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The spectrum of biopsy-proved kidney disease: A retrospective single center study in Erbil-Iraq

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ABSTRACT

Background: Renal biopsy is crucial to determine the pattern of the different types of renal diseases. It represents the gold standard of diagnostics for renal pathologies, including glomerular diseases, and it has an important value for the prognosis,monitoring disease progression, and planning the management protocol. **Aims and objective:** To report the frequency of different pathological lesions affecting the kidney in patients who were admitted to our medical centre. **Materials and methods:** This is a retrospective study of all patients with renal diseases who underwent percutaneous renal biopsy at the Erbil Kidney Centre for eight years(1st of January 2010 to 31st of December 2017). A total of 893 cases were biopsied and subsequently studied via histopathological examination and immunofluorescence microscopy. The study is ethically permitted by the Kurdistan Board for Medical Specialization. **Results:** The average age of the patients was 30.9 years. The most common clinical indication for biopsy included nephrotic syndrome (46.47%), acute renal failure (19.04%), chronic renal failure (15.34%),nephritic syndrome (7.39%), proteinuria alone (7.28%), and hematuria alone (4.48%). In patients with a primary glomerular disease, focal segmental glomerular sclerosis minimal change disease were the most frequent (27.44% and 16.01%) in the younger patients (18.61 ± 13.47 years), while membranous glomerulonephritis was more common in older patients (38.94 ± 13.69 years). Patients with a secondary glomerular disease were mainly diagnosed with lupus nephritis,amyloidosis,and diabetic nephropathy. **Conclusion:** The epitome of our study signifies that the spectrum of glomerular diseases varies based on age,sex,ethnicity, and geographical distribution. The implementation of renal biopsy proved to be a cornerstone in reaching the correct diagnosis. Future studies should implement the use of electron microscopy in conjunction with classical techniques of histopathology and immunofluorescence microscopy to diagnose equivocal cases of interest.

Key words: Renal Biopsy; Renal Insufficiency; Nephrotic Syndrome;Glomerulonephritis; Kurdistan.

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INTRODUCTION

Histological examination of the renal biopsies represents the gold standard for the diagnosis of different diseases affecting the kidney.[1] Nowadays, most medical centres employ the use of percutaneous renal biopsy using real-time ultrasonography as well as automated percutaneous devices.[2,3] Renal pathologies manifest in different ways and in the form of a spectrum from asymptomatic patients to those with life-threatening conditions.[4] Although nephrologist do implement an armamentarium of diagnostic utilities including biochemical and serological in addition to urine-based investigations, the implementation of biopsies and histopathological examination is still considered as the gold standard in reaching a diagnosis in various types of renal disorders.[5] Further, the percutaneous renal biopsy is considered as the most essential for the correct characterization of different types of diseases

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affecting the kidney and the renal system as a whole.[6] It has a critical role in diagnosing different types of tubulointerstitial and vascular diseases.[7] Hence, an adequate histological specimen is mandatory for an accurate interpretation as well as early detection of the specific ailment affecting the renal tissues.[8, 9]

The histopathological analysis plays a vital role in the evaluation of proteinuric patients not only for diagnosis but also to assess the response to specific therapeutic modalities.[10] It also gives significant information which provides an insight to estimate the progression of the medical condition and the prognosis of the existing renal disease.[7] However, a needle biopsy is not risk-free which must be weighed against the benefits and the advantages of the yield of data via histopathological analysis obtained from the procedure.[11,12] Our study aims to report the frequency of different pathological lesions among patients with renal diseases admitted to our medical centre. We shall also contrast our original data with the local (regional) and international data, based on the systematic review of the relevant body of literature, to see any concordance or discordance and we shall attempt to provide and postulate a reasonable explanation for any discrepancies from our results.

MATERIALS AND METHODS

Our study is retrospective in design, and it includes all the native kidney biopsies performed at the Renal Transplant Centre and the Renal Unit at Erbil Teaching Hospital for the period 2010-2017. The study has been ethically permitted by the institute review board and the related ethical committee of the Kurdistan Board for Medical Specialization. A total of 893 cases of different age groups were biopsied and included in this study.The indications for renal biopsy included patients with nephrotic syndrome, nephritic syndrome, renal insufficiency (failure) due to an unknown aetiology, and asymptomatic urinary abnormality. The biopsy procedure followed an established operative protocol. Prior to carrying out the procedure, laboratory technicians biochemically estimated the bleeding time, the clotting time, the prothrombin time, and the partial thromboplastin time.Abdominal ultrasonography was also a prerequisite in order to assess the renal or the lesional morphometric parameters including the dimensions, volume, the cortical thickness, and the status of the pelvicalyceal system. On the day of the procedure, a blood pressure more than 140/100 mmHg was an absolute indication to postpone the biopsy. The patients had to lay in a supine posture during the procedure. Following the acquisition of a successful biopsy, the patients were instructed to remain in bed, while their blood pressure is monitored regularly to prevent a catastrophic hypotensive episode or a hypovolemic shock. Besides, the urine output and its colour were checked for the occurrence of macroscopic hematuria.

The patients then were discharged home 6-8 hours after taking the biopsy given that they were hemodynamically stable and with no macroscopic hematuria. The patients were instructed to stay in the bed and avoid physical activities for the next twenty-four hours. All biopsies were obtained using a percutaneous trucut 14 gauge disposable needle. Two tissue samples were retrieved, one for the light microscopy and the other for immunofluorescence.Tissue sectioning and paraffin-embedding were prepared and stained with hematoxylin and eosin stain (H&E), Periodic acid–Schiffstain (PAS), and Masson's trichrome stain. All the renal biopsies were examined by an experienced pathologist and evaluated via light and immunofluorescence microscopy to reach a definite diagnosis.The authors conducted a comprehensive and systematic review of the literature via the relevant databases including PubMed, Embase, the Cochrane Library, CINAHL Plus, and Elsevier, as well as interactive social research websites including ResearchGate and Academia. The graphical presentation and statistical analysis were conducted via Microsoft Excel 2016 and the Statistical Package for the Social Sciences (IBM SPSS version 24).

RESULTS

The study involved biopsies taken from 893 patients including 472 males (52.86%) and 421 females (47.15%) with an age in the range of 6 months to 79 years and an average of 30.9 years.The number of biopsies executed for eight consecutive years (2010-2017) increased progressively but not consistently (Figure 1).The histopathology and immunofluorescence analysis of the biopsies revealed a heterogeneity of renal pathologies including focal segmental glomerulosclerosis (FSGS), minimal change disease (MCD), membranous glomerulonephritis (MGN), lupus nephritis (LN), diabetic nephropathy (DN), chronic glomerulonephritis (CGN), rapidly progressive glomerulonephritis (RPGN), acute tubular necrosis (ATN), tubulo-interstitialnephritis (TIN), membranoproliferative glomerulonephritis (MPGN), mesangio-proliferative glomerulonephritis (MesPGN), post-infectious glomerulonephritis (PIGN), IgA nephropathy (IgAN)=, and thrombotic micro-angiopathy (TMA).In relation to the pre-operative indications of renal biopsy, the most common clinical indication was nephrotic syndrome (415, 46.47%), followed by acute renal failure (170, 19.04%), chronic renal failure (137, 15.34%), nephritic syndrome (66, 7.39%), proteinuria alone (65, 7.28%) and hematuria alone (40, 4.48%) (Table 1).The frequency distribution

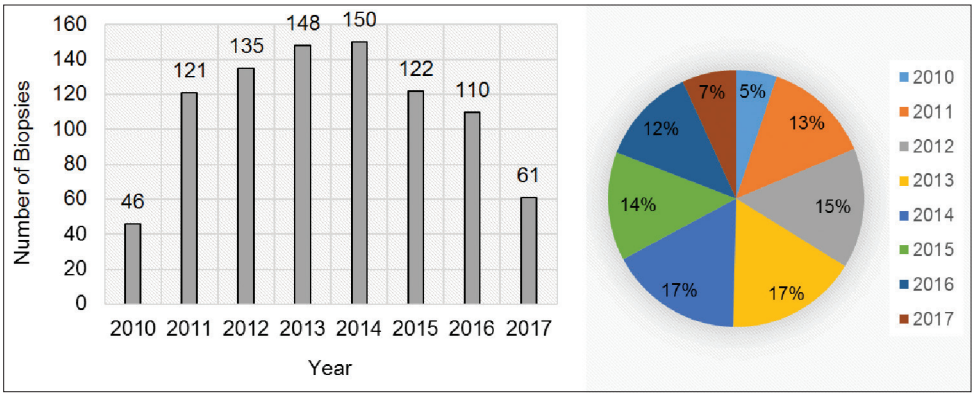

Figure 1: Componential Analysis of the Number of Biopsies for the Period 2010-2017

Table 1: Descriptive parameters of the patients (above) and the indications of renal biopsy (below)

Descriptive parameter		Value
Male-to-Female ratio		1.12:1
Average age (years)		30.9
Indications for biopsy	**Frequency**	**Percentage**
Nephrotic syndrome	415	46.47
Acute renal failure	170	19.04
Chronic renal failure	137	15.34
Nephritic syndrome	66	7.39
Proteinuria alone	65	7.28
Hematuria alone	40	4.48
Total	893	100

for the major glomerular diseases in descending order of frequency was FSGS (245, 27.44%), MCD (143, 16.01%), MGN (103, 11.53%), arteriosclerosis (61, 6.83%), LN (46, 5.15%), IgAN (39, 4.37%), CGN (39, 4.37%), amyloidosis (30, 3.36%), RPGN (28, 3.14%), ATN (27, 3.02%), Chronic TIN (20, 2.24%), MPGN (20, 2.24%), chronic pyelonephritis (15, 1.68%), acute TIN (13, 1.46%), MPGN (13, 1.46%), PIGN (13, 1.46%), DN (11, 1.23%), acute pyelonephritis (10, 1.12%), TMA (9, 1.01%), and myeloma (8, 0.90%) (Table 2).

The distribution of different types of glomerular diseases was variable based on age and sex of the patients. The typology is broadly categorized into primary glomerular diseases, secondary glomerular diseases, and tubulointerstitial diseases (Table 3). In relation to primary glomerular diseases, it is evident that FSGS, MCD, MGN, MesPGN, and PIGN were more common in males while RPGN and CGN were more common in females while MPGN was equal in distribution amongst males and females. In relation to secondary glomerular diseases, it is noticeable that DN, amyloidosis, and arteriosclerosis were more common in males while LN, myeloma and TMA were more common in females. In relation to tubulointerstitial diseases, it is observable that chronic TIN, acute TIN, and ATN were more common in males

Table 2: The frequency distribution of the renal pathologies based on the clinical and histopathological analysis of renal biopsies

Type of renal pathology	Frequency	Percentage
FSGS	245	27.44
MCD	143	16.01
MGN	103	11.53
Arteriosclerosis	61	6.83
LN	46	5.15
IGAN	39	4.37
CGN	39	4.37
Amyloidosis	30	3.36
RPGN	28	3.14
ATN	27	3.02
ChronicTIN	20	2.24
MPGN	20	2.24
Chronic Pyelonephritis	15	1.68
Acute TIN	13	1.46
MPGN	13	1.46
PIGN	13	1.46
DN	11	1.23
Acute Pyelonephritis	10	1.12
TMA	9	1.01
Myeloma	8	0.90
Total	893	100.00

while acute pyelonephritis and chronic pyelonephritis were more common in females (Table 3).To validate our results, we compared our data with the reported prevalence of glomerular and tubulointerstitial diseases in different countries based on data extrapolated from the published literature on the same topic (Table 4). Regarding primary glomerular diseases, MCD is more prevalent in India while FSGS is predominant in Pakistan and Oman.On the other hand, MGN is predominant in Iran. Regarding secondary glomerular diseases, it was found that LN is the most prevalent with an exception for Japan where DN is more predominant.

DISCUSSION

This study provides a comprehensive evaluation in relation to the demographic parameters, clinical presentation, and

Table 3: Descriptive statistics: The clinicopathological diagnosis of renal pathologies based on age, sex, and the number of the patients

Renal Pathology	Patients n (%)	Age (Mean±SD)	Male n (%)	Female n (%)
Primary glomerulonephritis				
FSGS	245 (27.44)	27.79±16.42	136 (55.51)	109 (44.49)
MCD	143 (16.01)	18.61±13.47	80 (55.94)	63 (44.06)
MGN	103 (11.53)	38.94±13.69	65 (63.11)	38 (36.89)
MPGN	20 (2.24)	33.65±17.98	10 (50.00)	10 (50.00)
MesPGN	13 (1.46)	31.58±6.60	8 (61.54)	5 (38.46)
IGAN	39 (4.37)	28.03±11.55	26 (66.67)	13 (33.33)
RPGN	28 (3.14)	39.43±16.35	13 (46.43)	15 (53.57)
PIGN	13 (1.46)	24.00±18.87	9 (69.23)	4 (30.77)
CGN	39 (4.37)	31.67±15.49	19 (48.72)	20 (51.28)
Secondary glomerulonephritis				
DN	11 (1.23)	41.64±12.09	7 (63.64)	4 (36.36)
LN	46 (5.15)	28.43±9.77	6 (13.04)	40 (86.96)
Myeloma	8 (0.90)	54.88±7.87	2 (25.00)	6 (75.00)
Amyloidosis	30 (3.36)	42.83±14.99	22 (73.33)	8 (26.67)
TMA	9 (1.01)	23.81±17.35	3 (33.33)	6 (66.67)
Arteriosclerosis	61 (6.83)	44.15±13.46	37 (60.66)	24 (39.34)
Tubulointerstitial disease				
Chronic TIN	20 (2.24)	35.30±17.14	13 (65.00)	7 (35.00)
Acute TIN	13 (1.46)	40.08±16.81	7 (53.85)	6 (46.15)
ATN	27 (3.02)	33.89±14.26	19 (70.37)	8 (29.63)
Chronic PN	15 (1.68)	29.58±7.31	1 (6.67)	14 (93.33)
Acute PN	10 (1.12)	35.00±17.13	4 (40.00)	6 (60.00)

Table 4: The prevalence of renal and glomerular pathologies in other countries based on the systematic review of the literature

Renal biopsy lesion	Current study	Pakistan, (Mubarak et al., 2011)	India, (Das et al., 2011)	Oman, (Al-Riyami et al., 2013)	Iran, (Ossareh et al., 2010)	Korea, (Chang et al., 2009)	Japan, (Sugiyama et al., 2013)
Duration (year)	2010-2017	1995-2008	1990-2008	1992-2010	1998-2007	1987-2008	2009-2010
Sample (n)	893	1793	1849	133	1407	1818	7034
Male: Female	1.12:1	1.6:1	1.5:1	0.56:1	1.2:1	1.02:1	-
Average age	30.9	32	32	-	36.5	36	-
FSGS	27.44	21.2	10.5	19.5	10.0	5.6	5.3
MGN	11.53	17.2	7.3	9.8	26.8	12.3	10.7
RPGN	3.14	5.2	4.5	1.5	5.8	-	6.3
MCD	16.01	5.8	15.1	-	8.3	15.5	12.1
MPGN	2.24	1.1	3.9	2.3	5.5	4.0	2.6
IGAN	4.37	1.5	4.4	3.0	11.0	28.3	29.3
MesPGN	1.46	1.9	5.2	4.5	0.9	-	38.8
DN	1.23	0.9	1.2	3.8	2.2	2.0	5.1
LN	5.15	4.9	14.2	36.1	11.0	8.7	4.8
Amyloidosis	3.36	4.6	1.5	2.3	3.3	-	1.4
Chronic TIN	2.24	2.8	3.7	-	0.3	0.3	1.8
Acute TIN	1.46	1.1	1.1	1.5	2.0	2.0	1.5
PIGN	1.46	3.9	5.6	-	-	-	1.8
TMA	1.01	0.6	0.3	1.5	0.8	-	-

the prevalence of kidney diseases. Patients had an average age of 30.9 years and they were younger in comparison with patients from other studies conducted in Pakistan, India, and Oman.[13-15] There was a slight male predominance in our study which is comparable to the other studies in contrast to the published work of Dawood and coworkers (Oman) and Sugiyama and colleagues (Japan) where the male-to-female ratio was different.[15,16] There are large differences in reporting the underlying causes of nephrotic syndrome in different regions of the world and among different ethnicities, for instance in the United States, where FSGS is the commonest underlying pathology with an increasing incidence among all ethnic groups.[17] IgA nephropathy was more frequent in European patients while FSGS is infrequent with no increment in the incidence.[18] On the other hand, in Asian countries including Korea and Japan

as well as India, MCD and IgAN were the most frequent aetiology of nephrotic syndrome.[14, 16, 19]

The primary glomerular disease was the most frequent type encountered in our patients while nephrotic syndrome was the most common clinical indication for a renal biopsy which is similar to the results reported in numerous other published research throughout the world.[13,14,20] Among primary glomerular diseases, FSGS was the most frequent pathological lesion (27.44%) encountered in our study which is similar to data from regional Asian studies.[13-15] However, these results depart from those reported in other published papers which show a relatively low incidence of FSGS.[18,21] MCD was found to be more common in the younger age group (18.61±13.47 years) and it was the second most frequent pathology encountered in our study (16.01%) which is identical to other studies from India, Korea, and Japan.[14,16,19] However, it differs from the results reported in other studies carried out in Pakistan and Iran.[13,20] In Oman, MCD was not detected among the diagnosed renal and glomerular pathologies which can be due to the higher age group of participants (patient) involved in that study.[15] MGN was more common in the older age group of our patients (38.94±13.69 years), and it represents the third most frequent diagnosis among patients with primary glomerular diseases which is identical data to other studies.[14,16,19] In Iran, MGN was the most frequent renal pathology encountered among patients with primary glomerular diseases.[20] On the other hand, the incidence of MGN is declining in Europe and North America over time.[17,22] IgAN is the most frequent glomerular disease in Japan and Korea and it was less encountered in our study which is compatible with data from other regional Asian studies.[14,15,16,19,23]

Secondary glomerular disease ranked 2nd following the most common primary glomerular disease. In our patients, Lupus nephritis was the most common secondary glomerular disease followed by amyloidosis and diabetic nephropathy which was identical to all other studies.[13-15,23] However, diabetic nephropathy was more frequent than lupus nephritis in Japan while diabetic nephropathy was more common than amyloidosis in Omani patients.[15,16] In tubulointerstitial diseases, the most common aetiology of acute and chronic TIN were drugs especially NSAID, and in our study, most of the patients in this category were relatively older. Chronic TIN was more common than acute TIN which is identical to other studies conducted in Pakistan, India and Japan.[13,14,16] The epitome of our study signifies that the spectrum of glomerular diseases varies based on age, sex, as well as the geographical mapping and the ethnic grouping. In primary glomerular diseases, we found that FSGS represented the most common incriminated pathology among the younger age group followed by MCD. Lupus nephritis was the most common pathology detected for secondary glomerular diseases especially in the young females group followed by amyloidosis and DN in higher age group. Minimal change disease and lupus nephritis were more frequent in the younger age group while MGN and Amyloidosis were more clustered in the middle age group.

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Authors Contribution:
Mudhafar Abdullah Ali- contributed to the study design, the review of the literature, histology-related workup, statistical analysis, and preparation of the manuscript. **Safa Ezzaddin Al-Mukhtar**- contributed to the study design and the supervision of the study. **Ahmed Al-Imam**- was responsible for the manuscript submission and correspondence with the editorial office of the journal.

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