Prevalence of Specific Types of Kidney Disease in Patients Undergoing Kidney Biopsy: A Single Centre Experience

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Accepted on
February 9, 2014

DOI Name
http://dx.doi.org/10.3126/jaim.v3i1.10695

Keywords
Kidney biopsy, Lupus Nephritis, FSGS, nephrotic syndrome

Citation
Mukunda Prasad Kafle, Dibya Singh Shah, Shailendra Shrestha, Mahesh Raj Sigdel, Kanak Bahadur Raut. Prevalence of specific types of kidney disease in patients undergoing kidney bopsy: a single centre experience. Journal of Advances in Internal Medicine 2014;03(01):5-10.

ABSTRACT

Background and aims: Prevalence of various types of kidney diseases in Nepalese population has largely been unknown. Knowledge of the prevalence of specific type kidney disease in renal patients has important implications in starting the treatment modalities and prognostification of these patients. We tried to find out the various types of kidney diseases in patient population undergoing kidney biopsy at our centre.

Methods: We retrospectively analyzed kidney biopsy reports of patients who underwent Kidney Biopsy from 2007 to 2009 in Tribhuvan University Teaching Hospital (TUTH), Kathmandu.

Results: Of the 194 kidney biopsy reports analyzed, 100(51.5%) were females and 94(48.5%) males. Most of the patients 75.773% (n=147) were 16-45yrs age (Mean age 33.7years). Biopsy reports showed Lupus Nephritis in 20.6%(n=40), Focal Segmental Glomerulosclerosis (FSGS) in 19.6%(n=38), IgA Nephropathy in 9.8%(n=19), MPGN 9.8%(n=19), Membranous Nephropathy 8.2%(n=16) and Minimal Change Disease (MCD) in 8.2%(n=16) of the population biopsied. Nephrotic syndrome was the commonest clinical indication for kidney biopsy.

Conclusion: Our study demonstrated that Lupus Nephritis is the commonest indication for kidney biopsy at our centre.

BACKGROUND

Renal diseases have remained understudied in Nepal. Glomerulonephritis (GN) hasn't been studied much often. Facilities for kidney biopsies are available in few centers only. There haven't been many publications in this subject.

Kidney biopsy is the investigation of choice to diagnose glomerular diseases, mainly primary and secondary glomerulopathies. Glomerular diseases are common causes of End Stage Renal Disease (ESRD).

In the developed countries, these diseases are the third most common cause of ESRD only after diabetes mellitus (DM) and hypertension (HTN) accounting for 10-15% of patients in the United States.[1] The rate of ESRD caused by glomerulonephritis has been unchanged, and also consistent with levels seen in the early 1990s.[2] However, many patients with renal failure attributed to hypertension probably have an underlying glomerular disease as the cause, so the numbers quoted for prevalence are probably low. Yearly incidence of biopsy proven glomerulonephritis (BPGN) was reported upto 12.3 out of 21·5 per 100,000 population per year undergoing renal biopsy in Australia.[3]

In the developing countries, glomerular diseases are expected to stand higher in the list as a consequence of various

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infectious agents. For every patient with clinically apparent glomerulonephritis receiving medical care, an estimated additional five to ten patients have undiagnosed subclinical disease.[4] Among those individuals without end stage renal disease at age 40 years, the lifetime risk of end stage renal disease is expected to be 2.66% for men and 1.76% for women.[5]

MATERIALS AND METHODS:

This is a retrospective study. We collected information from the pathology reports of our patients who underwent kidney biopsy at Tribhuvan University Teaching Hospital (TUTH), Kathmandu, Nepal. We recorded the pre-biopsy information and clinical indications mentioned in the biopsy reports as they were stated during histopathology requests. All the biopsies were reported at the Dr. Lal's Pathlabs New Delhi by renal histopathologists. Our protocol of renal biopsy is a real time ultrasound guided kidney biopsy by disposable Bard needle. We analysed the biopsy data of 194 patients who underwent renal biopsy at our centre from 2007 to 2009.

RESULTS

Patient Distribution:

Among the total patients undergoing kidney biopsy, 100 (52%) were female and 94 (48%) were male. [Table 1.] Mean age was 33.7±14 years (Range 11-76 years).

Table 1. Age and Sex Distribution of Patients

Age in years	Male	Female	Total (%)
10-19	15	18	33 (17%)
20-29	26	29	55 (28.3%)
30-39	24	24	48 (24.7%)
40-49	11	18	29 (14.9%)
50-59	7	6	13 (6.7%)
>59	11	5	16 (8.2%)
Total	94	100	194 (100%)

Biopsy Reports:

The most common biopsy diagnosis was Lupus Nephritis (LN) in 40 (20.6%) patients followed by Focal Segmental Glomerulosclerosis (FSGS) in 38 (19.6%), Membranoproliferative glomerulonephritis (MPGN) in 19 (9.8%) {Mesangiocapillary-1, Mesangioproliferative-2, Membranoproliferative-16}, Immunoglobulin A Nephropathy (IgAN) in 19 (9.8%), and Minimal Change Disease (MCD) in 16 (8.2%). Chronic Glomerulonephritis with advanced sclerosis was found in 13 (6.7%) of the total kidney biopsies. [Table 2.]

Table 2. Histological Diagnosis of Kidney Biopsies

S. No.	Histological Diagnosis	Number (%) n=194
1	Lupus Nephritis	40 (20.6)
2	Focal Segmental Glomerulosclerosis	38 (19.6)
3	Immunoglobulin A Nephropathy	19 (9.8)
4	Membranoproliferative Glomerulonephritis	19 (9.8)
5	Minimal Change Disease	16 (8.2)
6	Membranous Glomerulopathy	16 (8.2)
7	Chronic Glomerulosclerosis	13 (6.7)
8	Other Profilferative Glomerulonephritis	12 (6.1)
9	Acute Tubular Necrosis	6 (3.0)
10	Pauci-immune Glomerulonephritis	4 (2.0)
11	Thrombotic Microangiopathy (HUS/TTP)	2 (1.0)
12	No opinion due to Inadequate Sample	5 (2.5)
13	Malignant Hypertension	1 (0.5)
14	Post-Infectious Glomerulonephritis	1 (0.5)
15	Diabetes Mellitus	1 (0.5)
16	Amyloidosis	1 (0.5)

HUS: *Hemolytic Uremic Syndrome*

TTP: *Thrombotic Thrombocytopenic Purpura*

Clinical Information:

Pre-biopsy clinical information was available in 174 reports. It consisted of Nephrotic Syndrome (NS) as the most common clinical impression necessitating kidney biopsy in 71 patients. However, clinical information was not appropriately mentioned in 20 (10.3%) of the kidney biopsies. [Table 3.]

Table 3. Clinical impression before kidney biopsy

S. No.	Clinical Information	Number	% of total available(n=174)
1	Nephrotic syndrome	71	40.8%
2	Swelling of body	34	19.5%
3	Systemic Lupus Erythematosus	25	14.3%
4	Rashes / Joint pain	4	2.2%
5	Others (Nephritic syndrome, Hypertension etc)	40	22.9%
6	Information not available	20	

Nephrotic Syndrome: FSGS accounted for the commonest post biopsy diagnosis in 22 (30.9%) of the patients with clinical impression of nephrotic syndrome (n=71). [Table 4.]

Table 4. Histological diagnosis of patients with clinical impression of

nephrotic syndrome

S.No.	Cause	n=71	(%)
1	Focal Segmental Glomerulosclerosis	22	(30.9%)
2	Minimal Change Disease	12	(16.9%)
3	Membranoproliferative Glomerulonephritis	9	(12.6%)
4	Membranous Glomerulopathy	8	(11.3%)
5	Immunoglobulin A Nephropathy	6	(8.4%)
6	Lupus Nephritis	3	(4.2%)
7	Chronic Glomerulonephritis	2	(2.8%)
8	Diabetes Mellitus	1	(1.4%)
9	Others	8	(11.3%)

Majority of the patients whose measured UTP was >3.5g per day had FSGS, Membranous Glomerulopathy or Minimal Change Disease in histology apart from Lupus Nephritis. [Table 5.]

Table 5. Common histology of kidney biopsy compared to 24 hour urinary total protein (UTP)

S. No.	Diagnosis	24hour UTP >3.5Gm/D n=60	24hour UTP ≤3.5Gm/D n=47
1	Focal Segmental Glomerulosclerosis	14	11
2	Lupus Nephritis	10	11
3	Membranous Glomerulopathy	9	3
4	Minimal Change Disease	7	4
5	Immunoglobulin A Nephropathy	5	4
6	Membranoproliferative Glomerulonephritis	4	3
7	Chronic Glomerulosclerosis	4	4

Among the 40 patients with biopsy diagnosis of Lupus Nephritis, 32 (80%) were female and 8(20%) were male. WHO Class IV was the commonest pathological classification of LN. [Figure 1.]

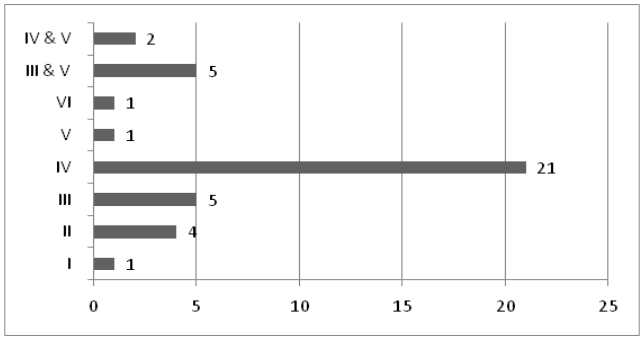

Figure 1. *Distribution of histological class of lupus nephritis*

DISCUSSION

Incidence and prevalence of GN varies worldwide. Studies from various parts of the world show different types of patterns of GN. The availability of high quality clinical trials in glomerular diseases is lacking. Some authors have suggested various reasons to the lack of strong clinical evidence: e.g.(i) low prevalence of disease; (ii) variability in clinical presentation; (iii) variability in treatment response; (iv) lack of consensus in definitions; (v) difficulty in recruiting patients; (vi) high costs of randomized controlled trials; and (vii) lack of collaborative efforts.[6]

Table 6. Comparison with other similar studies [7-11]

Diagnosis	Current Study	Aryal et al	Das et al	Balkrishnan et al	Mubarak et al	Parichatikanond et al
Reference No		*[7]*	*[8]*	*[9]*	*[10]*	*[11]*
Number	*n=194*	*n=137*	*1849*	*4035*	*1793*	*638*
Country	*Nepal*	*Nepal*	*India*	*India*	*Pakistan*	*Thailand*
Duration	*2007-2009*	*2001-2007*	*1990-2008*	*1990-2001*	*1995-2008*	*2003-2005*
Lupus nephritis	40	2	270	279	87	242
FSGS	38	11	195	677	380	32
IgA nephropathy	19	4	81	338	27	125
MPGN	19	30	169¶	412‡	54‡	20¶
MCD	16	14	279	437	104	8
MGN	16	58	129	384	308	64
Chronic GN	13	3	124	249†	208 +17∫	NR
TIN / ATN	6	2	124	144µ	209	NR
Pauciimmune GN	4	1	12	NR	94 Δ	NR
Post infectious GN	1	3	104	543	70	NR
Amyloidosis	1	2	27	41	83	5
Diabetic nephropathy	1	1	22	111	16	24
Other Diagnosis	15	6		420		118

FSGS=Focal Segmental Glomerulosclerosis; IgA= Immunoglobulin A; MPGN= Membranoproliferative Glomerulonephritis; MCD= Minimal Change Disease; MGN= Membranous Glomerulopathy; GN=Glomeruolnephritis; TIN= Tubulointerstitial Nephritis; ATN=Acute Tubular Necrosis. ¶=MesCGN+MPGN ‡=Mes PGN +MPGN †=ES Histology + Benign Nephrosclerosis ∫=Benign Neph µ=ATN+Inters Nephritis Δ=Cresc GN NR=Not recorded

Some relevant studies from neighboring countries have been shown in Table 6.[7-11] They have tried to study the distribution of various histological patterns of kidney biopsy results in corresponding setup.

Nephrotic Syndrome (NS) :

Nephrotic syndrome is pathognomonic of glomerular disease.[12] Our study demonstrates that NS is the commonest clinical indication for renal biopsy. This is also verified by the histological reports suggesting the most frequent findings in consistence with traditional causes of NS being at the top list. Similar results were obtained in other studies (Table 7). Nephrotic syndrome is the commonest indication for kidney biopsy worldwide.

Table 7. *Contribution of Nephrotic syndrome to Kidney Biopsy*

Country	Authors	Percent
Nepal	Aryal et al [7]	81.6%
India	Balkrishnan et al[8]	65.4%
India	Das et al[9]	49%
Pakistan	Mubarak et al[10]	49.9%

Urinalysis, which is cheap and easy, has been considered the first step for evaluation of kidney disease.[13] Whereas 24-hour protein excretion in urine remains the reference (''gold standard'') method for quantification of proteinuria in patients with glomerular diseases, spot urinary specimen testing are also being standardized.[14]

Proteinuria is both cause and result of kidney damage. Clinically, proteinuria is the simplest tool to detect kidney disease in hospitalized patients as well as in screening for kidney diseases. Proteinuria and its relation to the kidney disease has been described for centuries now. More recently, there has been increasing study of proteinuria and its relationship to kidney and cardiovascular disease, and as a potential target for intervention.[15]

Kidney Biopsy:

Kidney biopsy is mandatory for diagnosis of glomerular diseases. The single exception to this rule is Steroid Sensitive NS (SSNS) in children. Though kidney biopsy is mandatory, the role of clinical information is vital in the reporting of any biopsy specimen right from the staining procedure. Kidney Disease: Improving Global Outcomes (KDIGO) guidelines have also focused on the adequate clinical information to the histopathologist. The assessment of chronic damage from the biopsy must always be interpreted together with the clinical data to avoid misinterpretation if the biopsy is taken from a focal cortical scar.[14]

Lupus Nephritis (LN):

Lupus nephritis is the renal manifestation of Systemic Lupus Erythematosus (SLE). Our study demonstrates lupus nephritis to be the commonest indication for kidney biopsy. LN is the commonest secondary GN worldwide. Kidney Biopsy is indicated in patients with SLE with clinical renal abnormalities. Renal involvement in SLE starts far before clinical renal signs are evident. Mesangial changes are evident in patients with SLE even without clinical renal abnormalities.[16[

LN has varied clinical and pathological profile in varied population groups. Some ethnic groups have higher chances of having certain histopathological classes of LN lesions as compared to others. Certain ethnic groups may be more likely to have a serologic profile and renal lesions that were associated with more aggressive renal disease. Contreras et al. found that black patients were almost twice as likely to have WHO class IV lesions as white patients (51% versus 30%).[17] Different ESRD free survival rates have been described according to different classes of renal histopathologic lesions in LN.[18]

The Collaborative study found that the serology at presentation is different, the glomerular pathology is different, and the prognosis is significantly poorer for black compared with white patients with severe lupus nephritis.[18]

In our subcontinent, the most prevalent secondary glomerular disease in China and India is SLE.[19, 20] Higher frequency of LN cases in our cohort of renal biopsy may mean aggressive nature of SLE dominant in our study population.

Generally, GN is more common in the male than in the female population. Lupus nephritis is the major exception; the frequency is two or more times higher among the female than among the male population. However, since the female to male ratio of SLE is roughly ten, yet that of nephritis is only two to three, male patients with lupus seem more likely to develop nephritis than female patients.[3] Female preponderance in our study population is likely because of high number of LN patients, who are predominantly female.

Focal Segmental Glomerulosclerosis (FSGS): We found that FSGS is the commonest cause of NS in our study population contributing to 23% of cases with UTP>3.5gm/Day.

Idiopathic FSGS is often associated with a NS and may affect both children and adults. FSGS accounts for approximately 40% of cases of the nephrotic syndrome in adults, with an estimated incidence of 7 per 1 million.[21] Primary or idiopathic FSGS accounts for approximately 20% of cases of idiopathic NS in adults.

Studies have shown that FSGS stands as the commonest cause of primary NS in the US.[22] Braden et al reported an increasing incidence of FSGS as compared to Membranous GN.[20]

While the prognosis of FSGS is relatively good for patients with subnephrotic proteinuria, most patients with persisting proteinuria progress to ESRD in spite of glucocorticoid or immunosuppressive treatment. [24]

Renal biopsy is required to identify the pathologic class of FSGS, upon which the outcome of treatment may depend.[25]

Immunoglobulin A (IgA) Nephropathy:

IgAN is the most common form of GN worldwide, comprising 45% of all primary GN cases.[26] IgAN has been recognized as the most common form of primary GN in developed countries and remains an important cause of ESRD.[27,28] The frequency with which it is diagnosed varies between and within countries, mostly according to local policies regarding the indications for renal biopsy.[29] T

he prevalence of IgAN is higher in the western Pacific Rim and relatively low rates in the United States and Europe. Because of its high prevalence in Asian countries, IgAN is probably the most common form of GN worldwide.[30]

Almost 10% of our study population had IgAN. Commonest of the clinical impression in IgAN were NS, hypertension and hematuria. In general, NS is, however, not the commonest clinical presentation of IgAN as compared to episodic hematuria. Because most cases of episodic hematuria may not attend the hospitals till late, this result may not be the exact representation of the actual burden of diseases.

Membranous Nephropathy(MN):

Membranous nephropathy is the leading cause of NS in the adults. Idiopathic MN population that progresses to ESRD remains relatively small, the absolute numbers are large, and because it affects people predominantly in their 30s and 40s, it has an enormous long-term impact on their quality of life and productivity.[31] Because of its frequency, it remains the second or third most common type of primary GN resulting in ESRD. [32] Our study population comprised of 8.2% MN patients where MN contributed 15% to the total number of patients with UTP >3.5gm/D.

Minimal Change Disease(MCD):

MCD accounts for 10–15% of all cases of primary adult nephrotic syndrome.[33-34] Incidence of MCD is reported to be as low as 1 per million in the United Kingdom and up to 27 per million in the United States. It is more common in South Asians and Native Americans but is much rarer in African Americans. MCD is also relatively rare in developing countries, such as most countries in Africa and South America.[35] MCD comprised of 8.2% of our total study population, and 11.7% of those patients whose UTP was >3.5gm/D.

CONCLUSION: Our study demonstrates the commonest indication of kidney biopsy is SLE. Nephrotic Syndrome is the commonest clinical indication for kidney biopsy and LN is the commonest histological diagnosis. FSGS is the commonest cause of nephrotic syndrome in our study population.

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