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Change of pattern of histopathological analysis of kidney biopsy specimens in Kuwait; a five-year prospective study

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Abstract

Introduction: Among the different geographical areas, glomerulonephritis (GN) varies in incidence due to socioeconomic conditions, ethnicity, genetic variability and environmental factors.

Objectives: Our study aimed to determine change of pattern of histopathological analysis of kidney biopsy specimens in Kuwait over the preceding five years.

Patients and Methods: In a prospective study, we analyzed the clinical and histopathological data of 217 kidney biopsies that performed over the preceding five years during the period from November 2014 to November 2019. An automated gun was used to perform kidney biopsies percutaneously guided by ultrasound. The kidney biopsy specimens were processed for light microscopy and immunofluorescence examination. Kidney function tests, urine protein/day, virology, immunology profiles, age, gender, indications for kidney biopsy and histopathological findings were recorded for analysis.

Results: Primary GN was reported in 63.1%, secondary GN was reported in 31.8% and tubulointerstitial disease was reported in 5.1% of the 217 kidney biopsies studied. Among primary GN, immunoglobulin A nephropathy (IgAN) was the most common lesion (19.4%), followed by focal and segmental glomerulosclerosis (FSGS, 16.6%), and membranous nephropathy (MN, 14.7%). Among biopsies that showed secondary GN, lupus nephritis was the most common (11.98%), followed by diabetic nephropathy (DN) (5.1%) and membranoproliferative glomerulonephritis (MPGN) (4.6%). Among biopsies that showed tubulointerstitial disease, acute interstitial nephritis was the most common lesion (4.6%), followed by chronic interstitial nephritis (0.46%).

Conclusion: The present study revealed that IgAN is the most common primary GN, followed by FSGS, while lupus nephritis is the most common secondary GN, followed by DN. Our previous study in Kuwait, revealed that MN was the most common primary GN, followed by IgAN, while lupus nephritis was the most common secondary GN, followed by hypertensive glomerulosclerosis.

Keywords: Kidney biopsy, Glomerulonephritis, Immunoglobulin A nephropathy, Lupus nephritis

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Introduction

Inflammation within the glomeruli and other compartments of the kidney termed glomerulonephritis (GN) and is caused by a range of immune-mediated disorders (1). Primary GN is considered, when there is no associated disease elsewhere and secondary GN when glomerular involvement is part of a systemic disease, e.g. systemic lupus erythematosus (SLE) or polyarteritis nodosa. Primary GN can also be classified according to the clinical syndrome produced, the histopathological appearance or the underlying etiology (2).

Among the different geographical areas, GN varies in incidence due to socioeconomic conditions, ethnicity, genetic variability and environmental factors. Recent studies have determined a change of pattern of incidence of GN in different parts of the world (3). For instance, in a recent US study, the incidence of end-stage kidney disease (ESKD) due to focal segmental glomerulosclerosis (FSGS) has increased 11-fold in the past two decades (4). A previous Egyptian study of 1234 renal biopsies revealed a high prevalence of proliferative GN and FSGS (5) and previous Kuwaiti study indicated that MN was the most common primary GN, followed by IgAN, while lupus nephritis was the most common secondary GN, followed by hypertensive glomerulosclerosis (6).

Objectives

Our study was conducted to determine the histopathological pattern of kidney biopsies performed over the last five years, during the period from November 2014 to November 2019 at the Al-Khezam dialysis center, Al-Adan hospital, Kuwait.

Patients and Methods

Study design

In a prospective study, we analyzed the clinical and

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Implication for health policy/practice/research/ medical education

The present study analyzed the histopathological data of 217 kidney biopsies that were conducted over the preceding five years during the period from November 2014 to November 2019. Among primary GN, IgA nephropathy was the most common lesion (19.4%), followed by FSGS (16.6%), and membranous nephropathy (14.7%). Among biopsies that showed secondary GN, lupus nephritis was the most common (11.98%), followed by DN (5.1%) and MPGN (4.6%).

pathological data of all kidney biopsy samples (217 kidney biopsies) that were performed during the period from November 2014 to November 2019 at the Al-Khezam dialysis center, Al-Adan hospital, Kuwait. In Kuwait, Al-Adan hospital, Kuwait, is the largest tertiary referral hospital and plays an important role in health-care management. The main indications for kidney biopsy were nephrotic syndrome (urinary protein excretion >3 g/d), nephritic syndrome (active urinary sediment with/ without azotemia), sub-nephrotic proteinuria (<3 g/d), combined proteinuria and hematuria, kidney failure (acute and chronic) and isolated hematuria. Kidney biopsies were performed percutaneously using an automated gun guided by ultrasound. The biopsy samples were processed for light microscopy and immunofluorescence examination. Electron microscopy examination was performed only in selected cases. Age, gender, blood pressure, serum creatinine, blood urea, serum glucose, 24-h urinary protein, fundus examination for diabetic patients, virology, immunology profiles, indications for kidney biopsy and histopathological findings were recorded for analysis. Kidney biopsies with sole tubulointerstitial involvement were also included in the analysis.

Statistical analysis

Data were analyzed as means ± standard deviation (SD) using the MedCalc statistical software or number (%) using an online percentage calculator. Statistical analysis was performed with the aid of the SPSS computer program (version 12 windows).

Results

The kidney biopsy samples of 217 patients were referred for pathological assessment during the period of the study; they included 140 male and 77 female patients and 110 Kuwaiti patients and 107 non-Kuwaiti patients, and their mean age was 38.8 ± 13.06 years (range; 14-68 years).

The frequency of kidney diseases, male/female ratio, Kuwaiti/non-Kuwaiti patient ratio, mean age, serum creatinine, blood urea and 24-h urinary protein of primary GN, secondary GN and tubulointerstitial disease are illustrated in (Table 1). Primary GN was reported in 137 cases (63.1%), secondary GN was reported in 69 cases (31.8%) and tubulo-interstitial disease was reported in 11 (5.1%) of the 214 kidney biopsies performed (Table 1; Figure 1).

Among primary GN, immunoglobulin A nephropathy (IgAN) was the most common lesion (19.4%), followed by focal and segmental glomerulosclerosis (FSGS, 16.6%), membranous nephropathy (MN, 14.7%), minimal change disease (MCD, 6.5%), membranoproliferative glomerulonephritis (MPGN) (MPGN, 5.5%) and fibrillary GN (0.46%) (Figure 2). Among biopsies that showed secondary GN, lupus nephritis was the most common (11.98%), followed by diabetic nephropathy (DN) (5.1%), MPGN (4.6%), MN (4.1%), hypertensive glomerulosclerosis (3.2%), FSGS (1.38%), IgAN (0.9%) and crescentic GN (0.46%) (Figure 3). Among biopsies that showed tubulointerstitial involvement, acute interstitial nephritis was the most common lesion (4.6%), followed by chronic interstitial nephritis (CIN) (0.46%).

Post-biopsy complications included gross hematuria, which was seen in four cases (1.8% of kidney biopsies performed); two of them required blood transfusions and no other interventions, and the hematuria subsided spontaneously. Hypertension (HTN) was present in 29% with IgAN, 25% with FSGS, 20.3% of cases with MGN, 5.66% with minimal change disease (MCD), 51% with membranoproliferative GN (MPGN), 100% with fibrillary GN, 27% with LN, 58.3% with DN, 49% with secondary MPGN, 13% with MCD, 100% with hypertensive glomerulosclerosis, 100% with secondary FSGS, 13% with IgAN, 25.8% with crescentic GN and 64.6% of with acute tubular necrosis. Diabetes mellitus was present in 2.8% with IgAN, 4.6% of cases with MGN, 100% with DN, 13.4% with hypertensive glomerulosclerosis, 12.7% with crescentic GN, and 16.6% of cases with CIN. Hematuria/dysmorphic red blood cells were present in 69%/3% with IgAN, 8%/7% with FSGS, 33.93%/2.7% of cases with MGN, 48%/22% with MPGN, 48%/29% with LN, 26.38%/12.8 with DN, 88%/0% with secondary MPGN, 47%/0% with secondary MGN, 4.8%/3.8% with hypertensive glomerulosclerosis 98%/0% with secondary FSGS, 51.5%/31.6% with crescentic GN, 6.8%/6.2% with acute interstitial nephritis and 12.8%/0% with CIN.

Table 1. Frequency of kidney diseases in the 217 kidney biopsies studied

Variables	No. (%)	M/F	KWT/NKWT	Proteinuria (g/d)	Age (years)	S. creatinine (µmol/L)
Primary glomerulonephritis	137 (63.1%)	90/47	65/72	4.38 ± 4.01	40.78 ± 13.08	196.91 ± 169.6
Secondary glomerulonephritis	69 (31.8%)	42/27	39/30	4.93 ± 3.19	35.59 ± 12.45	312.37 ± 277.55
Tubulointerstitial nephritis	11 (5.1%)	8/3	6/5	0.305 ± 0.192	35.69 ± 11.98	232.69 ± 236.05
Total	217	140/77	110/107	4.37 ± 3.78	38.8 ± 13.06	220.96 ± 208.22

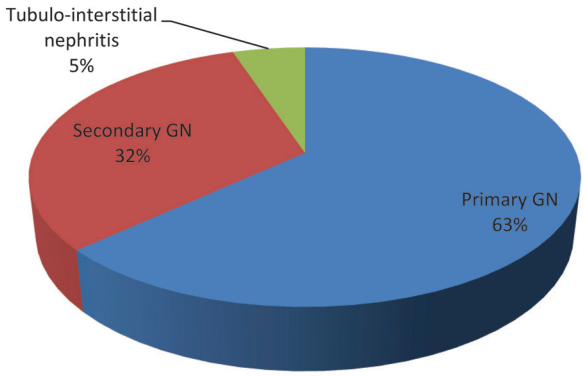

Figure 1. Frequency of kidney diseases in the 217 kidney biopsies studied.

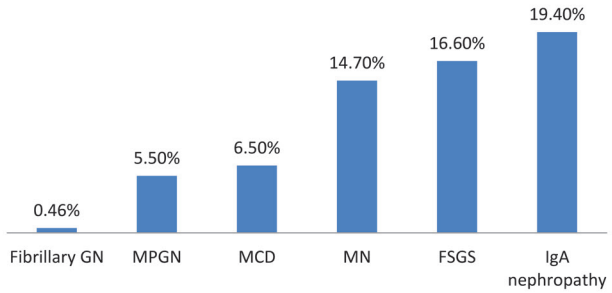

Figure 2. Frequency of primary glomerulonephritis in the kidney biopsies studied (n = 137/217).

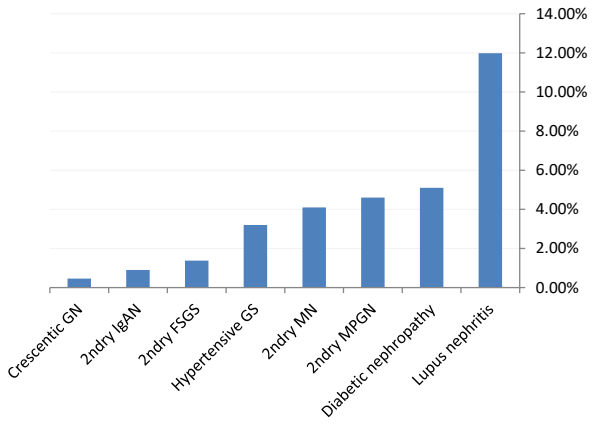

Figure 3. Frequency of secondary glomerulonephritis in kidney biopsies studied (n = 69/217).

Complement C3/C4 levels were both low in 43% of the cases with LN. Anti-hepatitis C virus and antibody/ hepatitis B surface antigen were positive in 20%/20% of cases with secondary MGN and positive in 50%/0% of cases with secondary MPGN.

Discussion

The present study showed that primary IgA nephropathy (IgAN) was the predominant forms of primary GN in the study population and LN was the predominant forms of secondary GN in the study population. IgAN (20.3%) was the most commonly encountered disease in the whole group, followed by MN (18.9%), FSGS (17.9%) and LN (12%).

IgAN was the most common primary GN reported in our study group (19.4%).

This is in agreement to the high incidence of IgAN in Europe (7,8), North America (9) and Far-East (10,11). IgAN was the second most common primary GN in the study of Abdallah et al (6) lower frequencies of IgAN have been reported in the neighboring countries in regions such as Saudi Arabia (12,13), Bahrain (14) and Iran (15). FSGS was the second most common primary GN among the study group (16.6%). In addition, it was the second most common lesion in a study from Bahrain (14). FSGS was the fourth most common primary GN in a study of Abdallah et al (9.3%) (6). FSGS was the predominant GN in studies published from Saudi Arabia (16,17), Kuwait (18), Jordan (19) and Egypt (20). FSGS is increasingly reported to be common in the USA in all ethnic groups (9,21). In the present study, MGN was the most third common primary GN among the study group (14.7%). MGN was the most common primary GN in the study by Abdallah et al (12.15%) (19). MGN was the fourth most common cause of primary MGN in a report from Egypt (7.03%) (20). MGN represented 9.9% of primary GN in a study from Saudi Arabia (16). This finding was in contrast to two earlier reports from the United Arab Emirates and Iran (22,15). The highest frequency of MGN was reported in Saudi Arabia (23), of 25.7% in the western region (range 3.5-25.7%). In the present study, MCD was the fourth most common primary GN among the study group (6.5%), while, MCD was the third common primary GN in the previous our study in Kuwait (9.8%) (19); it was the second most common cause of primary GN (17.7%) in Saudi Arabia (16) and the third most common primary GN in Egypt (8.5%) (20), while other studies have reported a wide range from 5.4% to 29% (23,12,13,24-27). In the western countries, MGN has a male predominance, with a Male:Female (M:F) ratio of 2:1, while we found a female predominance with a M:F ratio of 12/14 (9,10,28-30).

In the western population, IgAN demonstrated a male preponderance by 17/8. We also found a male predominance of IgAN by 32/12. We additionally found a male predominance (M: F 22/17) of FSGS, as reported in western countries, Egypt (20) and Saudi Arabia (16). While there was equally distributed of MPGN and MCD in both males and females; we found a male predominance in both lesions by a ratio of 14/8 and 9/5 respectively. In the present study, LN was the most common cause of secondary GN (12%) and this finding is in agreement with our previous study in Kuwait, where the most common cause of secondary GN was LN (11.7%) and LN was the most common lesion among female adults and in the middle-age groups (19). Secondary GN with increased prevalence of LN has been observed in several studies from Egypt (5,20), Sudan (31), Iran (15), Bahrain

(14), Jordan (19), Australia (32), Kuwait (18) and Saudi Arabia (16). DN was the most second cause of secondary GN (5.1%), the prevalence of DN in our previous study (6) was only 3.3%, similar to reports from Egypt (20) and Saudi Arabia (16). The reason for this could be that diabetic patients with diabetes mellitus are not biopsied unless there is atypical presentation of DN and there was no diabetic retinopathy. In the present study, hypertensive glomerulosclerosis was the fifth most common cause of secondary GN (3.2%) and this finding is in contrast to our previous study where hypertensive glomerulosclerosis was the second most common cause of secondary GN (10.3%) (6). Hypertensive nephropathy was the second most common cause of secondary nephropathies in Saudi Arabia (16). In this study, crescentic GN was seen in 0.46%, of the biopsies compared with 4.5% in Saudi Arabia (16), and 7.1% in our previous study (6), secondary MGN was seen in (4.1%) and 1.9% in our previous study (6), secondary MPGN was seen in (4.6%) and 0.9% in our previous study (6), secondary FSGS seen in (1.38%), and 0.46% in our previous study (6) and secondary IgA N was seen in 0.9% of the biopsies studied. In the present study, among biopsies that showed tubulointerstitial disease, acute interstitial nephritis was the most common lesion (4.6%), followed by CIN (0.46%). In the previous our study (19), acute interstitial nephritis was the most common, seen in 6.1%, CIN was seen in 2.8% and ATN was seen in 1.4%. In the United States and around the world, tubulointerstitial constitute 10-15% of all kidney diseases. In certain regions, such as the Balkans (i.e., Yugoslavia, Bosnia, Croatia, Romania and Bulgaria), interstitial diseases are more prevalent than elsewhere (33,34).

Conclusion

In conclusion, IgA nephropathy was the most common primary GN, followed by FSGS, while LN was the most common secondary GN, followed by DN in our present study from Kuwait.

Authors' contribution

EA was the principal investigator of the study. EA, BA, and RA were included in preparing the concept and design. EA, SK, WD, and MH revisited the manuscript and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the contents of the manuscript and confirmed the accuracy or the integrity of any part of the work.

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Conflicts of interest

The authors declare that they have no conflict of interest.

Ethical issues

The research followed the tenets of the Declaration of Helsinki written and informed consent taken from all participants before any intervention. Moreover, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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