Original Article

A Study of Diagnostic Yield, Efficacy and Complications of Ultrasound Guided Renal Biopsy in Different Renal Pathologies.

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Abstract

Introduction: Renal biopsy is an integral part of modern nephrology practice, being indicated in renal diseases in both native and transplanted kidneys. The purpose of this study was to evaluate diagnostic yield, efficacy and complications of ultrasound guided renal biopsy with automated biopsy gun.

Methods: This was a prospective cross sectional study involving 184 patients including renal transplant recipients. These patients with new onset renal symptoms or deteriorating renal function post transplant underwent free hand real time ultrasound guided renal biopsy with 18 gauge automated biopsy gun. The diagnostic yield, pathological and immunohistochemistry diagnosis and complications of the procedure were analyzed.

Results: 184 patients underwent the ultrasound guided biopsy, 17 were renal transplant recipients. Male and female ratio was almost equal (51.1% and 48.9%, respectively). Most patients were in age group of 20-40 years. Most cases presented clinically with nephrotic syndrome (38.04%), followed by equal number of lupus nephritic and nonnephrotic range proteinuria. The average number of glomeruli in the biopsy tissue was 11.8 per specimen. The average length of biopsy tissue was 1.15 cm in native kidneys and 0.9 cm in transplant kidneys. Renal biopsy yielded pathological diagnosis in 97.2% cases with adequate sample for diagnosis in 98.9% cases. Major life threatening complication was noted in a single patient. Rest of the patients showed minor or no complications.

Conclusion: Ultrasound guided percutaneous biopsy with automated biopsy gun is modality of choice for renal biopsy since it has the greatest yield, highest efficacy and least serious complication rates.

Keywords: glomeruli, nephrotic syndrome, renal biopsy, ultrasound

Introduction

The Kidney disease outcome qualitative initiative (K/DOQI) working group has defined chronic kidney disease in adults as: evidence of structural or functional kidney abnormalities (abnormal urinalysis, imaging studies, or histology) that persist for at least three months, with or without a decreased glomerular filtration rate (GFR) (as defined by a GFR of less than 60 ml/min per 1.73 m^2)[1]. The number of patients with chronic kidney disease worldwide is increasing rapidly.[2] The cost of treating patients with end stage renal disease is substantial and poses a great challenge to provision of care. More than 100 developing countries, together with a population in excess of 600 million, do

not have any provision for renal replacement therapy.[3] Consequently, more than a million people die every year worldwide from end stage renal disease. In Nepal, a door-to-door screening and intervention program was conducted. Among 3,218 people over 20 years surveyed, CKD was detected in 10.6%. Age and diabetes were particularly predictive.[4]

Renal biopsy is a common diagnostic procedure in nephrology, and can provide essential histological evidence of renal disease. It is an invasive procedure done for extraction of tissue for the diagnosis of renal diseases. Due to slow course of the disease, delayed presentation is common and the biopsy may not lead to major therapeutic decisons in such cases.[5] Moreover, renal biopsy is costly and potentially hazardous, so its potential benefits should be assessed.[6] However, with correct diagnosis by renal biopsy and with appropriate treatment, progression from acute into the chronic renal disease may be delayed.

Ultrasound guided biopsy is routinely practiced in our hospital. With the commencement of renal transplantation, this technique has further gained importance in cases with acute or persistent deterioration of renal function after transplantation. However, the safety, efficacy and complications of the procedure have not been evaluated in our set up. Hence this study is being carried out to evaluate diagnostic yield, efficacy as well as complications associated with this procedure.

Methods

This was a prospective cross sectional study involving 184 patients with various renal diseases referred for ultrasound guided renal biopsy. Medical ethics committee, Institute of Medicine, approved the study protocol and all the participants gave prior informed consent. Study was conducted in the Department of Radiology, Tribhuvan University Teaching Hospital from September 2008 to August 2009. Subjects with clinical diagnosis of glomerular hematuria, nephrotic syndrome, nonnephrotic range proteinuria, acute nephritic syndrome, lupus nephritis, acute renal failure of unknown origin and chronic renal failure of unknown origin were enrolled as cases. Also included were patients with renal diseases post renal transplant. Subjects with uncorrected bleeding diasthesis, solitary kidney, small echogenic kidneys, intractable hypertension uncontrolled by medications, hydronephrosis, multiple cysts and active urinary tract infections were excluded from study.

Ultrasonography was done before biopsy for localization and assessment of renal size, as well as to look for morphological abnormalities, cysts, or neoplasms. The procedure was carried out with a 3.5MHz curvilinear probe in Toshiba ultrasound machine (Toshiba Corporation, Japan). An automated biopsy gun of 18 gauge size and 22 mm penetration depth was used to obtain the renal tissue. Patients were kept in prone position for biopsy in native kidneys and in supine position for transplant kidneys. Site was selected and marked for percutaneous biopsy with ultrasound guidance. The distance between the skin surface and the capsule of the selected kidney was measured by ultrasound. The lower pole of kidney was selected for biopsy in native kidneys and upper pole was selected in transplanted kidneys. Under strictly aseptic precautions, local anesthesia was infiltrated at biopsy site and a small incision was made parallel to skin line. The loaded automated biopsy gun was passed through the incision site upto the level of capsule under ultrasound guidance and then the gun was fired. Two samples were obtained in native kidneys, one each for light microscopy and immunofluorescence study. In transplant cases, single sample was obtained for light microscopy only. Two passes were made to obtain the two samples in native kidneys, however, in cases of inadequate sample, upto maximum of four passes were made. Following the biopsy of a native kidney, the patient was kept in supine position for at least 6 hours to improve compressive hemostasis. Following the biopsy of a transplanted kidney, firm pressure was applied to the needle entry site for at least 5 minutes. Patients were instructed to remain under bed rest for 24 hours. The patients were asked to collect the urine sample in different containers after each void till 24 hours. In cases of no gross hematuria, routine urine examination was done to see microscopic hematuria. In cases of gross hematuria, patients were asked to collect urine till the urine was free of hematuria. Post biopsy ultrasound was performed to see for immediate complications like perinephric hematomas which were later evaluated for size changes. Routine hemoglobin examination was done in cases of persistent hematuria.

Data obtained were compiled and analyzed using standard statistical analysis. SPSS 16.0 was utilized for the data analysis and presentation.

Results

Ultrasound guided percutaneous renal biopsy was performed in 184 patients. These included patients with native kidneys and renal transplant recepients with deterioration in renal function. Ideally, two samples were taken from native kidneys and one from transplanted kidneys.

Patient demographics

Age ranged from 11 years to 76 years, the mean age was 32.9 years. Maximum numbers of patients were in the age range of 21-40 years (99 patients, 53.80%).

Table 1: Age group of patients

Age group of patients(years)	Number of patients	Percentage
0-20	39	21.20%
21-40	99	53.80%
41-60	35	19.02%
61-80	11	5.98%

94 (51.1 %) were male and 90 (48.9%) were female.

Clinical diagnosis

The clinical diagnosis of the patients was divided into 7 groups by history, clinical and laboratory findings (Table 2). Out of 167 patients with disease in native kidneys, most (70 cases, 38.04%) were of nephrotic syndrome.

Table 2: Clinical diagnosis of patients

Clinical diagnosis of patients	Number of patients	Percentage
Acute nephritic syndrome	15	8.1%
Acute renal failure of unknown origin	8	4.35%
Chronic renal failure of unknown origin	10	5.43%
Lupus Nephritis	32	17.39%
Nephrotic Syndrome	70	38.04%
Non Nephrotic Range Proteinuria	32	17.39%
Post renal transplant	17	9.24%

Number of biopsy gun passes

The mean numbers of passes were 1.99 with maximum 4 and minimum 1. In 144 patients numbers of passes were 2 and in one patient number of passes were 4. However in post transplant patients, single pass was made except in one case in which numbers of passes were 2.

Length of biopsy tissue

The mean length of first biopsy tissue was 1.15 cm with a minimum of 0.3 cm and maximum of 2 cm.

The mean length of second biopsy tissue was 0.9 cm with a maximum of 2.1cm and a minimum of 0.2 cm.

Number of glomeruli

The mean numbers of glomeruli were 11.84 with maximum of 45 glomeruli and minimum of 1 glomerulus per biopsy tissue. In two cases, no glomeruli were seen in the biopsy specimen in microscopic examination.

Biopsy lateralization

Renal biopsy was done in left kidney in 166 patients (90.22%) and in right kidney in 18 patients (9.78%).

Pathological diagnosis

The pathological diagnosis in native kidneys was made after light microscopy and immunofluorescence. However, diagnosis in transplant kidneys was made with light microscopy only.

In 184 patients, 167 (90.76%) biopsies were done in the native kidneys and 17 (9.24%) biopsies were done in transplant kidneys.

In five cases, no diagnosis could be made. Inadequate tissue was found in two cases; in others, the biopsy was inconclusive for reasons other than adequate sample (Table 3).

Table 3: Pathological diagnosis in native kidneys

Pathological diagnosis	Number of patients	Percentage
Minimal change disease	13	7.78%
Membranoproliferative glomerulonephritis	37	22.16%
Focal segmental glomerulosclerosis	30	17.96%
Post streptococcal glomerulo nephritis	2	1.2%
Cresentric glomerulonephritis	7	4.19%
Membranous nephropathy	9	5.39%
IgA nephropathy	16	9.58%
Lupus nephritis	36	21.56%
Tubulointerstitial nephritis	11	6.59%
Others (Wegners granulomatosis, Vasculitis, Amyloidosis)	3	1.8%
No Diagnosis	3	1.8%
	167	90.76%

In transplant cases, pathological diagnosis were as follows (Table 4)

Table 4: Pathological diagnosis in transplant kidneys

Pathological diagnosis	Number	Percentage
Acute antibody mediated rejection	2	11.76%
Acute tubular necrosis	2	11.76%
Cell mediated rejection	6	35.29%
IgM nephritis	1	5.88%
Interstitial nephritis	1	5.88%
No Diagnosis	2	11.76%
Normal findings	3	17.65%
	Total 17	

Post biopsy complications

Post biopsy complications were divided into four categories. Category I showed no complications. Category II comprised of microscopic hematuria. Category III comprised of gross macroscopic self limiting hematuria, perinephric hematoma (small in size with no significant change on repeated ultrasound examination and no further intervention required). Category IV comprised of persistent hematuria requiring intervention, hematuria requiring blood transfusion, large perinephric hematoma requiring drainage, loss of kidney and death.

Table 5: Post renal biopsy complications

Complications	No of patient (%)	Type
None	68 (36.96%)	
Microscopic hematuria	78 (42.39%)	
Minor complications	37 (20.11%)	Macroscopic hematuria, small perinephric hematoma requiring no intervention
Major complications	1 (0.54%)	Large hematoma or persistent hematuria requiring intervention, blood transfusion, loss of kidney, death

Discussion

Renal biopsy is an invasive modality for extracting tissue from kidneys for the diagnosis of medical renal diseases. Percutaneous renal biopsy, based on the use of an aspiration needle and patient in the sitting position was first described by Iverson and Brun in 1951.[7] They used intravenous urography to target the kidneys. In 1954, Kark and Muehrcke described the use of cutting Vim Silver man needle on patients in the prone position with substantial improvement in rate of success. Their technique laid the foundation for method used by nephrologists for the next 30yrs.[8]

Image guided renal biopsy is modality of choice since, with blind techniques, the yield of tissue is low and rate of complications are high. Real time ultrasound provides the direct visualization of the kidneys with appropriate selection of site and depth needed for biopsy. With the advent of newer automated biopsy guns, the yield of tissue for diagnosis is higher with lesser complication rates.

Out of 184 patients, renal biopsy was done in 167 native kidneys and 17 transplant kidneys. In patient with native kidneys, the most common clinical diagnosis was nephrotic syndrome (38.04%), followed by equal proportions of lupus nephritis and non nephrotic range proteinuria (17.39% each). The clinical profile of the patients undergoing biopsy in our study is partly similar to the study done by Kim et al.[9] Indications for biopsy in their series were proteinuria (38%), proteinuria accompanied by hematuria (31.3%), acute renal failure (9.6%), lupus nephropathy (9.6%), chronic renal failure (6%), and hematuria only (5.4%). The high proportion of nephrotic syndrome (and the proteinuria) in these studies reflect higher incidence of the condition among the renal diseases.

Our findings are in corroboration with previous studies studying the efficacy of image-guided biopsy and their comparison with blind biopsy. Maya et al[10] compared blind and real-time ultrasound-guided percutaneous renal biopsy in two group of patients and results showed the mean number of glomeruli per biopsy was higher in the ultrasound-guided group than in the patients with a blind biopsy (18 ± 9 versus 11 ± 9, $p = 0.0001$). Repeat biopsy due to inadequate tissue sample was not necessary in any of the ultrasound-guided biopsies but 16% of the blind biopsies ($p = 0.0006$). Mean glomeruli in our study were 11.8 and the glomeruli were absent in 1.08%. The absent glomeruli probably resulted from faulty technique since all of the biopsies were performed free hand and biopsy adapter was not used in any case.

We performed biopsy with the help of 18-gauge biopsy needle with good yield of tissue for pathological diagnosis in 97.2% cases; major complication was seen in a single patient (0.54%). Mostbeck et al[11] studied optimal needle size for renal biopsy, both in vitro (cadaveric kidneys) and in vivo in 141 patients. Results were obtained with a 16-gauge modified Menghini needle. In vitro, 9.7 ± 5.7 (mean ± standard deviation) glomeruli were retrieved, and

the average length of tissue core was 17.8 mm ± 8.2. In vivo, 10.63 ± 6.64 intact glomeruli were retrieved, and a definitive histologic diagnosis was achieved in 86% of patients. The frequency of major complications with this needle was 3.5%, and minor complications were seen in 5.8%. No major complications occurred when biopsy was performed with 18-gauge needles. Although the mean number of glomeruli with 18 gauge needle is less than 14 and 16 gauge, it is adequate for histological diagnosis. The rate of complications is also low with 18 gauge needles.

The number of glomeruli necessary to facilitate an adequate diagnosis ranges from 3 to 12.[12] Tisher and Croker[13] believed 12 glomeruli were adequate, Oberholzer et al[12] believed 6 to 10 were necessary, and some investigators believed 3 may be the minimum number[14]. It may require only one glomerulus to make the diagnosis of membranous glomerulopathy, sometimes more than six glomeruli may also not be sufficient in early focal glomerulosclerosis or in lupus nephropathy.[15]

The mean number of glomeruli obtained in our study were 11.84. The biopsy yielded adequate tissue in 182 (98.9%) patients and histopathological diagnosis by light microscopy and immmunofluoroscence could be made in 179 cases (97.2%). No diagnosis could be made in 5 patients. In 2 patients, the tissue was not adequate for diagnosis and in other 3 patients, results were inconclusive for reasons other than inadequate sampling. In study done by Olaf Hergesell et al[16] in 1090 consecutive cases, only 1.2% of specimens showed no glomeruli or even no renal tissue. Sufficient tissue for reliable histopathological diagnosis was obtained in almost all cases (98.8%). The median number of glomeruli was 9 (range 1–37) per specimen. A histological analysis, including conventional light and immunofluorescence microscopy, could be made by the pathologist in 99.1% of the successful biopsies. These findings are in close corroboration with our study.

The pathological diagnoses in native kidneys (total 167 cases) in our series were: membranoproliferative glomerulonephritis (22.16%), lupus nephritis (21.56%), FSGS (17.36%), IgA nephropathy (9.58%) and 0.9% each of amyloidosis, ATN and vasculitis. These diagnoses are different from a study in Korea by Dohum Kim et al[9] where IgA nephropathy (25.9%) was the commonest followed by, minimal change disease (16.3%), lupus nephritis (11.4%), membranous glomerulonephropathy (9.3%), membranoproliferative glomerulonephritis (5.4%), and others. This probably reflects the geographical variation in the pattern of the renal diseases among different parts of the globe.

Biopsy in 17 cases of transplant kidneys showed cell mediated rejection in 6 cases (35.29%), equal proportion of ATN and acute antibody mediated rejection (11.76%) and normal findings in 3 cases (17.65%).

Post biopsy complications were divided into four categories. Out of 184 patients, 68 cases (36.96%) showed no complications, 78 cases (42.39%) presented with microscopic hematuria, minor complications were noted in 37 cases (20.11%) and major complication was seen in a single case (0.54%). These findings are in close correlation with studies conducted by earlier authors.[16, 17]

The results show that serious biopsy-induced complications are extremely low with ultrasound guidance and with automated biopsy gun, good yield of tissue could be obtained for diagnosis of renal diseases.

Conclusion

Free hand real time ultrasound guided percutaneous renal biopsy with automated biopsy gun is modality of choice for renal biopsy since it has the greatest yield, highest efficacy and least serious complication rates.

Conflict of interest: None declared

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