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Renal Data from Asia – Africa

Complication Rate and Diagnostic Yield of Percutaneous Native Kidney Biopsies: A 10-year Experience at a Tertiary Care Hospital in Pakistan

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ABSTRACT. The use of an automated biopsy device, and real-time ultrasound for percutaneous kidney biopsies (PKBs) has improved the likelihood of obtaining adequate tissue for diagnosis and also has reduced the complications associated with the procedure. We aimed to determine the frequency and type of complications associated with PKB and to determine the diagnostic yield. It was a retrospective file-based review of cases who underwent PKB of native kidney between January 2003 and December 2013 at the Aga Khan University Hospital in Karachi, Pakistan. PKBs were performed by trained nephrologists or radiologists using an automated device with a 16/18-gauge needle under real-time ultrasound. The data obtained included age, gender, clinical and histopathological diagnosis, and complications associated with the procedure (minor: hematuria, local infections, and hematoma; major: transfusions, severe infections, surgery, nephrectomy, arteriography, embolism, and death. Yield of the procedure was based on the number of glomeruli obtained. Patients having major complications were compared with the patients who had minor or no complications. A total of 433 native kidney biopsies were performed. The mean age of the patients was 41 ± 15.9 years, and 58% of the patients were male. The main histological findings were membranoproliferative glomerulonephritis (17.6%) followed by focal and segmental glomerulosclerosis (16.4%) and interstitial nephritis (13.9%). Majority of the procedures were performed by nephrologists (67.4%). The overall complication rate was 14.2%. Among those, 21 patients (4.8%) had a major complication while the others had minor complications. Of those who had a major complication, 17 patients required blood transfusion(s) and had hematuria or a major hematoma, three had prolonged hospitalization >24 hours, and one patient required surgical intervention. Only 10 procedures (2.3%) had inadequate tissue to establish the histopathologic diagnosis. PKB under real-time ultrasound guidance is a safe and efficacious procedure to establish the histological diagnosis of the renal disease.

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Introduction

Percutaneous kidney biopsy (PKB) is an integral part of nephrology practice. It provides the essential diagnostic and prognostic information which plays a vital role in making the appropriate management plans. Since its inception in the 1950s, various technical advances have been made in performing PKBs which have improved the diagnostic yield as well as safety of the procedure. In the current era, most hospitals use real-time ultrasonography and automated percutaneous devices for the procedure.

PKB is an invasive procedure that can result in complications mainly related to bleeding (hematuria and hematoma). However, most of the complications are usually minor and without clinical significance. Major complications occur infrequently provided potential risk factors for bleeding are identified and rectified before the procedure.

At our institution, we have performed PKB using real-time ultrasonography and automated percutaneous device for almost a decade. In this study, we report the procedure-related complications and the diagnostic yield of PKB performed over a period of 10 years. Our study is the largest report from Pakistan describing complications as well as yield of PKB.

The objective of this study was to determine the frequency and type of complications associated with PKB and to determine the diagnostic yield in terms of obtaining enough material for diagnosis.

The yield of the procedure was determined depending on the number of glomeruli obtained and whether the pathologist considered the material to be adequate to establish a diagnosis.

Subjects and Methods

We retrospectively reviewed medical records of patients who had undergone native kidney biopsy between January 2003 and December 2013 at The Aga Khan University Hospital. The procedures were performed using real-time ultrasonography and automated percutaneous devices by either a consultant radiologist or a nephrologist with a 16- or 18-gauge (G) needles. Two cores of tissue were obtained and were processed separately for light microscopy and immunofluorescence. All patients had given written consent for biopsy and were observed for a period of 24 h after the procedure.

Clinical details including age, gender, indications for biopsy, and blood pressure (BP) at the time of biopsy were recorded from the case records. Laboratory profile including serum creatinine, hemoglobin (before and after biopsy), hematocrit, platelet count, coagulation profile, and histological diagnosis was also obtained from the records.

Complications were categorized as major or minor. Major complications included need for blood transfusion, surgical intervention, angioembolization, extended hospitalization beyond 24 h, and death related to the procedure. Minor complications were defined as transient gross hematuria or minor hematoma that resolved spontaneously and did not require any transfusions/intervention and did not require hospitalization beyond 24 h.

Patients who developed complications were identified and classified based on whether the complications were major or minor. Patients identified as having major complications were compared with the rest of the cohort (those with minor complications and those who did not present any complications) to identify potential risk factors for major complications. We analyzed the following independent variables: age, gender, BP at the time of the biopsy, indication for PKB, and histopathologic diagnosis. In addition, we examined the following prebiopsy laboratory variables: prothrombin time (PT), activated partial thromboplastin time, hemoglobin, platelet count, serum creatinine, and blood urea nitrogen (BUN).

Statistical Analysis

A descriptive analysis was made for demographic and clinical features. Continuous variables with normal and nonnormal distributions were reported as mean (standard deviation) and median, respectively, and number (percen-

tage) for qualitative variables. Comparisons between groups were performed by means of Chi-square tests for categorical data. For contrasts of continuous variables, independent sample *t*-test was used to assess the difference of means. All analyses were conducted using the Statistical Package for the Social Science (SPSS) (Release 19.0, standard version, copyright © SPSS; 1989-02). All *P*-values were two-sided and considered as statistically significant if <0.05.

Results

During the study period, a total of 433 native kidney biopsies were performed using an automated biopsy gun and real-time ultrasound guidance. Demographic characteristics and laboratory findings of the patients are shown in Table 1. The mean age of the patients was 41 ± 15.9 years, and 58% of the patients were male. The main clinical indications for a PKB were hematuria-proteinuria (31.2%), nephrotic syndrome (24%), and chronic renal insufficiency (18.2%) (Figure 1). The main histological findings were membranoproliferative glomerulonephritis (MPGN, 17.6%), followed by focal and segmental glomerulosclerosis (FSGS, 16.4%) and interstitial nephritis (13.9%) (Figure 2). Majority of the procedures were performed by nephrologists (67.4%). The overall complication rate was 14.2%. Among those, 21 patients (4.8%) had a major complication while the others had minor ones. Of the patients who had a major complication, 17 required a blood transfusion and had hematuria or a major hematoma, three had prolonged hospitalization >24 h, and only one patient required surgical intervention. Of the 433 native kidney biopsies, only 10 procedures (2.3%) had inadequate tissue to establish the histopathologic diagnosis. More than 10 glomeruli were present in 242 cases (55.9%), 149 cases had 6 to 10 glomeruli (34.4%), and 32 cases had 1 to 5 glomeruli (7.4%).

Table 1. Demographic characteristics and laboratory findings in the study patients.

Variable	Total (*n* = 433)	Major complication (*n* = 21)	Without major complication (*n* = 412)	*P*
Age, in years	41±15.9	39±14.8	40.9±16	0.57
Gender				
Male	250 (57.7)	14 (66.7)	236 (57.3)	0.49
Female	183 (42.3)	7 (33.3)	176 (42.7)	
Weight, kg		65.8±15.8	69.4±16.3	0.13
Prebiopsy laboratory test				
Serum creatinine (mg/dL), median [IQR]	2.5 [1.4−5.2]	3.8 [1.9−6.3]	2.5 [1.4−5.1]	0.12
Hemoglobin [g/dL]	10.9±2.2	10.3±2.4	11±2.2	0.23
Hematocrit (%)	32.6±6.4	30.9±6.9	32.7±6.4	0.24
Platelets ($\times 10^3/\mu L$)	252 [193–317]	221 [194–306]	257 [193–320]	0.38
Prothrombin time [s]	10.9±1.6	12.5±2.5	10.8±1.6	0.002
Activated partial thromboplastin time (seconds)	28±4.4	29.7±4.3	27.8±4.4	0.21
Systolic blood pressure (mm Hg)				
>140	140 (32.3)	5 (27.8)	135 (33.3)	0.79
<140	283 (65.4)	13 (72.2)	270 (66.7)	
Diastolic blood pressure (mm Hg)				
>90	96 (22.2)	5 (27.8)	91 (22.5)	0.57
<90	327 (75.5)	13 (72.2)	314 (77.5)	
Operator				
Radiologist	133 (30.7)	10 (47.6)	123 (30.4)	0.14
Nephrologist	292 (67.4)	11 (52.4)	281 (69.6)	

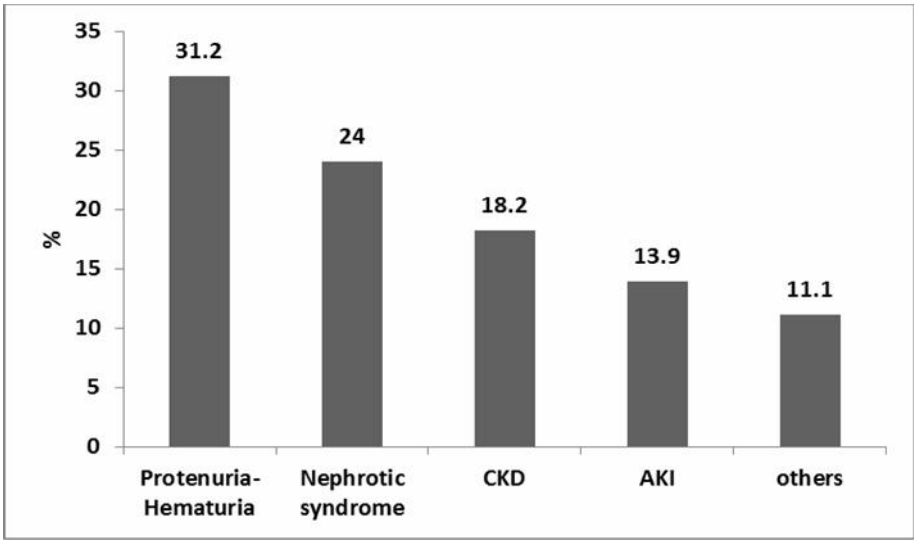

Figure 1. The most frequent indications for performing kidney biopsy.
CKD: Chronic kidney disease, AKI: Acute kidney injury.

Discussion

Our study analyzed 433 PKBs performed over a decade under real ultrasound guidance; the diagnostic yield was 97.7%, and the rate of major complications was 4.8%. Literature review reveals that the reported incidence of minor complications may range from 2% to 35% and major complications from 1% to 7%.[1] Differences in complication rates among studies vary substantially because of confounding issues such as the nature of the study (prospective or retrospective), the type of imaging used (real-time ultrasound, computerized tomography, or blind biopsies after ultrasound localization), the needle type or gauge used (manual versus automated and 14, 16, or 18-gauge), and who is performing the biopsy

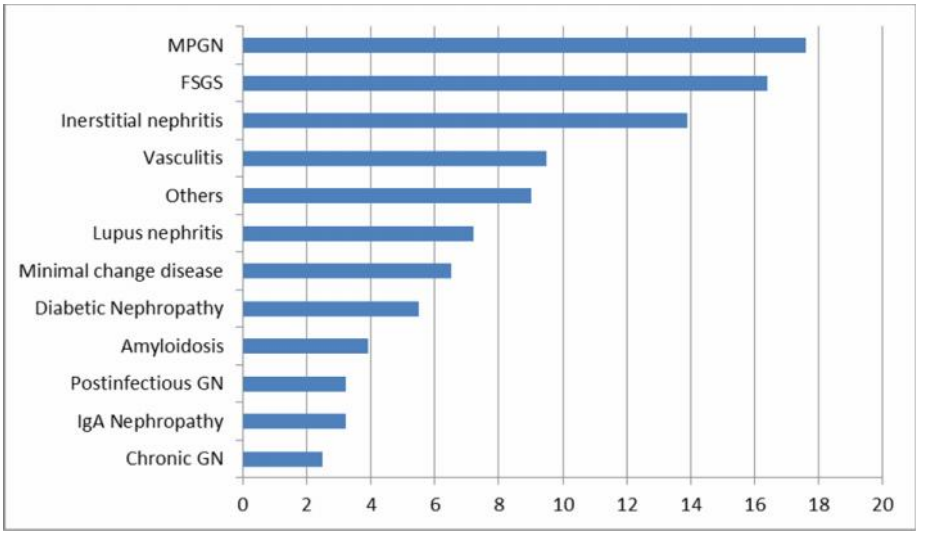

Figure 2. The most frequent histological findings in the study patients.
MPGN: Membranoproliferative glomerulonephritis, FSGS: Focal and segmental glomerulosclerosis, GN: Glomerulonephritis.

(nephrologists or radiologists). Amer Azhar et al from Peshawar, Pakistan, analyzed 200 PKBs and found that 10% developed complications (minor complications in 8% and major 2%).[2] In a study from India that included 320 renal biopsies in 305 patients over a period of five years, adequate tissue for pathologic diagnosis was obtained in about 79% of biopsy attempts, and the overall complication rate was 6.8%.[3] Corapi et al performed a systematic review of 34 retrospective and prospective studies that included 9474 adults who underwent native kidney biopsy using real-time ultrasound guidance.[4] They reported the approximate incidence of the different bleeding complications as transient macroscopic hematuria (3.5%), requirement for blood transfusion (0.9%), need for angiographic intervention to control bleeding (0.6%), nephrectomy (0.01%), and death (0.02%). In our study, 412 patients (9.4%) either had no or minor complications and only 21 patients (4.8%) had a major complication. Hence, our results are consistent with the results reported by the international series as well as with earlier studies from Pakistan. Torres Muñoz et al from Bolivia reported a complication rate of 17.6%, and out of this, only 2.24% had major complications.[5] Mishra et al reported complications in 5.8% and most of them were minor.[6] Jiang et al performed a retrospective cohort study of 475 biopsies and found an overall complication rate of 8.2% (6.9% minor and 1.3% major).[7] Whittier et al reported a series of 750 PKBs on native kidneys over a period of 20 years.[8] Complications occurred in 13% of the patients with 6.4% being major. Toledo et al have reported a major complication rate of less than 1% in their series.[9] Older series has described a slightly higher complication rate that had likely been associated with the use of manual devices and lack of real-time ultrasound guidance. Hence, the use of modern medical techniques and modifications, PKB has evolved into a safer procedure.

The risk factors for developing a complication are divided into those that are patient-associated (e.g., age, increased BP, elevated serum creatinine or reduced glomerular filtration rate (GFR), coagulopathy, increased bleeding time, and nature of underlying disease) and those related to the technique (e.g., needle type or size, use of imaging or not, and the number of passes). In their series, Corapi et al found systolic BP ≥130 mm Hg, serum creatinine ≥2 mg/dL, hemoglobin <12 g/dL, and age over 40 years to be the risk factors associated with significant bleeding complications.[4] Independent risk factors for major complications reported by other authors include a higher baseline serum creatinine level or reduced estimated GFR, diastolic BP >90 mm Hg, platelet count <120,000/μL, and BUN ≥60 mg/dL.[1-3] In our study, 96 patients (22.2%) had a diastolic BP >90 mm Hg while 140 (32.3%) had a systolic BP greater than 140 mm Hg. However, there was no difference in the rate of complications (both major and minor) between those who had a systolic/diastolic BP greater than 140/90 and those who did not. Previous reports have suggested an association between the risk of complications and underlying histopathologic diagnosis. Many diseases such as amyloidosis, acute tubular necrosis, and end-stage kidney disease were found to have an increased risk of bleeding. However, more recent studies have not shown this association.[1] In the current study, we found that only a prolonged PT before the procedure was associated with increased risk of major complications. The difference in the other clinical and laboratory parameters was not statistically significant between the two groups in relation to occurrence of major and minor complications (Table 1). The fact that we could not find a significant correlation between risk factors and major complications could be attributed to a small sample size.

The type of needle, gauge, and number of passes may have a link with the risk of complications. A larger needle is more likely to induce trauma and hence a greater complication rate. On the other hand, a smaller gauge needle may require more number of passes to obtain an adequate sample, which may also lead to higher complication rate.[10] At our institution, both 16-gauge and 18-gauge needles

are used to perform kidney biopsies. However, being a retrospective chart review, we could not gather precise information on the needle size and number of passes and that is a limitation of our study. Eiro et al have found that >5 needle passes is associated with a higher complication rate.[11] Manno et al and the Norwegian registry data reported no difference in the frequency of complications or diagnostic yield comparing 14-gauge with 16-gauge needles.[12,13] However, Corapi et al found that the use of 14-gauge needle was associated with an increased need of blood transfusion compared to 16- or 18-gauge needles.[4] As far as the difference between a manual and automated needle is concerned, the complication rate does not differ with the same needle gauge, regardless of the type.[13]

To have a conclusive histopathologic diagnosis, an adequate sample size must be obtained. Minimum sample size for diagnosis varies greatly with the specific diagnosis; for instance, membranous glomerulonephritis can be diagnosed from a single glomerulus.[14] For most light microscopic assessment to adequately assess severity and distribution of lesions, 8 to 10 glomeruli are needed.[14] Needle gauge has dramatic impact on sample obtained. Eighteen- or 19-gauge needles give very small, narrow samples and often may have inadequate representation of vessels. In our data, we had an adequate glomerular yield in 97.7 % of biopsies despite the fact that we did not have the facility to have a stereomicroscope and a renal pathologist at the site to check for sample adequacy.

In recent times, kidney biopsies have been taken over by nonnephrologists, particularly radiologists, in many institutions. Studies looking at the complication rates and glomerular yield of the procedures performed by radiologists versus nephrologists have not found any significant differences in outcomes.[15] Chung et al reported 568 native kidney biopsies performed by nephrologists or radiologists using the ultrasound-marked blind or real-time ultrasound-guided techniques.[16] No differences in postbiopsy complications were observed among the two groups. Similar observations have been made by Corapi et al.[4] A study by Gupta and Balogun reported 37 biopsies performed under real-time ultrasound guidance (23 biopsies (62%) were performed by a nephrology fellow while 14 biopsies (38%) were performed by a radiologist).[17] Mean complication scores and glomerular yield were similar in both the groups. However, severe complications were significantly less in nephrology fellow performed biopsies. In a case series from India, nephrologists performed real-time ultrasound-guided PKB on 37 patients. The results were then compared with those of a similar number of biopsies performed with a radiologist's support.[18] The diagnostic yield was similar between the two groups. However, the complication rate was higher in the radiologist group.[18] In our study, majority of the biopsies were performed by nephrologists (68%), and the complication rates as well as glomerular yield were not different whether the operator was a nephrologist or radiologist.

MPGN was the most frequent histopathologic diagnosis (17.6%) in our data followed by FSGS (16.4%) and interstitial nephritis (13.9%). An earlier retrospective analysis of 511 consecutive renal biopsies from the same center had reported MPGN to be the most common histological lesion (28%).[19] Another study from Pakistan, however, found FSGS as the leading histological diagnosis in their series of 1793 adult renal biopsies.[20] Despite the fact that the incidence of MPGN is declining all over the world, we have significant number of cases labeled as MPGN in our cohort of renal biopsies. One possible explanation for this might be the higher incidence of infections such as hepatitis B and C in our part of the world.

To the best of our knowledge, this is the largest study from Pakistan reporting the safety and yield of PKB. However, it has certain limitations which need to be addressed. Being a retrospective analysis has its engraved bias. There could be potential underreporting, reporting bias and lack of detailed information about other potential complications. This study cohort formed a small population which might

underestimate the frequency of complications. Since it is a single center study, the results cannot be generalized and hence may not be representative of the general population.

Conclusion

PKB with an automated gun under real-time ultrasound guidance is a safe procedure with excellent yield to establish the histological diagnosis of the renal disease. The most common complications are related to bleeding, and only rarely are these catastrophic.

Conflict of interest: None declared.

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