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Original Article

Renal Disease in Nepal, Under Microscope: One Year Study

Nirajan Mainali[1], Barsha Acharya[2], Upasana Lamichhane[2], Ganesh Phulara[2]

[1]*Department of Pathology, Kathmandu medical college teaching hospital, Kathmandu Nepal*

[2]*Department of Pathology, Pratham pathology laboratory private limited, Kathmandu, Nepal*

ABSTRACT

Introduction: Renal disease is a significant health problem in Nepal which is creating an increasing health and economic burden. Renal disease usually does not cause symptoms until reaching an advanced stage. Correct diagnosis of renal biopsy requires correlation of clinical, biochemical, serological parameters and histopathological examination by light microscopy, immunofluorescence and sometimes electron microscopic examination. The present study was conducted to study the histopathological patterns of all renal biopsy specimens in Nepal with the help of information obtained from Light microscopy and Immunofluorescence examination.

Materials and Methods: In this cross-sectional (Prospective study) undertaken at Pathology Department at Pratham Pathology Laboratory, Lazimpat over a period of 1year duration (January 1ST - December 31ST 2022), all renal biopsy specimen of patients with different glomerular diseases were enrolled. Final diagnosis was made by pathologist correlating with the histopathological along with immunofluorescence and other clinical and laboratory findings.

Results: A total of 195 patient renal biopsies specimen between aged (1-80years) were enrolled. Majority of patients were in the age group of 21-30 years (23.60%). The study showed slight female predominance with Male to female ratio of 1: 1.34. The most common renal disease was Lupus Nephritis with frequency of 64 with predominance of Lupus Type IV with frequency of 34 (17.45. Among all, 21 cases were of Chronic Glomerulonephritis and the most common leading cause for it was IgA Nephropathy with frequency of 8 (38.10%).

Conclusions: The most common diagnosed renal disease under microscope was Lupus Nephritis with frequency of 34 (17.45%). The leading primary glomerular disease for Chronic glomerulonephritis was IgA Nephropathy with frequency of 8 (38.10%).

Keywords: Chronic Glomerulonephritis; Chronic Kidney Disease; Glomerular diseases; Light Microscopy; Immunofluorescence

Correspondence:
Dr. Nirajan Mainali, MD
Associate professor, Department of Pathology, Kathmandu Medical College Teaching Hospital, Sinamangal, Kathmandu
ORCID ID: 0000-0002-6648-1914
Email: mainali_nirajan@hotmail.com

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INTRODUCTION

Renal disease has been recognized as a significant health problem in Nepal and is increasing health and economic burden.[1] Renal disease usually does not cause symptoms until reaching an advanced stage.[1] Incidence of renal diseases varies greatly in various part of the world and the prevalence changes with the time. [2 3] Moreover, renal diseases have remained understudied in Nepal. Its prevalence and specific knowledge regarding different types of kidney disease has important implication for planning treatment and predicting its prognosis in patient with renal disease.[4] Renal disease is most often caused by other conditions that put a strain on the kidney and high blood pressure and diabetes being the most common causes of kidney disease.[1]

Renal biopsy plays an important role in the diagnosis of kidney disease and identifies type of glomerular injuries, associated tubular, interstitial and vascular abnormalities involved in its cause. [5] There are two types of renal biopsy, native renal biopsy and transplant renal biopsy. A native renal biopsy is one in which the patient's own kidneys are biopsied. In a transplant renal biopsy, the kidney of another person that has been transplanted into the patient is biopsied.[6]

The biopsied tissue are processed for Immunofluorescence microscopy, electron microscopy and paraffin embedded tissue for light microscopy.[7] Light microscopy is used for the first classification of renal disease where it helps in understanding nephron structure and visualizing morphological alterations. For visualization of etiological and pathogenic factors in renal biopsy, immunofluorescence is used as a diagnostic procedure. [8]Therefore, correct diagnosis of renal biopsy requires correlation of clinical, biochemical, serological parameters and histopathological examination by light microscopy, immunofluorescence and sometimes electron microscopic examination .[9]

So, there is the need of identifying renal disorders at early stage in order to retard the rapid progression to end stage renal disease. In Nepal, there are very few published data on the spectrum of renal disease based on histopathological and immunofluorescence examination diagnosis.

The present study was conducted with an aim to study the patterns of renal disease in Nepal and recognizing its underlying pathology by light microscopy and immunofluorescence examination.

MATERIALS AND METHODS

This is a cross sectional (Prospective study) undertaken at Pathology Department at Pratham Pathology Laboratory, Lazimpat over a period of 1year duration (January 1st - Dec 31st 2022). A total of 195 patients undergoing renal biopsies with different glomerular disease received at the laboratory were enrolled in this study. Demographic data including age, sex, male female ratio and clinical diagnosis were recorded.

Final diagnosis was made by pathologist after correlating the histopathological findings along with immunofluorescence and other clinical and laboratory findings.

All patients with renal biopsy specimen received at the Pratham Pathology laboratory and patient party willing to give informed written consent were included in the study. Those who were unwilling to give consent were excluded from the study. All renal biopsies were processed following the standard processing technique, one each for Light Microscopy (LM) and Immunofluorescence (IF). For light microscopy, paraffin sections were stained for hematoxylin and eosin, Periodic Acid Schiff, Masson Trichome, Congo red. For Immunofluorescence the slides were stained with Anti Human IgG, IgA, IgM, C3 and C1q. Slides kept under the microscope and the diagnosis was recorded.

DEFINITION OF SOME RENAL DISEASES:

Chronic Kidney Disease (CKD): Is defined as per national kidney foundation and is present when kidney damage either functional/ structural, occurs or by a deterioration in GFR below 60ml/min/1.73m2 of body surface area for > 3months.[10]

Chronic glomerulonephritis (CGN): Is characterized pathologically by varying degrees of glomerular scarring which is always accompanied by cortical tubular atrophy, interstitial fibrosis, interstitial infiltration by chronic inflammatory cells, and arteriosclerosis.[10]

Pathological diagnosis of End Stage Renal Disease (ESRD) is concluded when the glomerular, interstitial, and vascular sclerosis worsen which eventually can reach a point at which histologic evaluation of the kidney tissue cannot show even the initial cause for the kidney injury.[11]

Data were entered in Excel v 11 after receiving at the laboratory and was checked after every 10 day entry and exported to SPSS (Statistical Package for Social Sciences) 2020 for statistical analysis. For Descriptive Statistics: frequency, Percentage (%) and Ratio were calculated along with graphical and tabular presentations were made.

RESULTS

A total of 195 Renal biopsies samples were studied during the study period. In this study, Majority of the patients were in the age group of 21-30 years (23.60%) followed by 31-40 years (21.54%) followed by 11-20 years (20.51%) followed by 41-50 years (13.33%) followed by 51-60 years (10.77%) followed by 61-70 years (5.13%) followed by 1-10 years and 71-80 years (2.56% each) .The minimum age of the patient was 5 years and maximum age was 75 years is shown in **(Table 1).** In this study, 112 (57.44%) were females and 83 (42.56%) were males with Male: Female (M: F) ratio of 1: 1.34.

Table 1: Age - wise distribution of the study population

AGE RANGE (Years)	FREQUENCY [n(%)]
1-10	5 (2.56)
11-20	40 (20.51)
21-30	46 (23.60)
31-40	42 (21.54)
41-50	26 (13.33)
51-60	21 (10.77)
61-70	10 (5.13)
71-80	5 (2.56)
Grand Total	195 (100)

Histopathological patterns of renal biopsies

Among 195 cases studied, the most common renal disease was Lupus Nephritis with frequency of 64 with predominance of Lupus type IV **(fig. 1)** showing frequency of 34 (17.45%) followed by IgA Nephropathy **(fig. 2)** with frequency of 21 (10.77%) followed by Acute kidney injury with frequency of 13 (6.67%) followed by Chronic Glomerulonephritis with frequency of 12 (6.15%) followed by Focal Segmental Glomerulosclerosis with frequency of 10 (5.13%) followed by other glomerular and tubular/interstitial diseases and the least common diseases were Acute Antibody mediated rejection, Alport syndrome, C1q Nephropathy, C3 Glomerulonephritis, Cortical necrosis,

Cryoglobulinemia, Medullary infection, Tacrolimus toxicity with the frequency of 1 (0.51%) in each case. One of the sample was inadequate for the study is seen in Table 2.

Table 2: Histopathological patterns of renal biopsies under microscope

Histopathological diagnosis		Frequency [n(%)]	Histopathological diagnosis	Frequency [n(%)]
Lupus Nephritis	**Type II**	5 (2.59)	**Acute Tubulointrstitial nephritis**	5 (2.56)
	Type III	11 (5.64)	**IgM Nephropathy**	4 (2.05)
	Type IV	34 (17.45)	**ANA negative Lupus Nephritis**	3 (1.54)
	Type V	14 (7.18)	**RPGN**	3 (1.54)
IgA Nephropathy		21 (10.77)	**Anti-GBM, RPGN**	2 (1.02)
Acute kidney injury		13 (6.67)	**Chronic Tubulointrstitial Nephritis**	2 (1.02)
Chronic GN		12 (6.15)	**Diffuse proliferative GN**	2 (1.02)
Focal Segmental Glomerulosclerosis		10 (5.13)	**Descriptive**	2 (1.02)
Hypertensive changes		9 (4.62)	**Acute Antibody mediated rejection**	1 (0.51)
Antineutrophilic cytoplasmic antibody (ANCA) associated nephritis	**ANCA associated GN**	6 (3.06)	**Alport syndrome**	1 (0.51)
	ANCA associated chronic GN	1 (0.51)	**C1q Nephropathy**	1 (0.51)
	ANCA associated Rapid GN	2 (1.02)	**C3- GN**	1 (0.51)
Minimal change disease		8 (4.10)	**Cortical necrosis**	1 (0.51)
Post-infectious glomerulonephritis		6 (3.06)	**Cryoglobulinemia**	1 (0.51)
Diabetic nephropathy		6(3.06)	**Medullary infection**	1 (0.51)
Membranous nephropathy		5 (2.56)	**Tacrolimus toxicity**	1 (0.51)
Inadequate sample		1 (0.51)	**Total**	195 (100)

GN= **Glomerulonephritis;** ***GBM*= Glomerular basement membrane;** ***RPGN:*** **Rapidly proliferative glomerulonephritis**

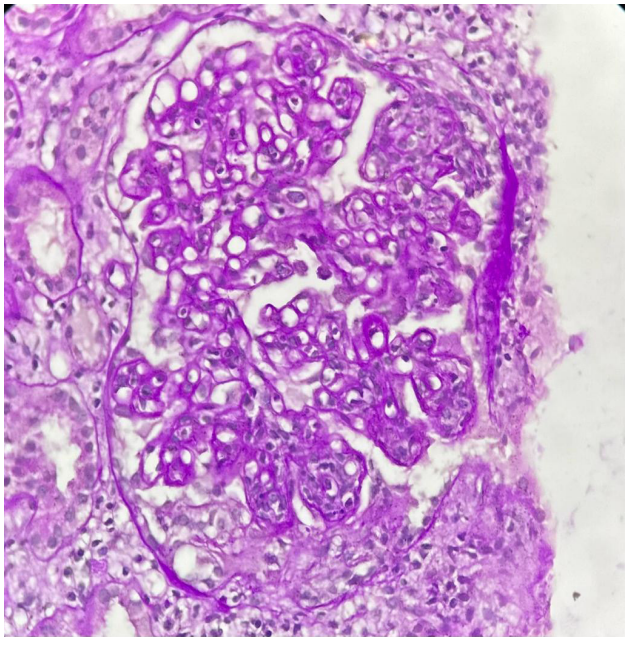

Figure 1: H&E section showing endocapillary proliferation associated with lupus nephritis (HE stain; 40X).

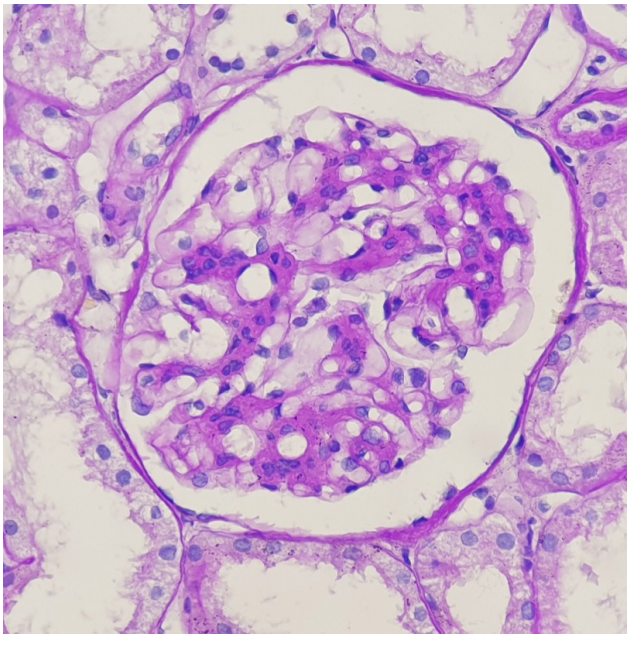

Figure 2: H&E section showing mesangial proliferation associated with IgA Nephropathy (HE stain; 40X).

Causes of Chronic Glomerulonephritis

Of the 195 cases included in this study, 33 cases were of Chronic glomerulonephritis. Among these 33 cases, 12 cases were due to progressive chronic glomerulonephritis itself and 21 cases were due to other causes. The most common cause for chronic glomerulonephritis was IgA nephropathy with frequency of 8 (38.10%) followed by Hypertensive changes and Diabetic nephropathy with frequency of 2 (9.52%) each. The least common causes were Lupus Nephritis Type IV+V with frequency of 1 (4.76%). Male and female were equally affected with slight male predominance where male having frequency of 11 and female 10 as shown in **[Table 3].**

Table 3: Causes of Chronic glomerulonephritis among the study populaiton

Causes	Frequency (n) [Male (M) and Female (F)]	Percentage (%)
IgA Nephropathy	8 (M = 4, F =4)	38.10
Hypertensive changes	2 (M =2)	9.52
Diabetic Nephropathy type IV	2 (F = 2)	9.52
Lupus Nephritis Type IV+ Type V	1 (M)	4.76
Post-infectious glomerulonephritis	1 (F)	4.76
Antineutrophilic cytoplasmic associated Chronic Glomerulonephritis	1 (F)	4.76
Rapidly Proliferative glomerulonephritis	1 (M)	4.76
Membranous Nephropathy	1 (M)	4.76
ANA negative lupus like nephritis	1 (F	4.76
Focal Segmental Glomerulosclerosis	1 (F)	4.76
Cryoglobulinemia	1 (M)	4.76
Diffuse proliferative glomerulonephritis	1 (M)	4.76
Total	21 (M =11, F =10)	100%

DISCUSSION

Renal disease is a significant health problem in Nepal which is creating an increasing health and economic burden. Incidence of renal diseases varies greatly in various part of the world and prevalence changes with the time. Renal disease usually does not cause symptoms until reaching an advanced stage. Early detection of renal disease leads to better therapy and reduction in morbidity and mortality.

Renal biopsy plays an important role in the diagnosis of kidney disease and identifies type of glomerular injuries, associated tubular, interstitial and vascular abnormalities involved in its cause. Chronic glomerulonephritis (CGN) is characterized pathologically by varying degrees of glomerular scarring which is accompanied by cortical tubular atrophy, interstitial fibrosis, interstitial infiltration by chronic inflammatory cells, and arteriosclerosis.

If the initial phase of renal injury is not halt, it eventually can reach a point at which histologic evaluation of the kidney tissue cannot show even the initial cause of kidney injury. Therefore, timely correct diagnosis of renal disease is essential where histopathological examination plays an important role. So, histopathological examination by light microscopy, immunofluorescence and sometimes electron microscopy examination is needed for the diagnosis of renal disease.

Study investigating the histopathological patterns of renal disease in Nepalese population using light microscopy and immunofluorescence are limited. Moreover, renal diseases have remained under studied in Nepal and there are very few studies where histopathological causes of chronic glomerulonephritis are elaborated.

This study provides detailed information about the histopathological patterns of renal diseases and the causes of chronic glomerulonephritis in biopsy specimen diagnosed using light microscopy and immunofluorescence examination, in Asian population of Nepal.

Age and Gender

In the present study, the highest number of cases was in the age group 21-30 years (23.60%) followed by 31- 40 years (21.54%) followed by 11-20years (20.5%). Study conducted by Maskey. A et al[3] on 175 patients and Khakurel S et al[12] showed similar findings. Another study conducted by Kafle P.M et al[4] on 194 cases showed maximum age group as 16-75 years. This slight discrepancy could be due to disease burden in younger age group for the sample received at the laboratory.

In the present study, 112 patients were females and 83 were male with Male: Female ratio of 1 : 1.34 and accounting (57.54%) and (42.56%) respectively with female predominance and was concordant with other studies done in Nepal.[3,4] Another study conducted by Modugumudi N.S.A et al on 137 biopsies showed, 89 males and 48 females with Male : Female ratio of 1.85:1 and accounting (65%) and (35%) respectively with male predominance. [13] This discrepancy may be due to small number of cases in study compared to the present study.

Histopathological patterns of renal biopsies under microscope

In the present study, the most common histopathological diagnosis was Lupus Nephritis with predominance of Lupus type IV followed by IgA nephropathy followed by Acute Kidney Injury followed by Chronic Glomerulonephritis accounting 34(17.45%), 21 (10.77%) ,13 (6.6%) and 12 (6.15%) respectively. This finding was concordant with the study done by Kafle P.M et al on 194 cases which showed most common histopathological disease as Lupus Nephritis Type IV accounting 40 (20.6%).[4] Similarly, in study conducted by Farah I.R et al on 209 renal biopsies study showed most common histopathological diagnosis to be Lupus Nephritis accounting 33.5% which is again similar to the present study.[14] Shrestha S conducted study on 160 renal biopsies showed most common histopathological diagnosis to be Lupus Nephritis Type IV accounting 34.3% which is again similar to the present study**.**

Another study conducted by Ghimire M on 75 biopsies study showed most common histopathological diagnosis to be

Mesangial Proliferative Glomerulonephritis followed by Minimal change disease and Lupus Nephritis accounting 18 (24%), 16 (21.3%) and 10 (13.3%) respectively which is in opposition to the present study. [15] The reason could be due to less number of cases studied then in the present study and also all cases not undergoing renal biopsy as many of the Lupus cases are follow up in rheumatology clinic .

Frequency of causes of Chronic Glomerulonephritis

In the present study, there were 21 cases of Chronic glomerulonephritis and among them, the most common cause of CGN was IgA Nephropathy accounting for 8 (38.10%). Alyousef A et al showed the most common cause of CGN as IgA nephropathy (63%) accounting for 85 (23.9%) . This finding was in near concordance with the present study.[16] Another study conducted by Rafique . Z et al showed the common cause of CGN as Focal segmental glomerulonephritis (primary cause) and Lupus Nephritis (secondary cause) accounting for 2 5(30.9%) and 8 (9.9%) respectively which is in opposition to the present study. [17]

CONCLUSIONS

The most common age of renal biopsies specimen received in Pratham pathology laboratory was in the age group of (21-30 years) and least common was in (1-10 years and 71-80 years) and showed slight female predominance. The most common diagnosed renal disease under microscope was Lupus Nephritis Type IV with frequency of 34 (17.45%) while Acute Antibody mediated rejection, Alport syndrome, C1q Nephropathy, C3 Glomerulonephritis, Cortical necrosis, Cryoglobulinemia, Medullary infection, Tacrolimus toxicity with frequency of 1 (0.51%) in each case were the least common disease. The leading cause for Chronic Glomerulonephritis was IgA Nephropathy with frequency of 8 (38.10%).

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