*Original Article*

# Real time Ultrasound Guided Percutaneous Native Renal Biopsy- Approach, Safety and Complications

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## Abstract

**Introduction:** Ultrasound guided percutaneous renal biopsy (PRB) is a relatively safe procedure; however, life threatening complications may occur even in current practice. There has been considerable decrease in the risk associated with percutaneous renal biopsy (PRB) in last few decades due to modifications in the biopsy needle as well as advancement in the image guidance.

**Objectives:** To determine the complications and efficacy and to determine relationship between the clinical/ laboratory findings with rate of complications.

**Material and methods:** We retrospectively evaluated hospital records of total of 150 patients who underwent PRB between September 2014 to August 2016 in the department of Radio diagnosis and Imaging at B. P. Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal. The renal biopsies had been performed with the current automated biopsy gun under real-time ultrasound guidance. The collected data were entered in MS excel.

**Results:** In the total 150 patients, the efficacy (adequacy of the sample) of the procedure was 97.3%. The complications were seen in 13 cases (8.6 %). Five out of these complications were major with 2 cases requiring blood transfusion. The univariate analysis demonstrated the risk factors for developing complications as follows: low platelet count, prolong PT/INR, elevated Blood Urea Nitrogen (BUN) and serum creatinine value and elevated systolic and diastolic blood pressure. However, elevated diastolic blood pressure and prolong PT/INR were associated with complications in multivariate logistic regression analysis.

**Conclusions:** The percutaneous renal biopsy is the safe and efficacious procedure to establish histological diagnosis of renal parenchymal disease.

**Keywords:** Complication, Efficacy, Percutaneous Renal Biopsy (PRB), Safety.

## Introduction

Renal biopsy has been an integral part of nephrology practice for diagnosis, prognosis and treatment of various renal diseases since Iverson and Braun first introduced renal biopsy in clinical practice in 1951.[1] Ultrasound guided renal biopsy has transformed the diagnosis, treatment and long-term outcome of glomerular disease. There has been considerable decrease in the risk associated with percutaneous renal biopsy (PRB) in last few decades due to modifications in the biopsy needle as well as advancement in the image guidance. Nowadays, automated cutting needle biopsy gun is widely used in place of true cut needle. However, even in today's era, percutaneous renal biopsy is not still complication free; there can be post procedural bleeding leading to increased hospital stay, need for transfusion, increased treatment cost and need of additional surgical/ radiological intervention to control bleeding. Life threatening complications like persistent hematuria requiring blood transfusion and radiological/ surgical intervention can still occur in today's practice.

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A number of factors are associated with increased risk of complication associated with biopsy which include: the size of biopsy needle, number of passes (i.e. needle piercing the renal parenchyma), associated hypertension, and deranged coagulation profile, although some of these factors are not consistent in the literature.[2,3] We reviewed clinical and laboratory parameters in two groups (with and without complications) with the aim to find out the risk factors of complications.

So, present study was carried to determine the complications and efficacy of percutaneous renal biopsy and to determine the relationship between the clinical/ laboratory findings with rate of complications.

**Material and Methods**

It is a hospital based retrospective study carried out over a period of three months from February to June 2017 in the department of Radio diagnosis and Imaging at B. P. Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal. We evaluated hospital records of total of 150 patients who underwent PRB between September 2014 to August 2016, for a period of 2 years.

Ethical clearance was obtained from institutional review board, BPKIHS. All biopsies were performed in Department of Radio-diagnosis and imaging of BPKIHS with real-time ultrasonography guidance by radiologist. All patients were admitted in the medical ward with preprocedural work up which included clinical history and examination, screening for uncontrolled blood pressure, uncontrolled diabetes mellitus, bleeding / clotting/ coagulation disorder and urinary tract infection. Patients' age, gender, blood pressure at the time of the biopsy, indication for PRB, pre-biopsy laboratory parameters i.e. Haemoglobin, platelet counts, PT/INR, Blood Urea Nitrogen (BUN), Serum creatinine, Serum Cholesterol and total urinary protein were recorded on a structured proforma. Percutaneous Renal Biopsy was performed under real time ultrasound guidance using an automated biopsy gun with a 14 or 16-gauge needle in all the cases. All biopsies were performed with local anesthesia in prone position. Cortical tangential approach with a trajectory passing from the interpolar renal cortex to the lower pole cortex with needle tip directed away from the central echogenic hilum was chosen so as to pierce the cortex near Brodel's line which is a relatively avascular zone between anterior and posterior segmental renal arteries.

No pathologists were present during the biopsy procedure and the adequacy of the sample was judged by the performing physician with visual inspection of the sample. After performing biopsy, all patients were hospitalized, vital signs were monitored regularly and each voided urine sample was examined for gross hematuria for 24 hours. All patients were followed up with USG in the evening and next morning before discharge. If there were any, complications detected were recorded in the file.

The efficiency of the procedure was determined based on whether the pathologist considered the sample to be sufficient to establish a diagnosis.

Safety was evaluated on the basis of the presence or absence of major or minor complications. We considered major complications as those that required a blood transfusion, surgical intervention and extended hospitalization, whereas a minor complication was defined as a complication that did not require transfusion or surgical intervention (usually minor hematomas or transient hematuria that resolved spontaneously and did not prolong hospitalization over the 24-hour period after the procedure). Patients identified as having major complications were compared with the rest of the population (those with minor complications and those who did not present any complications) to identify potential risk factors for major complications.

The collected data were entered in MS excel. The data were analyzed by using descriptive (mean standard deviation, frequency and percentage) and inferential statistics (univariate and multivariate logistic regression analysis) by using SPSS version 16. A p-value less than 0.05 was considered significant.

**Results**

A total of 150 PRBs performed in 150 patients using an automated biopsy device under real-time ultrasound guidance over the period of 2 years were studied. Demographic characteristics and laboratory findings are shown in Table 1. The mean age of the patients was 34.91 ± 13.5 years with male: female ratio 1.4:1.

**Table 1: Demography and pre-procedure laboratory findings of 150 patients included in the study.**

| Variable | Total number of patients (Mean± SD) | Patients without complication (Mean± SD) | Patients with complication (Mean± SD) |
|---|---|---|---|
| Age (years) | 34.91± 13.54 | 35.02± 13.68 | 33.77± 12.42 |
| Glomeruli number per sample | 13.83± 6.31 | 13.91± 6.31 | 13.08± 6.52 |
| Urea (mg/ dl) | 55.16± 35.47 | 47.22± 32.63 | 81.15± 49.14 |
| Creatinine (mg/ dl) | 1.20± 0.78 | 1.15± 0.72 | 1.98± 1.0 |
| INR | 1.22± 0.41 | 1.16± 0.36 | 1.85± 0.37 |
| HB (gm/ dl) | 11.81± 1.52 | 11.86± 1.46 | 11.30± 2.0 |
| Platelets ($x10^3$ per $\mu L^{)}$ | 244.54± 62.65 | 251.16± 611.10 (240 median) | 174.76± 254.03 (median 180) |
| Total Cholesterol (mg/dl) | 244.54± 62.65 | 236.66± 53.29 | 245.08± 46.72 |
| SBP (mm.Hg.) | 125.33± 10.27 | 124.96± 9.86 | 129.23± 13.82 |
| DBP (mm.Hg.) | 84.57± 8.63 | 83.221± 7.66 | 98.15± 6.18 |

The most common clinical diagnosis/ indication for renal biopsy in our study was Nephrotic syndrome (nephrotic range proteinuria) 55 (36.7%) cases; followed by acute kidney injury 46 (30.7%), lupus nephritis 31 (20.7%), non-nephrotic range proteinuria 15 (10%) and chronic kidney disease 3 (2%) cases respectively.

In our study, lupus nephritis and non-proliferative glomerulonephritis were the main histological findings, 29(19.5%) cases each; followed by focal segmental glomerulosclerosis (FSGS), IgA nephropathy and membranous nephropathy each in 16 (10.7%) cases. Biopsy diagnosis of other primary glomerulopathies were diffuse proliferative glomerulonephritis 11 (7.3%) cases, masangioproliferative glomerulonephritis 11 (7.3%) cases, tubulointerstitial disease 7 (4.7%), chronic sclerosing nephropathy 6 (4%) and crescentic glomerulonephritis 5 (3.3%) cases respectively.

**Efficiency evaluation**

Out of total 150 biopsies analyzed, there were 146 biopsies (97.33%) with an adequate sample (representative) to establish the histopathological diagnosis. There were four procedures (2.66%) with inadequate histological material or no renal tissue to establish a diagnosis. Of all 150 biopsies, 111 biopsies had more than 10 glomeruli (74%), 32 (21.3%) biopsies had 6 to 10 glomeruli and 3 (2%) biopsies had 1 to 5 glomeruli.

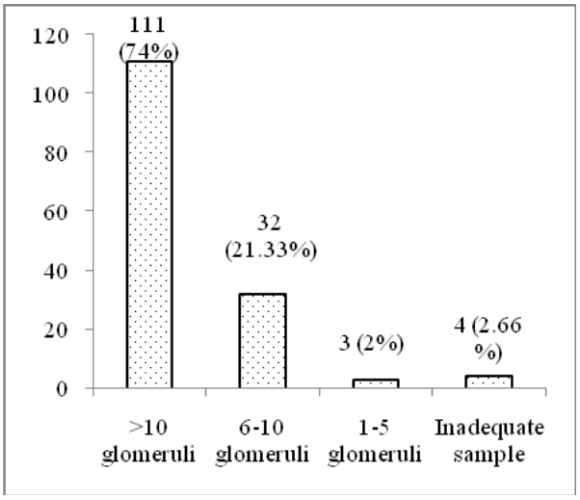


**Figure 1: Bar diagram showing number of glomeruli per biopsy sample**

**Safety evaluation**

The present study observed a total of 13 complications (8.66%). Among these complications, 8 (5.33%) were minor and 5 (3.33%) were major. The most frequent minor complication was the presence of an ultrasound-detected subcapsular hematoma, which occurred in 6 cases (13.9%), followed by transient hematuria in 2 cases (1.2%) which did not require transfusion. Of major complications (5 cases), perinephric hematoma was seen in 3 cases which prolonged patients' hospital stay for pain management and observation. The major hematoma requiring blood transfusion was seen in 1 case and gross persistent hematuria leading to fall in hematocrit and requiring transfusion was seen in 1 case. Any complications requiring surgical/ interventional radiology treatment or nephrectomy or intestinal perforation were not observed in any of our patients.

To find out the risk factors associated with complications, we compared pre-procedure clinical and laboratory parameters of patients who developed complications (*n*= 13) with those patients who had no complications (*n*= 137). As a result of the univariate analysis, the following variables were found to be significantly associated with complications: hemoglobin ≤10 g/dl, prothrombin time ≥14 s, platelets count ≤150 × $10^3$/µl, serum creatinine ≥1.2 mg/dl, and BUN ≥60 mg/dl, diastolic blood pressure > 90 and systolic blood pressure >140. However, in the logistic multivariate regression analysis, only diastolic blood pressure >90 mm Hg. ($p< 0.001$) and prothrombin time >14 Sec (PT) / INR ($p< 0.05$) were found to have an independent effect.

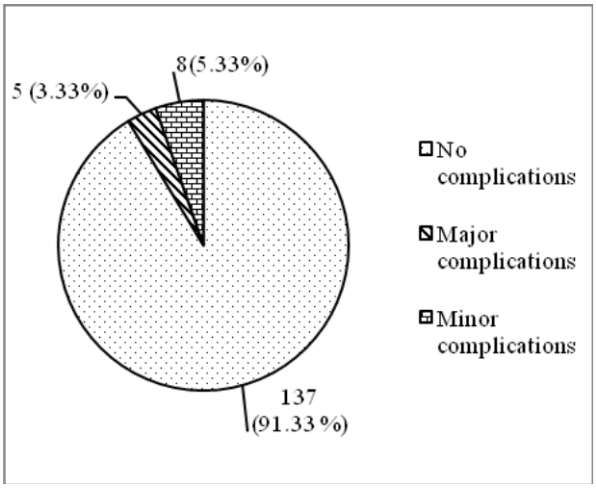


**Figure 2: Pie chart showing Complications in PRB**

**Assessment of Risk factors for major complications**

**Discussion**

We analyzed 150 native PRBs that were performed using an automated biopsy device under real-time ultrasound guidance over the period of 2 years.

The cortical tangential approach with a trajectory which passes from the interpolar renal cortex to the lower pole cortex with needle tip directed away from the central echogenic hilum was chosen so as to pierce the cortex near Brodel's line i.e. a relatively avascular zone between anterior and posterior segmental renal arteries. The effectiveness of percutaneous renal biopsy is improved with real time ultrasound guidance because the puncture of renal cortex is visualized in real time as compared to the blind technique where one cannot be sure of renal tissue before histological examination.

Glomerular disease is reported as the most common cause of end-stage renal disease in Nepal,[4] and the pattern of glomerular disease

was studied by light microscopy and membranous GN (MN) and membranoproliferative (MPGN) were reported as the most common causes of GN.[5] Several other reports revealed that the most common glomerular disease was IgA nephropathy in Asia, accounting for 58.2% in China[6] and 45% in Singapore.[7] In our study, lupus nephritis and non-proliferative glomerulonephritis were the main histological findings 29 each (19.5%) cases; followed by focal segmental glomerulosclerosis (FSGS), IgA nephropathy and membranous nephropathy each in 16 (10.7%) cases. Some authors consider renal biopsy representative or adequate biopsy, when glomeruli obtained are between 8 and 10 per sample; however, others consider biopsy representative if pathologists consider it possible to make a histological diagnosis. We considered biopsy sample adequate, if the reporting pathologists considered sample adequate irrespective of the number of glomeruli in the sample. In our experience, adequate tissue diagnosis was established in 97.33% cases. The efficacy of procedure is comparable to the other studies available in the literature: Castro et al., Burstein DM et al.[8], Hergesell O et al.[9], Munoz AT, et al.[10] and Tondel C[11], where efficacy rate were 92.3, 98.9, 98.8, 97.6 and 94% respectively.

In our study, the mean number of glomeruli was 13.83 per sample with 74% of the sample more than 10 glomeruli and 2.66% had inadequate sample. In a study by Hergesell *et al*., the median number of glomeruli per specimen was 9. In a study by Tondel C et al., 3% of biopsies had no glomeruli, and the sample size was significantly smaller in biopsies done with 18-gauge needles, a median of 9 glomeruli per biopsy; as compared with 12 glomeruli with either the 16- or 14-gauge needles.[9,11]

The rate of complications resulting in death decreased from 0.12% to 0.02% during the last 50 years.[3,12-13] In fact, during the last 20 years, death resulting from PRB of native kidneys has been extremely rare, with no deaths reported in a number of recent studies.[14-20] Nonetheless, despite the improved safety of the procedure, clinically significant bleeding complications do occur in 4%- 7% of biopsies on average[3,12-13], and rates as high as 25% to 30% have been reported in a number of recent studies despite the use of newer technologies.[15,19,21,22]

Although the majority of complications resolve spontaneously, in up to 9% of biopsies, the complication can be more severe and potentially life threatening, resulting in the need for intervention.[13,23-25]

There were no biopsy related mortality, nephrectomy, need for surgical / interventional radiological management, however, some form of bleeding complications occurred in 8.66% cases with two patient requiring blood transfusion. Minor complications were seen in 5.33% and major complications were seen in 3.33% of cases. Total complication rate in our study is similar to the result of the study by Hergesell et al. (complication rate 7.8%).[9]

Major complications in our study were (5.33%) which is comparable to Castro et al. (4.3%) and Whittier and Korbet et al. (6.4%).[3] However, it is higher than the study by Hergesell et al. (0.3%) and Munoz AT et al. (2.24 %).[9,10] We observed higher rate of major complications as compared to other studies which may be due to our case definition of major complications which was any complication that may prolong patient's hospital stay.

The analysis of risk factors using multivariate logistic regression analysis showed significant association between diastolic blood pressure of ≥ 90 mmHg ($p< 0.001$) and PT > 14 Sec ($p< 0.05$). Similar association with diastolic blood pressure of ≥ 90 mmHg and the risk of complications were described by Munoz AT and Diaz-Buxo.[10,26] In the same way, Eiro *et al*. showed that hypertension (systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg) was an independent risk factor for post-biopsy bleeding.[15]

Using univariate analysis; we found that the statistically significant risk of complications

were associated with hemoglobin ≤ 10 g/dl, prothrombin time ≥ 14 s, platelets count ≤ 150 × $10^3$/μl, serum creatinine ≥ 1.2 mg/dl, and BUN ≥ 60 mg/dl, diastolic blood pressure > 90 and systolic blood pressure > 140. However, these relations except DBP and PT/INR did not persist in multivariate logistic regression analysis.

In the present study, we observed a significant increase in the number of complications in patients with BUN levels ≥ 60 mg/dl; similar to other studies who suggested that there is an increased risk of developing a hemorrhagic complication after PRB in patients with uremic syndrome.[10,27,28] This finding could be related to the role of uremia in platelet dysfunction. Our study showed significant association between serum creatinine and risk of complication by univariate analysis as demonstrated by Parrish A et al.[29] but this relation could not be shown using multivariate logistic regression analysis in our study.

## Conclusion

In our experience, adequate tissue diagnosis was established in 97.33 % cases with mean number of glomeruli 13.83 per sample and 74% of the sample had more than 10 glomeruli. Some form of bleeding complications occurred in 8.66% cases with two patients requiring blood transfusion. Minor complications were seen in 5.33% of cases. We found that diastolic blood pressure ≥ 90 mmHg and PT > 14 Sec were significantly associated with development of complications by multivariate logistic regression analysis and thus, must be taken into account to reduce the frequency of complications.

## Limitation of the study

Present study is a retrospective done from the hospital records of the patients who had undergone biopsy. We relied upon the documented information in the patients' records which were limited. We were unable to study the effect of needle size in the occurrence of complications. Similarly, the effect of number of passes i.e. biopsy needle piercing the renal parenchyma on complication rate also could not be studied. The success of any invasive procedure may also depend on the expertise performing the procedure, which was again not evaluated in our study. Moreover, the study analyzed the profile of biopsies done for 2 years duration only, which is not a long duration and not all patients of glomerular diseases were biopsied.

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