Clinico-pathological Profile of Kidney Biopsy Patients in a Tertiary Hospital of Central Nepal

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ABSTRACT

Background

Kidney biopsy is an important diagnostic tool in Nephrology. As of now, we don't have a central kidney biopsy registry in our country and there are many studies showing heterogeneous patterns of pathologies observed in the country. We thought of looking on the clinico-pathological profile of kidney biopsy patients prevailing in our centre.

Objective

This study was carried out with an objective to know the clinico-pathological profile of kidney biopsy patients prevailing in our centre.

Method

This was a hospital based, prospective, observational study carried out in a tertiary teaching hospital of Chitwan over a period of 3 years from May 2016 to April 2019. All the consecutive kidney biopsy patients were included in the study. The indication of kidney biopsies were the standard indication based on clinical presentation and investigations. The patient`s demographic profile, indication of kidney biopsy and histological patterns were studied and analysed using appropriate statistical tools.

Result

A total of 210 kidney biopsies were analysed over a period of three years, that makes around 5-6 biopsies per month. The mean age of the patient was 35.7 ± 14.9 years. Male were 106 (50.5) and females were 104 (49.5) with male to female ratio of 1.01. The average number of glomeruli was 23.4 ± 11.0. The commonest indication of kidney biopsy and histological pattern were nephrotic syndrome 56 (26.7) and IgA nephropathy 51 (24.2) respectively. Among nephrotic syndrome group, the commonest histological pattern was minimal change disease 21 (37.5). Non-diabetic kidney diseases in diabetes were seen in eight (53.4) diabetic patients making it a significant problem in diabetes and the commonest histological pattern in them were minimal change disease and idiopathic cresentic glomerulonephritis two (13.3) each.

Conclusion

The commonest indication and histological pattern of the kidney biopsy were nephrotic syndrome 56 (26.7), and IgA Nephropathy 51 (24.2) respectively. Non-diabetic kidney diseases in diabetes were seen in eight (53.4) of the diabetic patient making it a significant problem in diabetes and the commonest histological pattern in them were minimal change disease and idiopathic cresentic glomerulonephritis two (13.3) each.

KEY WORDS

IgA nephropathy, Kidney biopsy, Nephrotic syndrome

INTRODUCTION

Kidney biopsy is an important diagnostic tool in Nephrology. It is useful not only in diagnosis but also in prognosis of the disease.[1] The histo-patholological study of kidney biopsy has maintained its charm even today and is still the gold standard for the diagnosis and prognosis of disease.[2] Unfortunately as off now, we don't have a central kidney biopsy registry and there are heterogeneous patterns of pathologies observed within the country. There are several possible reasons for this heterogeneity. These include: small numbers of patients in the studies, differences in the indications for biopsies, referral bias, geographical differences and the non-availability of the tool like electron microscopy.

We had realized that the kidney diseases are growing health problem in our hospital. Patients from different parts of the country and across the border come for the diagnosis and treatment in our centre. Many of them need kidney biopsy. Although we had one study on kidney biopsy from our center.[3] And, we thought of looking again on the clinico-pathological profile of kidney biopsy patients as the nature of the kidney disease may change with the time and the sample size.

METHODS

This was a hospital based, prospective, observational study carried out in a tertiary teaching hospital of Chitwan over a period of three years from May 2016 to April 2019. All the consecutive kidney biopsies were included in the study. The clinical diagnosis of the renal diseases were made by a nephrologist with an experience of > five years in clinical nephrology and all the diagnoses were supported by relevant biochemistry, radiology and pathology reports. The indication of kidney biopsies were the standard indication based on clinical presentation and investigations. Kidney biopsy was done by a nephrologist. A self-adjustable, automated, spring loaded biopsy (needle) gun of 16 to 18 G size (Bard Monotopy USA 16-18 G) was used for kidney biopsy. Kidney biopsy was performed under ultrasonography guidance with the help of radiology resident or junior consultant. Two cores of renal tissue were removed, one for light microscopy (LM) and other for Immunofluorescence (IF). These two cores were kept, one in N/10 normal saline and the other in michel media for LM and IF respectively. The tissues were then transported to Ranbaxy Clinical Reference Laboratories in India within 24-48 hours. In the Ranbaxy Clinical Reference Laboratories the tissues were processed in a standard protocol and procedure and examined for LM and IF for histopathological pattern. The data including demographic profiles, indications of kidney biopsy and histological patterns were recorded. The data were then entered in the MS XP sheet and were transferred to SPSS version 20 (Chicago, IL, USA) programme for analysis. The data were analysed using appropriate statistical tools. The continuous variables were expressed as mean ± standard deviation (SD) and ratio. The categorical variables were expressed as frequency and percentage. The approval to conduct the study was taken from the ethical committee of the hospital. A written consent was taken from each patient for the enrolment and for the procedure, after explaining the risk and benefit of the procedure.

RESULTS

A total of 210 kidney biopsies were analysed over a period of three years, that makes around 70 biopsies per year and around 5-6 biopsies per month. The mean age of the patient was 35.7 ± 14.9 years. The age ranges of patients were from 9 years to 76 years. The youngest one to undergo biopsy was a child of 9 years with an indication of steroid resistant nephrotic syndrome and the eldest was of 76 years with an indication of adult onset nephrotic syndrome.

Table 1. Age distribution of patients (n=210)

Age (in years)	Male n(%)	Female n(%)
1-20	25(45)	20(21.4)
21-40	43(91)	48(43.3)
41-60	33(65)	32(30.9)
61-80	5(9)	4(4.3)

The male were 106 (50.5%) and females were 104 (49.5%) making the male to female ratio of 1.01. Out of 210 renal biopsies, 136 (64.7%) patients were of age < 40 years and remaining 74 (35.3%) were of age ≥ 40 years. The average size of biopsy tissue obtained was 0.9 ± 0.3 cm. The minimum size being 0.3 cm and the maximum size was 1.8 cm. The average number of glomeruli was 23.4 ± 11.0. The minimum number was 2 and the maximum was 76. Of 210 biopsies, glomeruli number less than 10 were seen in 10 (4.76%) patients.

Table 2. Indications of kidney biopsies (n=210)

Indication of Kidney Biopsy	Number of patients (%)
Nephrotic syndrome	56 (26.7)
Unexplained chronic kidney disease	33 (15.7)
Lupus Nephritis (LN)	28 (13.3)
Nephrotic/Nephritic Syndrome	23 (10.9)
Rapidly Progressing Glomerulonephritis	15 (7.1)
Non-diabetic kidney disease on Diabetes Mellitus	15 (7.1)
Subnephrotic range proteinuria	10 (4.7)
Asymptomatic microscopic hematuria	9 (4.2)
Unexplained Acute Kidney Injury	8 (3.8)
Nephrotic range proteinuria without features of Nephrotic Syndrome	8 (3.8)
Acute Nephritic Syndrome	3 (1.4)
Episodic macroscopic hematuria	1 (0.5)
Henoch Schonlein purpura with renal involvement	1 (0.5)

Table 3. Histological patterns of kidney biopsies (n=210)

Histological pattern of Kidney Biopsy	Number of patients (%)
IgA Nephropathy	51 (24.2)
Minimal Change Disease (MCD)	29 (13.8)
Lupus Nephritis (LN)	28 (13.3)
Membranous Glomerulopathy (MGN)	21 (10)
Focal Segmental Glomerulosceloris (FSGS)	18 (8.6)
Idiopathic Cresentic Glomerulonephritis	15 (7.1)
Diffuse Proliferative Glomerulonephritis	10 (4.8)
Diabetic Nephropathy	7 (3.3)
Acute Tubular Necrosis (ATN)	6 (2.8)
Myeloma kidney	5 (2.4)
Hypertensive Nephrosclerosis	5 (2.4)
Glomerulonephritis (MesPGN)	4 (1.9)
Amyloidosis	4 (1.9)
Nonspecific Chronic Glomerulonephritis	3 (1.4)
Normal kidney biopsy	3 (1.4)
Nonspecific Chronic Interstitial Nephritis	1 (0.5)

Among the Nephrotic syndrome (n=56), the male were higher in number 36 (64.2%) than females 20 (35.8%) making the male to female ratio of 1.8. Out of 56 nephrotic syndromes, 37 (66.1%) were of age < 40 years and remaining 19 (33.9%) were of age ≥ 40 years.

Table 4. Histological patterns in nephrotic syndrome group (n=56)

Nephrotic syndrome Group	Number of patients (%)
MCD	21 (37.5)
MGN	17 (30.4)
FSGS	7 (12.5)
IgA Nephropathy	5 (8.9)
Amyloidosis	4 (7.1)
Diffuse Proliferative Glomerulonephritis	1 (1.8)
Idiopathic MesPGN	1 (1.8)

The different classes of lupus nephritis seen were class II two (7.1%), class III two (7.1%), class IV 13 (46.4%), class V four (14.3%), class III+V two (7.1%) and class IV+V five (17.8%).

Table 5. Histological patterns seen in diabetic patients (n=15)

Diabetic patients with kidney biopsy	Number of patients (%)
Diabetic Nephropathy	7 (46.6)
MCD	2 (13.3)
Idiopathic Cresentic GN	2 (13.3)
MGN	1 (6.7)
FSGS	1 (6.7)
IgA Nephropathy	1 (6.7)
Idiopathic MesPGN	1 (6.7)

DISCUSSION

Majority of the patients in our study were of age less than 40 years, suggesting that renal diseases were common problem of young age. Similar observations were made in studies done by Manandhar et al. and Subedi et al.[4,5] The paediatric age group (1 to 16 years) who had undergone biopsy were 18 (8.6%). This low prevalence of kidney biopsy in paediatric patients, indirectly suggested either a higher age of onset of the renal diseases or stringent criteria for biopsy or a hesitancy and fear of subjecting biopsy in children. Similar observations of lower rate of kidney biopsies in children were reported from Italy, and Romania.[6,7] The male and females were almost equal in number, making the male to female ratio of 1.01, signifying that this disease is equally important for both males and females. Similar observations were made in studies from European countries like and Romania and Serbia.[7,8] There is considerable regional variation in the gender distribution within and across the country. Some studies from Nepal had shown female preponderance while others male.[3,5,9-11] So, we need larger multicentric study to see the real gender difference.

Nephrotic syndrome was the most common indication for renal biopsy 56 (26.7%) in our study. Similar studies from other centres had also shown nephrotic syndrome to be the commonest presentation.[4,5,10,11] Similar observation was made in a study from northwest India.[12] Likewise, in a review of ten-year registry of native kidney biopsy from a single centre in China from 2000 to 2010, the most common indication for renal biopsy was NS (52%).[13] This highlights that nephrotic syndrome is the commonest clinical presentation worldwide. In our previous study, the commonest clinical presentation was subnephrotic range proteinuria 40 (53.3%), however the current study showed nephrotic syndrome as the dominant clinical presentation signifying that with change in time and sample size the dominant clinical syndrome can change.[3]

We found unexplained chronic kidney disease (uCKD) as the second most common indication of renal biopsy, which was not documented in studies from Nepal.[4,5,9-11] This might be a message that the unexplained CKD are increasing in our population. LN was the third common clinical presentation suggesting that LN is also a significant problem in our region. However, the classical acute nephritic syndrome was not a common presentation seen only in three (1.4%) cases, which was similar to an Italian survey.[6] This observation of low prevalence of classical acute nephritic syndrome in our study, was surprising for us as we had expected more of it considering a high burden of infectious diseases in our region.

We had seen a good trend of doing kidney biopsy in diabetes patient. Fifteen (7.14%) diabetic patients had undergone kidney biopsy with a suspicion of non-diabetic kidney disease. Different studies had established that diabetic patients do have underlying non diabetic kidney

disease.[14,15] The average size of the biopsy tissue was 0.9 ± 0.3 cm and the mean number of glomeruli was 23.4 ± 11.0. It is said that the average number of glomeruli needed for the optimal interpretation of kidney biopsy is around ten.[17] More than 200 (95.2%) patients in our study had glomeruli more than ten signifying that the glomeruli numbers were good enough for the optimal interpretation.

There seems a considerable regional variation in the patterns of the kidney biopsies within the country.[4,6,10,12] As evidenced by some of the studies from Nepal.[3,5,9-11,16] Like studies by Manandhar et al., Tuladhar et al., and Khakurel et al., had shown MCD as the commonest pattern whereas Sharma et al. and Aryal et al. had shown MGN as the commonest pattern.[4,9,10,11,16] A uniform pattern was not observed. So we need larger multicentric study and central kidney biopsy registry to see the true pattern prevailing in our country. Also the true patterns are underrepresented, as not all patients with renal disease are biopsied.

The most common histological pattern seen in our study was IgA Nephropathy 51 (24.9%). Similar observation was made by Subedi et al. from eastern Nepal.[5] The observed incidence of IgA nephropathy might be underestimated considering the indolent and asymptomatic nature of the disease and restricted biopsy practice pattern. Similar to our study, IgA nephropathy was the commonest pathology observed in studies from China (50.7%) and Korea (28%).[18,19] Likewise, in Australia and USA also the most common diagnosis was IgA nephropathy, accounting for 34% and 21% of the cases respectively.[20,21] IgA nephropathy was reported to be the commonest type of glomerulonephritis in several parts of the world making it the commonest pattern worldwide. In our previous study, the commonest histopathological pattern observed was idiopathic mesangio-proliferative glomerulonephritis 18 (24.0%), however the current study showed IgA nephropathy as the dominant histological pattern signifying again that the pattern can change with sample size and the time.[3]

MCD was the second most common pattern 29 (13.80%) observed in our study. Unlike our study, MCD was the commonest pattern observed in studies done by Manandhar et al., Tuladhar et al. and Khakurel et al.[4,9,10] MCD has a variable geographic distribution, being more common in Asia than in North America or Europe.[22]

In a study conducted by Rathi et al. from India, incidence of MCD was found to be 14.8%, which was similar to ours 29 (13.8%).[23] Similarly, the incidence was comparable to the study done by Suryawanshi et al., where 15.8% of the patients had MCD.[24]

LN was the most common secondary glomerulonephritis seen worldwide.[2,23,25] Lupus nephritis was the third most common pattern observed in our study. These observations are reflecting that lupus nephritis is a significant problem in our region also and merits a separate study. The dominant class of Lupus nephritis in our study was class IV 13 (46.4%) with majority (> 50%) being from class III and IV. Similar observations were made by Huong et al., where the majority had a class III and IV (49.0%).[26] The higher prevalence of proliferative disease class III and IV observed in the study might be because of higher number of biopsy subjected in these patient, as they usually present with overt nephritis.

MGN was the fourth common pattern 21(10.0%) observed in our study. A study by Aryal et al. showed MGN to be the commonest form of GN (42.3%).[16] FSGS 18 (8.6%) was the fifth common pattern observed in our study but lately FSGS is emerging as the commonest pattern of primary nephrotic syndrome as shown by Rathi et al.[23] Similar observations were made in the studies from Senegal, India and Sudan.[27-29] However, in some of the studies done in Nepal by Khakurel et al. and Sharma et al.[10,11] FSGS was found to be the second most common pattern. This suggests that there is a considerable regional variation in the patterns of the kidney biopsies within and across the country.

In Nephrotic syndrome group (n=56), the three most common histological pattern observed were MCD 21 (37.5%) followed by MGN 17 (30.4%) and FSGS seven (12.5%). This observation highlights that the histological pattern may vary within different group of clinical syndrome and sample size as one pattern may step up or down the list when assessed in different group or in totality. The pattern may vary according to the region, race and the ethnicity within the country. Thigh highlights the need of large multicentric studies in various provinces of Nepal.

Many studies had shown diabetic patients to have non diabetic kidney disease.[15,16] In our study eight (53.4%) of the diabetic patient had non diabetic kidney disease. The most common pattern of non-diabetic kidney disease was MCD two (13.3%), idiopathic cresentic GN two (13.3%) followed by MGN one (6.7%), IgA Nephropathy one (6.7%), FSGS one (6.7%) and idiopathic MesPGN one (6.7%). Similar observation was made in a study done by Das et al., where MCD was the commonest non diabetic kidney disease.[16] In another study done by Erdogmus et al. the most common non diabetic kidney diseases were membranous nephropathy (29.2%), tubulointerstitial nephritis (20.8%) and IgA nephropathy (12.5%).[30] This can be an area of research in future to better understand the nature of non-diabetic kidney disease in diabetes patients prevailing in our region.

There were few limitations in this study. Foremost being an observational study; all the inherent limitations of an observational study were there in the study. This was also a single centre study, so the results might not be generalizable/generalized to whole region and the country, highlighting the need for multicentric studies with uniform protocol.

CONCLUSION

There was almost equal distribution of males and the female in the study with male to female ratio of 1.01. The mean age of the patient was 35.7 ± 14.9 years. The most common indication of the kidney biopsy was nephrotic syndrome 56 (26.7%) and the most common histological pattern was IgA Nephropathy 51 (24.2%). Non-diabetic kidney disease in diabetes was present in eight (53.4%) of the diabetic patients. The commonest non diabetic kidney disease in diabetes was minimal change disease and idiopathic cresentic glomerulonephritis two (13.3%) each. There seems a considerable regional variation in clinical presentation and histological pattern of the kidney biopsy within the country and the clinical and histological patterns of kidney biopsies can change with time and sample size. So we need a larger and multicentric study and also a central kidney biopsy registry to precisely understand the true pattern of the disease prevailing in our country.

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