Spectrum of Glomerular Diseases at King Hussein Medical Center

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ABSTRACT

Objective: To determine the histopathological patterns of glomerulonephritis according to the clinical presentation.

Methods: This is a retrospective analysis of light microscopy results of native kidney biopsies done during the period of January 1st, 2005 until December 31st, 2008. There were 273 native kidney biopsies performed during this period. Data were collected from the computer data base of Princess Iman Research and Laboratory Center, King Hussein Medical Center, Amman, Jordan. All biopsies were examined by our renal histopathologist.

Results: The most common indication was nephrotic syndrome and the most common cause of nephrotic syndrome in our patients was membranous glomerulonephritis. The main cause of subnephrotic proteinuria was minimal change disease and focal and segmental glomerulosclerosis. Membranoproliferative glomerulonephritis was the most frequent finding in patients presenting with microscopic hematuria. In acute nephritis the most common lesions were crescentic, diffuse proliferative and necrotizing glomerulonephritis. Acute tubular necrosis was the most common cause of acute kidney injury. Changes of end stage kidney disease were the most frequent findings in patient with chronic kidney disease. In patients with systemic lupus erythematosus with renal involvement, the most common lesion was class IV lupus nephritis.

Conclusion: Kidney biopsy is an extremely helpful investigation and it should be performed once indicated. There is a need for a national registry of kidney biopsies. The histopathological findings are similar to other studies done in Jordan and in the neighboring countries.

Key words: Chronic kidney disease, Diagnostic procedure, Glomerulonephritis, Kidney biopsy

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Introduction

Glomerulonephritis (GN) is one of the leading causes of chronic kidney disease (CKD) and end stage renal disease (ESRD). GN has been found as the second most common cause of CKD in north of Jordan, the first being diabetes mellitus.[1] The etiologies of glomerular insults vary, but include systemic disorders, hereditary diseases, drugs and toxins besides primary glomerular pathologies.

Accurate diagnosis of glomerular diseases depends on histopathological examination of kidney biopsy.

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Table I. Presentation categories of the study group

	No. of Patients	%
Proteinuria	139	50.9
SLE	38	13.9
Abnormal KFT	53	19.4
Acute Nephritis	21	7.7
Hematuria	12	4.4
ARF	9	3.3
Kidney Donor	1	0.4
Total	273	100

Table II. Demographic data of the patients

Number of patients	273
Male:	134 (49 %)
Female:	139 (51%)
Age: (years)	
Range	14 - 75
Average	35.36
SD	14.07

In a patient with renal disease, kidney biopsy provides tissue that can be used to determine the diagnosis, indicate the etiology, predict the prognosis, and direct therapy.[2,3,4]

Kidney biopsy is a core procedure in the nephrology practice. Confidence and competence in performing this procedure should be one of the goals of training in nephrology, as in the majority of nephrology training centers in the United States.[5] Kidney biopsy is indicated in a patient with renal disease when all the three of the following conditions are met.[6]

1. The cause cannot be determined or adequately predicted by less invasive diagnostic procedures.
2. The signs and symptoms suggest parenchymal disease that can be diagnosed by histopathological evaluation.
3. The differential diagnosis includes diseases that have different treatment, different prognosis or both.

In order for golmerular lesion to be diagnosed with confidence, kidney biopsy should be adequate (containing six or more glomeruli for light microscopy). The results of kidney biopsy will help in studying the natural history of glommerular diseases, identify the patients at risk, and predict their prognosis.[6]

We present our experience during four years to report the findings and to compare with previous national, regional and international studies.

Methods

This is a retrospective analysis of light microscopy results of native kidney biopsies performed for adult patients in King Hussein Medical Center, Amman, Jordan, during the period from January 2005 to December 2008. There were 273 native kidney biopsies.

The results of light microscopy examination of these biopsies were collected from the computer data base of Princess Iman Research and Laboratory Center, King Hussein Medical Center, Amman, Jordan. All the biopsies were examined by our renal histopathologist.

Patients presenting with proteinuria whether nephrotic (3.5gm or more of urinary proteins per 24 hour), or subnephrotic (less than 3.5gm of urinary proteins per 24 hour) and / or hematuria, unexplained acute kidney injury, nephritic presentation, or those with unexplained abnormal renal function were investigated by kidney biopsy. (see Table I)

Patients scheduled for kidney biopsy were admitted to the hospital at least one day prior to the procedure. Blood pressure and coagulation profile were deemed normal before the biopsy. The procedure was performed by an experienced nephrologist under ultrasonograghic guidance.

Indications for kidney biopsy were:

1. Nephrotic syndrome.
2. Persistent sub-nephrotic proteinuria.
3. Unexplained abnormal kidney function test.
4. Acute kidney injury.
5. Acute nephritic presentation.
6. Hematuria (after excluding urological causes).
7. Assessment of serologically confirmed systemic lupus erythematosus with renal involvement.
8. Evaluation of kidney donor.

A standard procedure in our center is to have three specimens from each patient for light microscopy, immunoflourescene and electron microscopy.

Post biopsy, patients were observed for at least 24 hour for vital signs monitoring, development of persistent hematuria and documentation of their hematocrit level.

Kidney biopsy was not performed for patients with known cause of renal pathology, i.e. diabetic patients with microvascular complications, patients with resolving acute kidney injury secondary to specified causes (medications, prerenal or postrenal causes), furthermore kidney biopsy was not

Table III. Clinical indications for kidney biopsy

	Male		Female		Total	
	Number	**Age *years* *Average (SD)***	**Number**	**Age *years* *Average (SD)***	**Number**	**Age *years* *Average (SD)***
Nephrotic Syndrome	53	35.7 (12.6)	48	36.4 (12.5)	101	36 (12.5)
Sub nephrotic proteinuria	22	36.8 (16.4)	16	34.8 (14.5)	38	35.9 (15.4)
Abnormal KFT	30	40.6 (15.5)	23	35.7 (14.2)	53	38.05 (15)
Microscopic hematuria	8	36.5 (17.9)	4	44 (16.4)	12	39 (17.7)
Nephritic syndrome	13	34.3 (16.2)	8	31.4 (17.5)	21	32.4 (15.8)
Acute renal failure	4	57 (6.8)	5	29 (5.2)	9	41.4 (15.7)
SLE	4	33 (11.2)	34	25.8 (8.2)	38	26.5 (8.7)
Evaluation of kidney donor	--	--	1	37	1	37
Total	134		139		273	

performed for patients with contraindication for kidney biopsy such as:

1. Uncorrectable bleeding diathesis
2. Small kidneys (less than 9 cm in length)
3. Multiple bilateral renal cysts or any space occupying lesion (tumor)
4. Significant hydronephrosis
5. Active urinary tract infection
6. An uncooperative patient
7. Solitary kidney
8. Uncontrolled hypertension

Results

A total of 273 native kidney biopsies were performed during the period between January 2005 and December 2008. Female patients were 139 (51%), and age range was 14 – 75 years, with an average of 35.3 years (SD+\-14). Table II summarizes the patients' demographic data.

The most frequent indication for the biopsy was proteinuria found in 139 patients (50.9%), and 101 (72.7%) of these had nephrotic syndrome. Hematuria was the indication for kidney biopsy in 13 patients (4.8%). One of them was a potential kidney donor for her son, found to have microscopic hematuria.

Patients with unexplained chronic kidney disease were 53 patients (19.4%), while 21 patients (7.7%) presented with a picture of acute nephritis. Renal involvement in systemic lupus erythematosus (SLE) was the indication in 38 patient (13.9%) and unexplained acute renal failure was the indication in nine patients (3.3%) (see Table III).

Some patients had more than one indication for kidney biopsy (e.g. proteinuria and hematuria, or proteinuria and impaired kidney function). Those were put in a group according to the main presenting symptom.

Patients who presented with acute nephritis were the most serious ones, whether according to clinical picture or to the biopsy results. Those were 21 patients, 13 males (62%) and eight females (38%). Their age ranged from 14 to 70 years, with an average of 33.19 years (SD+\-16.2). Their biopsy results are shown in Table IV.

Patients with unexplained acute kidney injury for whom kidney biopsy was performed (other than those who presented with acute nephritis) were nine patients; there were five females (55.6) and four males (44.4). Their age ranged from 21 to 67 years, with an average of 41.4 year (SD+\-15.8). Biopsy results are shown in Table V.

Kidney biopsy was done for 13 patients with hematuria after systemic and urological causes were excluded. There were eight males (61.5%) and five females (38.5%). Their age ranged from 21 to 75 years with an average of 39 years (SD+\-17.7). Results of kidney biopsies are shown in Table VI.

Patients presented with unexplained deterioration of kidney function (chronic kidney disease) with preserved kidney morphology on ultrasound evaluation were 53 patients, 30 males (56.6%) and 23 females (43.4%). Their age ranged from 18 to 72 years with an average of 38.5 years (SD +\-15). Histopathological findings of their kidney biopsies are shown in Table VII.

The majority of the patients presented with nephrotic syndrome. They were 101 patients, 53 male (52.5%) and 48 female (47.5%). Their age ranged from 14 to 72 years, with an average of 36 year (SD +\-12.5). Histopathological findings of their kidney biopsies are shown in Table VIII.

Patients with subnephrotic proteinuria were 38, males were 22 (57.9%), and females were 16 (42.1%). Age range was 15-70 years, with an average of 36.4 years (SD+\-15.9).

Table IV. Histopathological lesions in patients presenting with acute nephritis

	No. of Patients	%
Crescentic GN	5	23.8
Diffuse proliferative GN	5	23.8
Necrotizing GN	5	23.8
MPGN	2	9.5
Post infectious GN	3	14.3
Scleroderma renal crisis	1	4.8
Total	21	100

Table V. Histopathological lesions in patients presenting with unexplained acute renal failure

	No. of Patients	%
ATN	4	44.44
Resolving ATN	2	22.22
Myeloma kidney	3	33.33
Total	9	100

Table VI. Histopathological lesions in patients presenting with hematuria

	No. of Patients	%
Hypertensive changes	1	8.3
IgA nephropathy	3	25
MPGN	4	33.3
Normal findings	2	16.7
Post infectious GN	1	8.3
Inadequate specimen	1	8.3
Total	12	100

Table VII. Histopathological lesions in patients presenting with chronic kidney disease

	No. of Patients	%
Amyloidosis	1	1.9
Chronic GN	6	11.3
ESRD	23	43.4
Diabetic nephropathy	1	1.9
FSGS	5	9.4
Hypertensive changes	4	7.5
MPGN	6	11.3
Interstitial nephritis	2	3.8
Ischemic nephropathy	1	1.9
Myeloma kidney	1	1.9
Inadequate specimen	3	5.7
Total	53	100

Histopathological findings of their kidney biopsies are shown in Table IX.

Kidney biopsy was done for 38 patients with newly diagnosed systemic lupus erythematosus (SLE) for various indications (acute renal failure, proteinuria,active urinary sediment). They were 34 females (89.5%) and four males (10.5%). Their age range was 14-55 years, with an average of 26.5 years (SD+\-8.7). Histopathological findings of their kidney biopsies are shown in Table X.

Inadequate specimens were obtained in 12 (4.4%) biopsies out of the total number of our series. These biopsies were either containing less than six glomeruli, or containing renal medullary tissue, or non renal tissue. Patients whom biopsies were inadequate were biopsied again with satisfactory results.

The most common complication of the procedure was pain at the biopsy site, seen in 53 patients (19.8%). Significant drop in the hematocrit (more than 3% drop from the base line hematocrit) was seen in three patients (0.01%), one of those three patients developed gross hematuria, requiring blood transfusion, and none needed any further intervention apart from ultrasonographic follow up, which showed subcapsular hematoma that was treated conservatively. None of the patients developed life threatening complications or loss of renal tissue.

Discussion

Glomerular lesions manifest clinically as proteinuria, hematuria, fluid retention, hypertension, progressive loss of kidney function of variable severity, or a combination of all these presentations, and occasionally it may be asymptomatic.

Our purpose was to outline the type of variable glomerular diseases among patients presented or referred for nephrology care or opinion at King Hussein Medical Center. Analysis of the data was done according to the main presenting symptoms and the main indication for biopsy.

There were 273 adult kidney biopsies during the period between 1st of January, 2005 until 31st of December, 2008. Surgical specimens, transplant and pediatric kidney biopsies were excluded.

The largest number of patients for whom kidney biopsies were performed, were those presenting with the nephrotic syndrome. These were 101 patients (37%) and this was almost the same percentage as in previous similar national,[7,8] regional[9] and international[10,11] studies. This reflects a fairly common presentation and the necessity of tissue

Table VIII. Histopathological lesions in patients presenting with nephrotic syndrome

	No. of Patients	%
Amyloidosis	4	3.9
MCD	23	22.8
Membranous GN	36	35.8
Diabetic nephropathy	6	5.9
FSGS	22	21.8
MPGN	6	5.9
Post infectious GN	1	0.9
Inadequate specimen	3	2.9
Total	101	100

Table IX. Histopathological lesions in patients presenting with subnephrotic proteinuria

	No. of Patients	%
Amyloidosis	2	5.3
MCD	6	15.8
Membranous GN	5	13.1
Diabetic nephropathy	1	2.6
FSGS	6	15.8
Hypertensive changes	6	15.8
Interstitial nephritis	3	7.9
Inadequate specimen	2	5.3
MPGN	3	7.9
ESRD	1	2.6
Focal proliferative GN	1	2.6
Normal	2	5.3
Total	38	100

Table X. Histopathological lesions in patients presenting with SLE

	No. of Patients	%
Normal	1	2.6
Class II	2	5.3
Class III	7	18.4
Class IV	18	47.4
Class V	6	15.8
Class VI (ESRD)	1	2.6
Inadequate specimen	3	7.9
Total	38	100

diagnosis in the management of the nephrotic syndrome. The main histopathological finding was membranous glomerulonephritis (MGN), followed by minimal change disease (MCD), then by focal and segmental glomerulosclerosis (FSGS). These glomerulonephritis are the main causes of the nephrotic syndrome which is similar to what has been described before[7-12] but with a different profile. In some studies the predominant lesion was MCD,[12] while in other it was FSGS.[8,9] However our results are similar to previous finding in Jordan[7] and in Iran.[10]

Patients presented with subnephrotic proteinuria comprised 13.9% of the sample. Their biopsy results showed the main glomerular lesions as MCD, FSGS and hypertensive changes as the predominant causes followed by MGN. This is broadly similar to the etiology of the nephrotic syndrome with a different pattern of frequency. The mechanism of glomerular injury and proteinuria is similar in the same disease that may produce nephrotic or subnephrotic proteinuria, the difference may be due to functional and other associated glomerular insults,[9,13] or the presence of other co morbid conditions.

Abnormal kidney function test (KFT) was the indication in 19.4% of the patients. This may represent a selection bias as patients presenting with known causes of CKD or those who were found to have small kidneys were not biopsied. However, the primary pathology of patients presenting with CKD would be of interest, even in patients requiring renal replacement therapy. This is of particular importance knowing that certain glomerular pathologies may recur after kidney transplantation. Almost in half of our patients the glomerular disease was identified. The most common pathologies identified were MPGN, FSGS and hypertensive nephrosclerosis. This finding is the same as what has been described in Jordan.[7]

Patients with hematuria (macroscopic or microscopic) not secondary to urological causes comprised 4.8% of the study group. This is similar to previous data.[9] MPGN and IgA nephropathy were the most common causes of glomerular hematuria among our patients. MPGN was the predominant cause in an Asian study[14] while IgA nephropathy was the predominant cause in Europe.[15] As compared to the total number of biopsies performed, those patients with IgA

nephropathy are 1.4%, similar to what was reported in Jordan,[1] probably reflecting high threshold to perform kidney biopsy in patients with isolated hematuria.

Our single case of kidney biopsy for a prospective kidney donor was for a 42 year old healthy female found to have microscopic hematuria during pre kidney donation for her 10-year old son. All her investigations were normal including renal angiogram and cystoscopy. Her kidney biopsy was normal. She donated a kidney for her son and follow up showed normal kidney function for both of them. (Our study examines only the results of light microscopy)

Patients' presenting with the frank nephritic syndrome were categorized separately from those presenting with acute kidney injury due to non nephritic causes. This is due to the nature of the glomerular pathologies leading to nephritic syndrome, which is considered as the most aggressive of renal diseases requiring advanced and aggressive management.

Nephritic syndrome was the indication in 7.7% of our patients. As expected, the majority of these cases turned to have aggressive forms of GN. The most frequent ones were crescentic GN, diffuse proliferative GN, and necrotizing GN (vasculitis). Similar results, similar age group but with a greater percentage of patients has been described in other studies.[9,16] The lower percentage of patients in our study can be attributed to the separation of patients presenting with the nephritic syndrome from those with non nephritic acute renal failure. In these cases, it was proved beyond any doubt that kidney biopsy is an extremely valuable diagnostic procedure in patients presenting with rapidly declining kidney function, as the early and aggressive management is highly rewarding.

Acute kidney injury due to non nephritic presentations was the indication in only 3.3% of patients, probably reflecting selection bias, as kidney biopsies were performed for patients who did not respond or showed sluggish response to conventional management to acute kidney injury.

Acute tubular necrosis was the major cause, strikingly in one third of acute kidney injury cases the cause was myeloma kidney. The renal involvement in multiple myeloma varies and can be due to many causes and it has been reported that multiple myeloma may present itself as ARF.[17-20] Multiple myeloma was mentioned as a cause of CKD in Jordan.[7] This may represent late referral to nephrology care or unawareness of the patients of the slow development of the disease process of multiple myeloma until presenting as renal failure.

Kidney biopsies were performed in 38 patients with serologically confirmed SLE with evidence of renal involvement. Renal involvement in SLE is most likely to occur on its own and these patients need more close follow up than those without renal involvement.[21] Kidney biopsy in SLE patients with any criteria of renal involvement was of major benefit as almost half of our lupus patients proved to have the aggressive class IV lupus nephritis. The management of lupus nephritis is entirely dependent on histological diagnosis to classify the lesion according to the International Society of Nephrology/Renal Pathology Society lupus nephritis classification[22] which carries diagnostic, therapeutic and prognostic criteria.[23] This was the case with our SLE patients, as in order to reverse or at least retard the aggressive presentation, aggressive management including immune – modulating therapy[24-27] was indicated.

Conclusion

Kidney biopsy is an extremely helpful investigation in the hands of nephrologists. Certainly, it should be performed only when indicated, and if there are no contraindications. The findings in our study are similar to previous local and regional studies. In some aspects our findings differ from those of other international studies, probably due to demographical or environmental factors. A national registry for kidney biopsy is needed to determine the frequency of various glomerulonephritis which may help to prevent or delay the development of advanced stages of CKD.

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