An Audit Of Kidney Biopsy Findings In A Tertiary Care Nephrology Department: 2010-2013.

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ABSTRACT:

BACKGROUND:

Renal biopsy, although an invasive procedure, still remains the last court of appeal in patients with clinical suspicion of glomerulonephritis. In most of the cases it will establish the diagnosis, stage the disease and provides information about the potential therapeutic modalities that can be employed.

We report our experience with renal biopsy in our tertiary care setup. A comparison with local and international data will follow.

METHODS:

This was a retrospective analysis of renal biopsies conducted at Department of Nephrology, Fatima Memorial Hospital in the period between February 2010 to August 2013 (three years and 6 months).

RESULTS:

During the period between February 2010 and October 2013, a total of 260 biopsies were conducted on the native kidneys. There were 137 (52.5%) females and 124 males (47.5%). The mean age was 31.40 + 13.63 years (median: 28 years, range: 3 – 77 years). In all patients at least two cores were taken. 22 (8.5%) biopsies failed to yield glomeruli sufficient to make a diagnosis. Mean number of glomeruli obtained were 12.29 + 7.72 (median: 10, range: 1 – 46). Out of the total cohort 38.3% (n=100) had PGD, 48.3% (n=126) had SGD and rest of the patients (5%; n=10) had other diagnoses**.**

LIMITATIONS:

Immunostaining could not be carried out on all specimens.

CONCLUSIONS:

The renal biopsy findings in our centre are similar to those reported elsewhere in internationally.

KEY WORDS:

Renal Biopsy, Ultrasound guided, Pathology, Immunostaining,

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INTRODUCTION:

Renal biopsy, although an invasive procedure, still remains the last court of appeal in patients with clinical suspicion of glomerular disease. In most of the cases it will establish the diagnosis, stage the disease and provides information about the potential therapeutic modalities that can be employed.

We report our experience with renal biopsy in our tertiary care setup. A comparison with local and international data will follow.

MATERIALS AND METHODS:

It was a retrospective observational study. Renal biopsy was performed by nephrology team using ultrasound guidance and spring loaded biopsy needle and the samples were carried immediately to the Department of Pathology. The specimen was processed for light microscopy (hematoxylin and eosin, John's methanamine silver and Periodic acid Schiff stains and other stains if required) and immunostaining. Weekly nephron-pathology meetings were held for appropriate diagnosis. We evaluated our biopsy records and findings were recorded in a specialized proforma. For the purpose of discussion the etiology was divided into three broad categories: **Primary Glomerular Diseases (PGD)** included Focal Segmental Glomerulosclerosis (FSGS), Membranous Glomerulonephritis (MGN), Membranoproliferative Glomerulonephritis (MPGN), IgA Nephropathy (IgAN), Mesangioproliferative Glomerulonephritis (MesPGN), Post Streptococcal Glomerulonephritis (PSGN), Minimal Change Disease (MCD) and Crescentic GN (CGN). **Secondary Glomerular Diseases** (SGD) included Lupus Nephritis (LN), Diabetic Nephropathy (DN), Amyloidosis and rarer entities like Thrombotic Microangipathic Glomerulonephritis. The third category comprised of entities such as End Stage Renal Disease (ESRD), Acute Tubular Necrosis (ATN), Tubulointerstitial Nephritis (TIN) and Primary Hyperoxaluria (PH).

RESULTS:

During the period between February 2010 and October 2013, a total of 260 biopsies were conducted on the native kidneys. There were 137 (52.5%) females and 124 males (47.5%). The mean age was 31.40 $\pm$ 13.63 years (median: 28 years, range: 3 – 77 years). In all patients at least two cores were taken. 22 (8.5%) biopsies failed to yield glomeruli sufficient to make a diagnosis. Mean number of glomeruli obtained were 12.29 $\pm$ 7.72 (median: 10, range: 1 – 46). Out of the total cohort 38.3% (n=100) had PGD, 48.3% (n=126) had SGD and rest of the patients (5%; n=10) had other diagnoses, Table 1 .

Table 1: general characteristics of 261 kidney biopsies performed at Fatma Memorial Hospital Hopsital from 2010-2013

Number of Biopsies: 261
Mean age of patients: 31.39 ± 13.61 years (median: 28 years, range 3 – 77 years)
Gender distribution: Males 47.5% (n=124), Females 52.5% (n=137)
Mean number of glomeruli: 12.29 ± 7.72 (median: 10, range: 1 – 46).
Primary Glomerular Diseases: 38.3% (n=100)
Secondary Glomerular Diseases: 48.3% (n=126)
Diseases not characteristic of glomerular disorder: 5% (n=13)
Missed biopsies: 8.4% (n=22)

DISCUSSION:

Renal biopsy has proven to be the gold standard for diagnosis of glomerular disease. Since the first biopsy was performed in 1901[1], the technique has come a long way making it a safe procedure. The information obtained from renal biopsy can potentially alter management decisions.

The distribution of glomerular diseases in our cohort was such that PGD accounted for 38.3%, SGD 48.3% and disorders not characteristic of glomerular pathology accounted for 5%. This is in contrast to Li L et al[2], Gesualdo L[3] and Rabbani[4] MA et al. However in our cohort the main reason of high rates of SGD is the presence of large number of cases of Lupus Nephritis. This is also supported by a study by Al Riyami et al[5] where a distinction was not made between primary and secondary glomerular disorders and Lupus Nephritis was the most common pathology.

The mean age of our cohort at the time of biopsy was 31.31 ± 13.69 years (median: 28 years; range: 3 – 77 years). This is in agreement with most of the local and international studies [2,4,6,7,8]

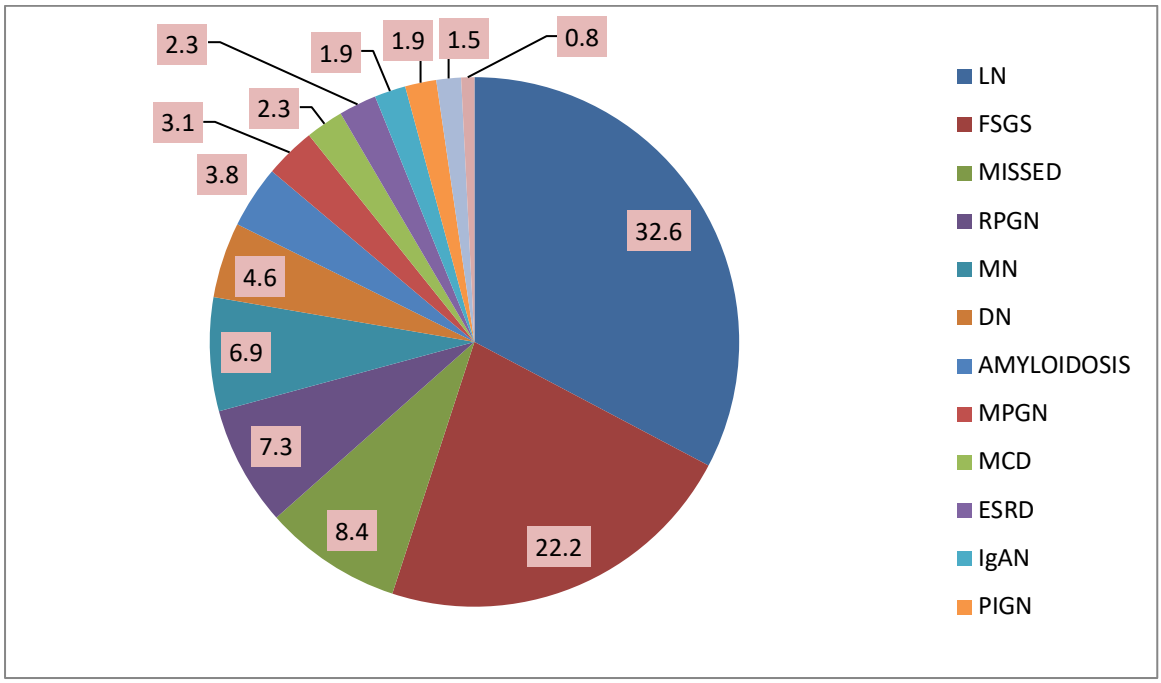
Focal Segmental Glomerulosclerosis was the most common PGD (58%) 22.2% of the total cohort). This is in agreement with Osmani MH et al[9] who reported the incidence at around 15% (however this study only included 152 biopsies) and Sabir et al[10] (although their study included only 60 cases), however our finding is different from Anwer et al[11], their study took into account patients with nephrotic syndrome above 40 years of age. Our findings are also different from Khan Y et al[6]; their study gives the incidence of FSGS at 7% only. Our finding is more in accordance with the international data and notion that FSGS is fast becoming most common GN worldwide[12,13,14,15,16]. These studies also indicate that large urban hospitals are reporting FSGS at a higher frequency. The reason behind this observation remains unknown although possible causes may include more renal biopsies performed due to better economic circumstances.

Among the PGD, **Membranous GN** was the second most common pathology recognized (18%, 6.9% of the total cohort). The mean age of the patients was 40.72 ± 11.15 years (range: 17 – 63 years). This pathology has been recognized to be common in our local literature[9,11]. The overall incidence of MGN internationally has been thought of giving way to FSGS as discussed above[12,13,14,15,16,17].

Crescentic GN was also a common pathology which made up 15.1% of the primary glomerular diseases and 7.3% of the whole cohort. The mean age of the patients was 37.76 ± 15.69 years

(range: 18 – 72 years). This is in contrast to findings reported by Al Wakeel et al[8] (1.7%), Li et al[2] (1.9%), Zhou et al (2.64%)[18], Rabbani et al[4] (6.4%) and Muzaffar S et al[19] (6.3%) but

Figure 1: Distribution Of Glomerular Diseases reported on 261 native kidney biopsies.



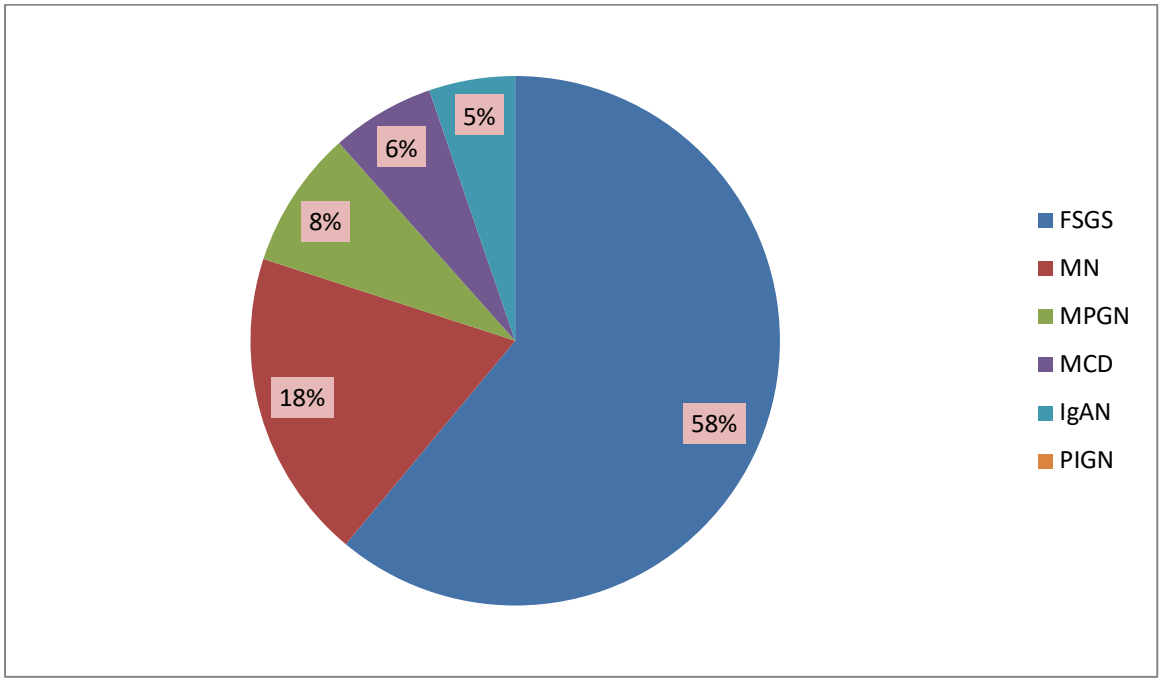
closer to Covic A et al[20]. It is also to be appreciated that in some studies crescentic GN has shown an increase in the recent periods[21]. In case of Crescentic GN the timing of biopsy is important. Late biopsies may not reveal epithelial crescents and advanced tubule-interstitial findings may make the biopsy sample non-specific for diagnosis. Our practice is to do a renal biopsy as soon as possible after presentation. Even in patients presenting with indications of dialysis, we usually perform a biopsy on the third day of presentation after two sessions of dialysis. This may partially account for higher rates of crescentic GN as seen in our study.

MPGN was also common among PGD at 8% (3.1% of the total cohort). The mean age of the patients was 19.3 $\pm$ 7.6 years (range: 14 – 31). This finding is again different from Khan Y[6] (22%) and Rabbani et al[4]. The latter study puts the rate of MPGN at 28.2% which is particularly high even when compared to loco-regional data[9,10,11,22] and international data[2,12,23]. Our findings closely resemble those of Sabir et al[10] (1.6%), Li et al[2] (3.38%), Mitwalli et al[23] (9.5%), Osmani[12] et al (9.86%) and Swaminathan S[9] et al (13%). It must be mentioned that care was taken to exclude secondary causes of MPGN in our study and we believe that the cohort of MPGN that we had was idiopathic MPGN. The apparent differences in the rates of incidence would be explained on the basis of regional differences as evidenced in other studies from across the world.

Minimal Change Disease was seen in 6% of PGD (2.3% of the total cohort). This is not surprising because our study did not include a big population of children where it is considered to be the most common GN and biopsy is usually not performed in these patients. Nevertheless local data places the incidence at 11% (Osmani MH et al)[9] to around 16% (Rabbani et al)[4] and 17% (Khan Y et al)[6]. We are unable to explain such high incidence of MCD in the earlier reports from Pakistan although it may have to do with the catchment area of the population and thus inclusion of pediatric biopsies (Rabbani et al)[4]. It is also to be appreciated that the differential in these cases includes early lesions of MGN and FSGS especially if immune-

staining studies and electron microscopy are not carried out. We also suspect that studies reporting such high rates may have included patients with secondary MCD, most likely Non-Steroidal Anti Inflammatory Drugs associated MCD. We suspect that the incidence of MCD in supposedly adult population as reported by our contemporaries may have been lower if immune-staining and electron microscopy were routinely carried out or cases suspected of having Secondary MCD ruled out. However our incidence is similar to some international studies[2,3,12,24].

Figure 2: Distribution of Primary Glomerular Diseases among the 100 out of 261 native kidney biopsies.

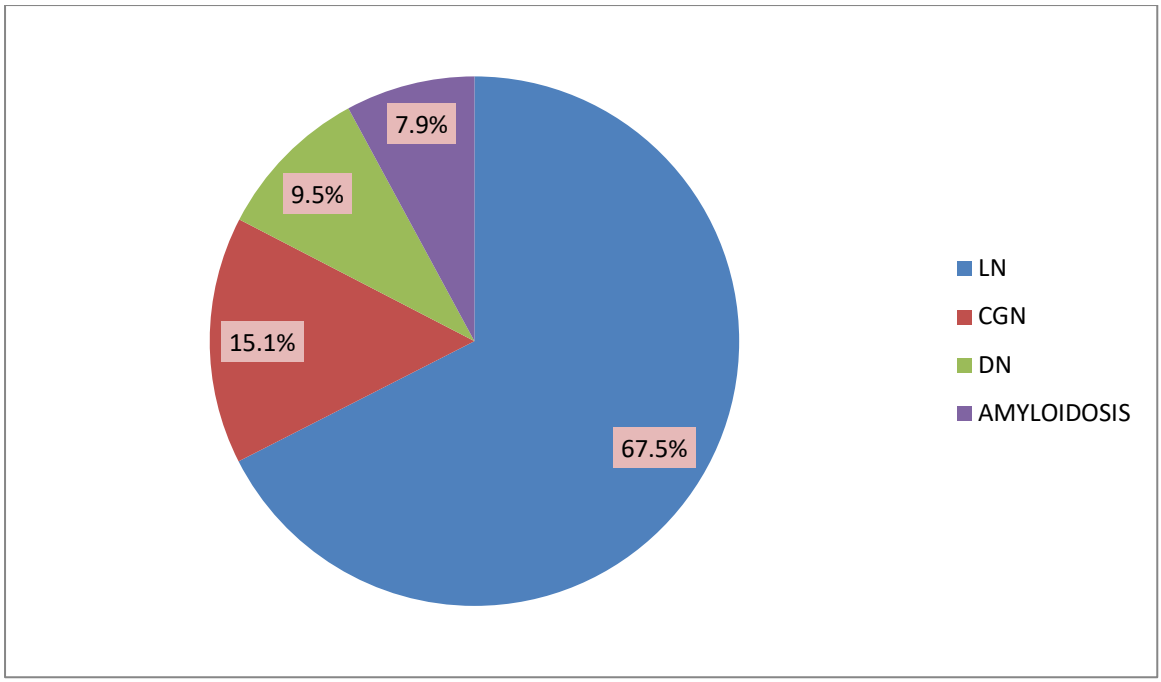


IgA Nephropathy was found in only 5% of the PGD (1.9% of the total cohort). The mean age of the patients was 32.75 ± 16.43 years. (range: 14 – 48 years). This is close to the incidence reported by Rabbani et al but is surprisingly low when compared to renal biopsy data from different regions of the world.[2,22,23,25,26] Another study from Pakistan reported the incidence at around 12.6%.[19] This disease can be asymptomatic and patients may have been biopsied while having unexplained microscopic hematuria in setups where there is regular screening of the urine e.g. Japan. We may have missed IgA Nephropathy cases when our institute was not carrying out regular immune-staining. The histopathology in early cases may be normal and the only ways in which diagnosis can be made would be to immune-stain the biopsy specimen or do an electron microscopy.

Post infective GN (Non IgA) was found at a frequency of 5% of the PGDs (1.9% in total). The mean age of the patients was 21.2 ± 9.03 years (range: 13 – 30 years). All of these cases were likely post streptococcal GN except one patient who had GN secondary to infective endocarditis. Rabbani et al[4] reported same incidence (10/511 biopsies (1.9% calculated); 9.2% of the SGD)). Al wakeel J[8] et al reported the incidence to be 3.3% of the PGD. Khan Y[6] et al found Acute PIGN to be around 9% of the total cohort of the patients with significant proteinuria. Distinction was not made between IgA and Non IgA cases. Sabir S[10] reported the incidence to be 1.6%. Anwer N et al[11] report similar findings but they included patients who

were more than 40 years of age. Generally our rate of PIGN is lower than the rates reported from the region. Golay V et al[15] report the incidence to be around 5%. However higher rates have also been reported from some regions e.g. Malafronte et al (12.5% of the SGD). The low incidence being reported from this region as compared to other countries may also have to do with the racial difference as proposed by Golay V et al[15].

Figure 3:Distribution of Secondary Glomerular Diseases among 126 out of 261 native kidney biospies.



Our data shows that the most common secondary GN was **Lupus Nephritis** (LN) (67.5%, 32.6% of the total cohort). The mean age of patients was 27.17 ± 10.83 years (range: 12 – 62 years). The age at presentation was similar to other studies reported from Pakistan[4]. Gender distribution was 73 females and 5 males (ratio: 14:1). Our incidence of LN on biopsy is in agreement with Al Riyami et al who reported an incidence of LN to be around 36% in his case series[5]. It must be mentioned that our institute has a referral centre for systemic lupus

Table 2: detailed description of kidney biopsies with diagnosis of lupus nephritis.

Lupus Nephritis (Class)	**Frequency (n=85)**	**Immunostain (n=53)**	**Frequency**
I	1.2%	IgM	30.6%
II	20.%	IgG	56.5%
III	17.6%	IgA	35.3%
IV	45.9%	C3	20%
V	7.1%	C1q	22.4%
VI	4.7%		
III + V	1.2%		
IV + V	1.2%		

erythematosus patients hence the difference of our data from the rest of the local data where LN was not the major cause of GN[9,11]. The frequency of different classes is shown in table 2. This is generally in accordance with data reported from this region.[27,28]. The immune-stain was carried out in 48 patients (60.8%) and the pattern is given in the Table 2.

Another common secondary GN was **Amyloidosis** which occurred with a frequency of 7.9% (3.8% of the full cohort). The mean age was 43.2 $\pm$ 7.88 years (range: 25 – 51 years). This agrees with the local data by Khan Y[6](7%) whereas Sabir et al[10] places it at 1.6%. Both these authors do not make distinction between PGD and SGD in their papers. The incidence of amyloidosis by Rabbani et al[4] (22% of the SGD) and Anwer N et al[11] (12.5% of total biopsies) is quite high as compared to local data (including ours). Balakrishnan et al[22] places the incidence at 1% of the total biopsy proven renal diseases whereas Li et al[2] places the incidence at 2.2% of the secondary glomerular disorders. Our incidence shows that in this region amyloidotic kidney disease occurs at a variable rate. It must be kept in mind that classical apple green birefringence may be difficult to pick up and technical mistakes in the application of the stain may underestimate the true incidence.

Diabetic Nephropathy was diagnosed in 9.5% specimens (4.6% of the total cohort). The mean age of these patients was 42.18 $\pm$ 9.72 years (range: 26 – 55 years). The usual indications for biopsy in diabetic patients were followed. Our incidence is similar to Rabbani et al[4] (10.1%) and Al Riyami[5] (3.8% of the total cohort). Some local studies excluded diabetic patients from their study population (Khan Y et al and Anwer N et al). The regional and international data varies in this regard: Balakrishnan et al[22] (2.8% of the total cohort), Malafronte P et al[7] (6.2% of the secondary GN) and Al Khunaizi[25] (14%). The variable incidence of diabetic nephropathy may suggest variable approach to biopsy in diabetic patients in different regions of the world.

Rest of the patients were found to have **ATN** (n=4, 1.5%), histopathological findings characteristic of **ESRD** (n=6, 2.3%), rare cases of **Tubulointerstitial Nephritis** (n=2, 0.8%) and one case of **primary hyperoxaluria** (0.4%) with characteristic crystals in the interstitium and tubules.

CONCLUSION:

Our data is generally similar to the data being reported from the region but exceptions are also seen. These exceptions may be due to approach of our nephrology team towards the procedure of renal biopsy. However to resolve these differences we strongly recommend creation of renal biopsy registries at local, provincial and national level.

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