephritis (GN), acute tubulointerstitial nephritis, and other acute injuries can be diagnosed mainly with the help of an

adequate kidney biopsy specimen.The aim of this study is to analyze the histopathological spectrum of native kidney biopsies in the north Karnataka population.

Materials & Methods: A total of 772 patients who underwent kidney biopsies at Department of Nephrology KIMS Hubli from January 2000 to December 2020 were included in the study. Medical records of these patients were studied retrospectively to analyze the patterns of renal diseases. There were 526 males and 246 females, with a mean age of 36.77 ± 25.15 years. The indications for renal biopsy included proteinuria, unexplained hematuria and systemic diseases with evidence of kidney involvement, unexplained renal impairment and renal impairment in post-transplant patients. Biopsy samples were obtained by a percutaneous method using a trucut needle underultrasound guidance. Two renal biopsy samples were taken from each patient, which were subjected for light microscopy and immunofluorescence studies. Sections were made from formalin-fixed paraffin-embedded tissue and stained by hematoxylin-eosin, Periodic-Acid Schiff (PAS) and Jones stains for light microscopy; special stains such as congo-red stain were also used where indicated. All samples were examined by a certified histopathologist. Re-biopsies were performed in case of inadequate tissue for light microscopy and immunofluorescence examination with the help of a radiologist under real-time ultrasound.The immunofluorescence microscopy panel included staining for IgA, IgM, IgG, C3, C 1q and fibrinogen. Patients' data were obtained from the previous medical records. Essential investigations including complement levels, auto-immune profile, ANCA antibodies extractable nuclear antigens, ASO titers and virology results were also recorded..

Statistical Analysis: Results were analyzed by using Statistical Package for Social Sciences (SPSS) version 20.0. The quantitative variables were expressed as the mean with standard deviation while qualitative variables were expressed as numbers and percentages.

Result: As shown in Table 1, 772 patients underwent renal biopsy during the study period among which there were 68.13% (526) males and 31.86%(246) females.   The mean age of patients was 36.77 ± 25.15 years.

Glomerular disease constituted 66.19% of the total renal biopsies. Of the patients with glomerular diseases, 335 patients were male and 176 were female. The most common histopathological diagnosis made was of primary glomerular disease (57.77%), followed by Tubulo-interstitial disease(17.61%), while the least common was the vascular disease (1.8%). Though in all categories, the number of male patients outnumbered female patients, this difference was most stark in cases of vascular disease. Disrtrubution of biopsy finding is shown in Table 1.

Glomereular disease is the most common histopathological finding among renal biopsies. The histopathological profile of renal biopsies among glomerular disease shown in table2. Among glomerular diseases primary glomerular disease constituted for 87.2% and secondary glomerular disease constituted for 12.7%. The mean age group among patients with primary glomerular disease was 32.95 ± 17.26 years and mean age group among secondary glomerular disease was 41.75 ± 19.62 years.

Among primary glomerular diseases Minimal change disease was the most common finding noted in 23.31% of cases followed by Focal segmental glomerulosclerosis(18.16%),IgA nephropathy (14.57%),Membranous GN(11.88%),Membrano proliferative GN(10.98%),Mesangiocapillary GN (10.76%),Complement mediated GN (5.1%),Crescentic GN21 (4.7%), IgM nephropathy (0.4%)was the least common finding among glomerular diseases. Males outnumbered females among all primary glomerular disease patients. Mean age group among IgM nephropathy was 11.50 ± 17.68 years as compared to mean 32.95 ± 17.26 years.

Among secondary glomerular diseases most common finding was Lupus Nephritis seen in 21(32.30%) patients among 65 patients followed by amyloidosis (30.70%), diabetic nephropathy (29.23%) and Hypertensive nephropathy (7.60%). Lupus nephritis was found in younger population (mean age 25.04+12.57 years) as compared to mean age of secondary Glomerular disease patients. Although males were majority even in secondary glomerular disease, females outnumbered males in lupus nephritis and diabetic nephropathy.

Tubulointerstitial diseases in histopathological specimen of renal biopsy was the second most common finding after glomerular diseases seen in 17.61% of all biopsies. Mean age was 36.34+16.72 years. Acute tubulointerstitial nephritis was seen in majority of renal biopsies seen 52 patients out of 136 patients followed by Acute interstitial nephritis, Acute tubular injury, Pyelonephritis, Granulomatous kidney disease was the least common finding seen in only 3 patients. Among all Tubulointerstitial diseases seen in histopathological specimens males were majority except in Granulomatous kidney disease where females were majority. Mean age and other data regarding Tubulointerstitial diseases has been depicted in table3.

Renal vascular diseases was the least common finding among all renal biopsies constituting only 10 patients out of 772 patients with mean age 46.2+ 15.89 years with males being majority. seven patients with transplanted kidneys underwent renal biopsies at our centre because of unexplained deterioration of graft function; four patients had acute cellular rejection, while the other three had features of chronic allograft dysfunction. All of these patients received transplant kidneys at different hospitals and were only followed-up at our center. Further details regarding primary renal disease, tissue matching and induction of immunosuppression was available.Thrombotic microangiopathy (TMA) was seen in only 3 patients with mean age 42+13.15 years with males being the majority.

Renal biopsy revealed chronic renal disease in 115 patients among total patients of which chronic GN was seen in majority of patients(51.30%) followed by Chronic intertstitial nephritis (31.30%) and Chronic tubulointertstitial nephritis (17.39%) with mean age 41.59+17.85 years. Males were majority among chronic renal disease patients.

Discussion: In the literature, there is paucity of epidemiological data on the spectrum of biopsy-proven renal diseases from India. Our institution being the major tertiary care centre in north Karnataka receives majority of patients with renal disease. However the rate of biopsy-proven renal diseases underestimates the true prevalence of diseases, as not all patients with renal disease are biopsied**.**

In our study of 772 cases, was observed that among the total biopsies conducted males outnumbered females which is similar to various Indian and international studies. [2-5]

Mean age group among patients with primary glomerular disease was 32.95+17.26 years and mean age group among secondary glomerular disease was 41.75+19.62years. which is comparable to some other recent studies though in a few studies, the mean age is shown as low as 15.4± 12.0 years. [6-9]

One important finding in the present study is that glomerular diseases (primary and secondary) account for 66.19% of all cases, and MCD is not only the commonest primary glomerular disease (23.31%) but also overall, the most frequently encountered histological diagnosis (n=104), mean age among patients with MCD was 27.69±18.14 years.

A study done in in a single center of South India shows almost similar finding about MCD being the most frequent histopathological diagnosis among patients with primary glomerular disease. [2] In our study, the most common cause was MCD, followed by FSGS, IgAN ,MN, MesGN, and MPGN, which is in similarity with other previous studies from our country.[10] In Korea and other northeast Asian countries

like Japan, the most common BIOPSY was MCD, followed by MN and IgAN. [11-12] Our results are consistent with the results of these studies to some extent.

In contrary to this , in Czech registryMN and IgAN were the most frequent . [13] On the other hand, study in Serbia reported MN as the most common biopsy finding and in Brazil, FSGS was the most common biopsy finding , followed by MCD and MN. [14-15] Our study is not comparable with these series.The distribution pattern of FSGS was also variable. There is a worldwide increase in the incidence of FSGS despite multiple variations. [16-17] It was the second most common PGD found in the present study. In contrast, FSGS is the most common in some studies reported from our neighboring countries and Brazil. [5,14,18,19]

Secondary GN accounted for 8.4 % of cases in our study, contrary to sunita et al [20] where 16 % of total cases were due to secondary glomerulonephritis ,it was 21.6% according to study by kumar et al[21] and 18.2% according to study by das et al[2].lupus nephritis was the most common secondary glomerular disease, which is similar with some other studies. [20,22][2]

In contrast to our study in a study conducted by Kumar et al [21] it was observed that DN was commonest of the secondary glomerular diseases and similar observation was also done bymultiple studies. [23-24] other causes of secondary glomerulonephritis in the present study were amyloidosis,diabetic nephropathy and hypertensive nephropathy.male preponderence was observed even in secondary glomerulonephritis.

Among tubulointerstitial (17.61%)group, Acute tubulointerstitial nephritis was the most common diagnosis,38.23% of alltubulointerstitial group. This was in consistent with study conducted by kumar et al. [21]

Other findings in renal biopsy were vascular changes that accounted for 1.2% this was in consistent with a study by kumar et al. [21] Among vascular changes graft   rejection was the most common finding followed by thrombotic microngiopathies.

Conclusion: To conclude, from the study and data analyzed, a wide variation of major histological groups in the primary glomerular diseases has been observed with most common being minimal change disease . however, among most countries of tHE world, the most common secondary glomerular disease has been documented as LN.The spectrum of glomerular diseases varies widely depending upon a number of factors like age and sex, as well as the geographical mapping and the ethnic grouping. even tubulointerstitial diseases also constitutes the major part among the renal biopsies.

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Table 1: Pattern of kidney diseases in a tertiary care referral hospital in north Karnataka : an overview through histopathological findings in biopsy-proven cases

Diagnosis	No and percentage	No of males and percentage	No of females and percentage	Mean age with SD in Years
Primary glomerular disease	446(57.77%)	297(66.5%)	149(33.4%)	32.95±17.26
Secondary glomerular disease	65(8.4%)	38(58.46%)	27(41.53%)	41.75±19.62
Tubulo-interstitial disease	136(17.61%)	101(74.26%)	35(25.73%)	36.34±16.72
Vascular disease	10(1.2%)	8(80%)	2(20%)	46.2±15.89
Chronic kidney disease	115(14.89%)	82(71.30%)	33(28.6%)	41.59±17.85
Total	772	526(68.13%)	246(31.86%)	36.77±25.15

Glomerular diseases	No. of cases(%)	Male	Female	Mean age ± SD in years
Primary Glomerular Diseases	**446**	**297**	**149**	**32.95±17.26**
Minimal change disease	104 (23.31%)	65	39	27.69±18.14
Focal segmental glomerulosclerosis	81 (18.16%)	49	32	37.27±18.55
Membranous GN	53 (11.88%)	41	12	38.59±14.87
Mesangiocapillary GN	48 (10.76%)	32	16	30.10±17.63
Membrano proliferative GN	49 (10.98%)	27	22	30.79±17.73
IgA nephropathy	65 (14.57%)	52	13	33.87±12.95
IgM nephropathy	02 (0.4%)	01	01	11.50±17.68
Crescentic GN	21 (4.7%)	14	07	29.76±17.09
Complement mediated GN	23 (5.1%)	16	07	32.52±19.30
Secondary Glomerular Diseases	**65**	**38**	**27**	**41.75±19.62**
Amyloidosis	20 (30.70%)	14	06	47.7±18.15
Diabetic nephropathy	19 (29.23%)	09	10	50.73±70.93
Lupus nephritis	21 (32.30%)	10	11	25.04±12.57
Hypertensive nephropathy	05 (7.60%)	05	00	54±11.95

Table 2: Histopathological profile among glomerular diseases

Table 3: Histopathological profile among Tubulointerstitial diseases

Tubulointerstitial diseases	136	101	35	36.34+16.72
Acute interstitial nephritis	36 (26.47%)	30	06	39.2+15.57
Acute tubular injury	36 (26.47%)	26	10	41.57+16.79
Acute tubulointerstitial nephritis	52 (38.23%)	38	14	29.67+16.36
Pyelonephritis	09 (6.61%)	06	03	43.11+12.39
Granulomatous kidney disease	03 (2.20%)	01	02	35.66+16.74

Table 4: Histopathological profile among Renal vascular diseases

Renal vascular diseases	10	08	02	46.2+15.89
Graft rejection	07 (70%)	06	01	48+17.57
Thrombotic microangiopathies	03 (30%)	02	01	42+13.15

Table 5: Histopathological profile among Chronic Renal disease

Chronic Renal disease	115	82	33	41.59+17.85
Chronic GN	59 (51.30%)	40	19	37.06+15.41
Chronic intertstitial nephritis	36 (31.30%)	27	09	49.52+18.23
Chronic tubulointertstitial nephritis	20 (17.39%)	15	05	40.65+19.79