Original Article

A Clinicopathologic Study of Glomerular Disease: Experience of the King Fahd Hospital of the University, Eastern Province, Saudi Arabia

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Published studies from different centers in Saudi Arabia have reported contradicting results regarding glomerular lesions. In this retrospective study, we report our experience in King Fahd Hospital of the University at Al-Khobar in the Eastern province, including a description of the morphologic and clinical characteristics of primary and secondary glomerular disease. The study included 233 renal biopsies obtained from patients presenting with glomerular manifestations over a period of 23 years (1986–2008), investigated by light microscopy, immunofluorescence (149 cases) and electron microscopy (34 cases). One hundred and eighty-seven cases (80.3%) were primary glomerulonephritides. Minimal change glomerulopathy was the most common type of primary glomerulonephritis found (29.4% of primary glomerulonephritides), followed by mesangioproliferative glomerulonephritis (19.8%), and focal/segmental glomerulosclerosis (15.5%). Membranoproliferative glomerulonephritis was found in 9.6% of cases, membranous glomerulopathy in 8.6%, IgA nephropathy in 6.4%, end-stage glomerulopathy in 5.9%, crescentic glomerulonephritis in 3.2%, and IgM nephropathy in 1.6%. Of the secondary glomerulonephritides (46 cases constituting 19.7% of the biopsies), lupus nephritis was the most frequently diagnosed disease (71.7% of secondary glomerulonephritides). Diabetic glomerulosclerosis was found in 10.9% of cases, amyloidosis in 6.5%, and Alport syndrome in 4.3%. Wegener's granulomatosis, Henoch-Schönlein purpura nephritis and hypertensive nephrosclerosis each represented 2.2% of cases (one case each). Other than a significantly higher incidence of minimal change glomerulopathy and lupus nephritis ($p<0.001$) and a significantly lower prevalence of membranoproliferative glomerulonephritis ($p=0.029$), our results are generally comparable to those reported by the Saudi registry for glomerulopathy and in some neighboring countries. Age- and sex-adjusted analyses revealed that minimal change glomerulopathy and lupus nephritis were also the most prevalent primary and secondary glomerulopathies in the pediatric age group (below 15 years) as well as in adults, females and males. [*Hong Kong J Nephrol* 2010;12(1):20–30]

Key words: crescentic glomerulonephritis, glomerulonephritis, glomerulopathies, primary glomerulonephritis

來自沙地阿拉伯不同院所的研究，對於腎小球病灶的描述並不一致。在本回溯性研究中，我們歸納了 King Fahd 大學醫院 (位於東部省的 Al-Khobar) 的經驗，對原發性及次發性腎小球疾病的形態學及臨床特徵作出描述。其中的研究材料是來自過去 23 年 (1986–2008) 間，腎小球疾病患者共 233 個腎臟活組織檢體，檢驗方法包括光學顯微鏡、免疫螢光測試 (149 宗)、及電子顯微鏡 (34 宗)。數據顯示在全體 233 宗個案間，187 宗 (80.3%) 屬於原發性腎小球腎炎，其中以極微變化性腎小球病變爲主 (佔原發性腎小球腎炎的 29.4%)，其他診斷依序包括繫膜增生性腎小球腎炎 (19.8%)、局部節段性腎小球硬化 (15.5%)、膜狀增生性腎小球腎炎 (9.6%)、膜性腎小球病變 (8.6%)、IgA 腎病變 (6.4%)、末期腎小球病變 (5.9%)、新月

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型腎小球腎炎 (3.2%)、及 IgM 腎病變 (1.6%)。在次發性腎小球腎炎 (共 46 宗，佔所有個案的 19.7%) 中，狼瘡性腎炎爲最常見 (佔次發性腎小球腎炎的 71.7%)，其他診斷依序爲糖尿性腎小球硬化 (10.9%)、類澱粉沉積症 (6.5%)、及 Alport 綜合症 (4.3%)；Wegener's 肉芽腫症、Henoch-Schönlein 紫癜性腎炎、及高血壓性腎硬化則均佔 2.2% (各 1 宗)。整體而言，除了極微變化性腎小球病變及狼瘡性腎炎的比率明顯較高 ($p < 0.001$) 及膜狀增生性腎小球腎炎的比率明顯較低 ($p = 0.029$) 之外，我們的數據大致與沙地阿拉伯及鄰近國家的登錄數據一致。對年齡及性別校正後的分析顯示，不論在兒童 (15 歲以下)、成人、或兩性之間，極微變化性腎小球病變及狼瘡性腎炎均分別是最常見的原發性及次發性腎小球疾病。

Introduction

Glomerular diseases are the leading cause of end-stage renal disease globally. Cases in which the kidneys are the predominant organs involved are known as primary glomerulonephritides (glomerulopathies) and constitute the most common form of glomerular disease. Primary glomerular diseases include several types that vary widely with regard to the morphology of the glomerular lesions. The glomeruli may also be injured during the course of a number of systemic diseases, e.g. autoimmune disorders such as systemic lupus erythematosus, vascular diseases like hypertension, metabolic diseases like diabetes mellitus and hereditary diseases such as Alport syndrome. The glomerular lesions in these cases constitute secondary glomerular diseases.

Studies published so far from different centers in Saudi Arabia concerning glomerular disease have reported conflicting results regarding the types of primary and secondary glomerular lesions encountered. Herein, we report our experience in King Fahd Hospital of the University (KFHU) at Al-Khobar in the Eastern province, including a description of the morphologic and clinical characteristics of primary and secondary glomerular disease, and compare this with studies reported from other parts of the Kingdom and from some other countries. Located in the Eastern Province of Saudi Arabia, KFHU is one of the leading teaching hospitals in the Kingdom serving a population of about 170,000.

Materials and Methods

In this retrospective study, 233 renal biopsies obtained from patients who presented with glomerular manifestations to KFHU over a period of 23 years (1986–2008) were investigated. Cases with transplanted kidneys were not included in the study. Clinical, laboratory, and photographed immunofluorescence and electron microscopic findings were retrieved from patients' files, while original or newly prepared paraffin sections were reviewed under a light microscope by one pathologist experienced in renal pathology (MS).

The indications for biopsy were: nephrotic syndrome, proteinuria of more than 1 g/day with active urine sediment, systemic disease with renal involvement, and unexplained renal insufficiency. Histologic evaluation by light microscopy was available in all cases, combined with direct immunofluorescence in 149 cases and electron microscopy in 34 cases. Light microscopic evaluation was performed on standard paraffin sections stained with hematoxylin and eosin and by the periodic acid-Schiff (PAS), Masson's trichrome and Jones methenamine silver techniques. Immunofluorescence included studies performed on frozen sections using FITC-labeled anti-IgG, IgM, IgA and C3 antibodies. In cases in which immunofluorescence and/or electron microscopic data were unavailable, paraffin sections of the biopsies were reviewed by all five pathologists participating in the study under a 10-headed light microscope and a consensus about the diagnosis was established.

Glomerular diseases were classified using the diagnostic criteria formulated by the World Health Organization [1]. Statistical analysis was performed using the SPSS software program (SPSS Inc., Chicago, IL, USA). Descriptive and nonparametric statistics were adopted.

Results

Of the 233 cases studied, 118 (50.6%) were male and 115 (49.4%) were female. The age ranged from 7 to 70 years. The clinical presentations of patients included: nephrotic syndrome, proteinuria, hematuria, acute renal failure, rapidly progressive glomerulonephritis, impaired renal function, chronic renal failure, and hypertension, singly or in various combinations.

There were 187 cases (80.3%) of primary glomerulonephritides. Minimal change glomerulopathy was the most common type of primary glomerulonephritis (observed in 55 cases, 29.4% of primary glomerulonephritides), followed by mesangioproliferative

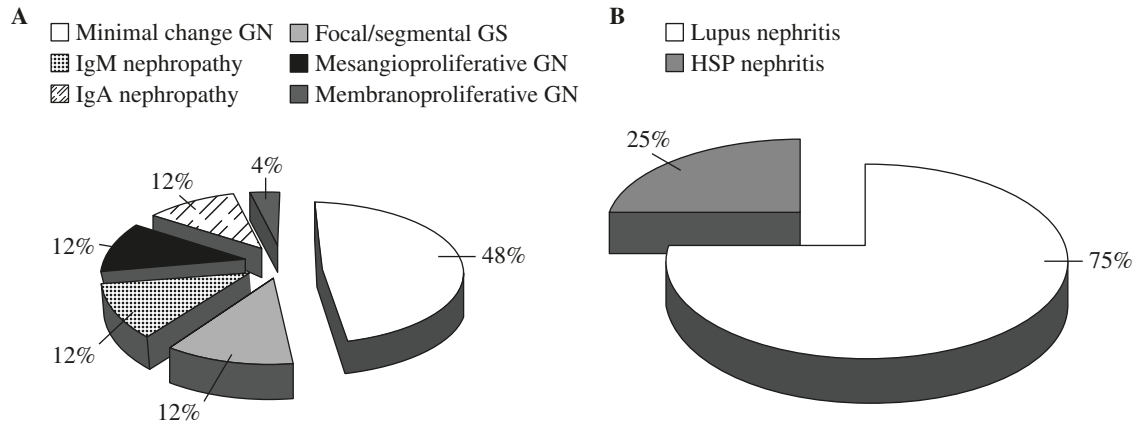

Figure 1. Frequency distribution in the pediatric age group (<15 years old) of: (A) primary glomerulonephritides; (B) secondary glomerulonephritides. GN=glomerulonephritis; GS=glomerulosclerosis; HSP=Henoch-Schönlein purpura.

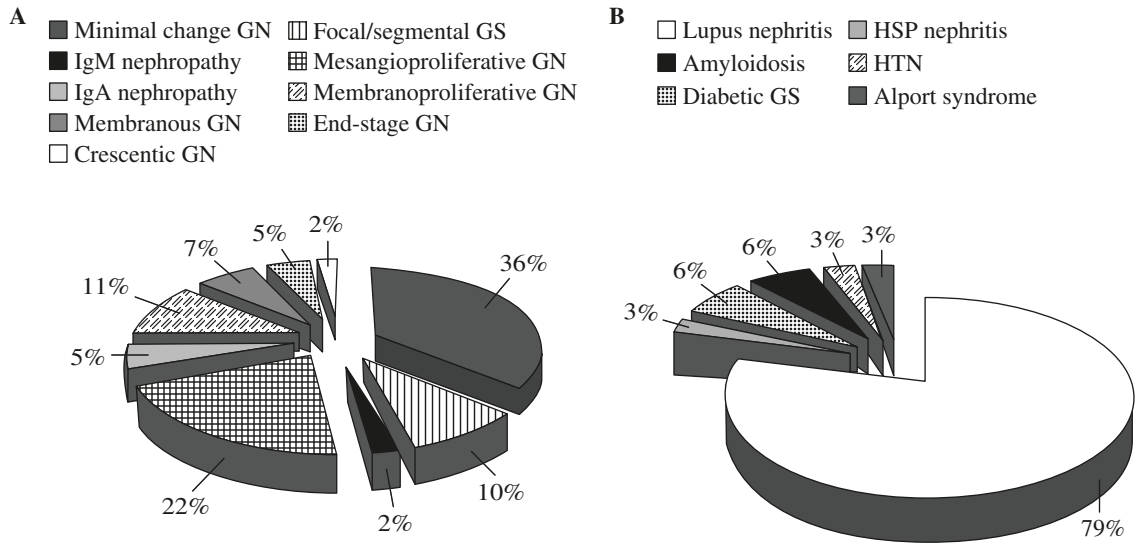

Figure 2. Frequency distribution in females of: (A) primary glomerulonephritides; (B) secondary glomerulonephritides. GN=glomerulonephritis; GS=glomerulosclerosis; HSP=Henoch-Schönlein purpura; HTN=hypertension.

glomerulonephritis (37 cases, 19.8%) and focal/segmental glomerulosclerosis (29 cases, 15.5%). Membranoproliferative glomerulonephritis was found in 9.6% of cases (18 cases), membranous glomerulopathy in 8.6% (16 cases), IgA nephropathy in 6.4% (12 cases), end-stage glomerulopathy in 5.9% (11 cases), crescentic glomerulonephritis in 3.2% (6 cases), and IgM nephropathy in 1.6% (3 cases).

In the pediatric age group (<15 years of age), the most common primary glomerulopathy was minimal change glomerulopathy (Figure 1), seen in 12 out of a total of 25 cases (48%), followed by mesangioproliferative glomerulonephritis, focal/segmental glomerulosclerosis, IgA nephropathy and IgM nephropathy, each seen in three cases (12%), and finally membranoproliferative glomerulonephritis in only one case (4%). Membranous glomerulopathy, crescentic glomerulonephritis and end-stage glomerulopathy were not encountered in the pediatric age group. It should be noted that minimal change glomerulopathy was also the most common primary glomerulopathy in adults (≥15 years of age), seen in 43 out of 162 cases (26.5%).

Minimal change glomerulopathy was also the most prevalent primary glomerulopathy encountered in females (Figure 2), in 30 out of 83 (36.1%), followed by mesangioproliferative glomerulonephritis (18, 21.7%), membranoproliferative glomerulonephritis (9, 10.8%), focal/segmental glomerulosclerosis (8, 9.6%), membranous glomerulopathy (6, 7.2%), IgA nephropathy and end-stage glomerulopathy (4 patients each, 4.8%), and finally crescentic glomerulonephritis and IgM nephropathy (2 each, 2.4%). Minimal change glomerulopathy was also the most common primary glomerulopathy encountered in males, seen in 25 out of 104 cases (24%).

Of the secondary glomerulonephritides (46 cases, constituting 19.7% of the biopsies), lupus nephritis was

Table 1. Frequency distribution and epidemiologic and clinical data of primary and secondary glomerulonephritides

Disease	Patients, *n* (%)	Age (yr), mean ± SD (range)	Male, *n* (%)	Female, *n* (%)	Clinical picture
Primary (*n* = 187)					
Minimal change GN	55 (29.4)	27.2 ± 12.9 (7–61)	25 (45.5)	30 (54.5)	NS (85%), proteinuria, hematuria, HTN
Mesangioproliferative GN	37 (19.8)	31.5 ± 13.8 (7–70)	19 (51.4)	18 (48.6)	NS (62%), proteinuria, hematuria, HTN, SCD, CRF
FSGS	29 (15.5)	32.1 ± 11.8 (7–53)	21 (72.4)	8 (27.6)	NS (62%), proteinuria, HTN
Membranoproliferative GN	18 (9.6)	28.9 ± 10.3 (13–54)	9 (50)	9 (50)	NS (72%), proteinuria, HTN, SCD, NF1
Membranous glomerulopathy	16 (8.6)	38.4 ± 10.3 (23–62)	10 (62.5)	6 (37.5)	NS (68.7%), proteinuria, hematuria, ESRD, SCD
IgA nephropathy	12 (6.4)	31.5 ± 14.6 (7–46)	8 (66.6)	4 (33.4)	Proteinuria (50%), NS, hematuria, RI, HTN
Chronic (end-stage) GN	11 (5.9)	36.5 ± 10.4 (21–51)	7 (63.6)	4 (36.4)	CRF (45.4%), NS, HTN, proteinuria
Crescentic GN	6 (3.2)	28 ± 8.6 (17–43)	4 (66.7)	2 (33.3)	RPGN (66.6%), CRF, vasculitis
IgM nephropathy	3 (1.6)	12 ± 0 (12)	1 (33.3)	2 (66.7)	NS, relapsing/steroid-dependant
Secondary (*n* = 46)					
Lupus nephritis	33 (71.7)	23.8 ± 9.2 (13–52)	8 (24.2)	25 (75.8)	NS, proteinuria, hematuria, HTN, RI
Diabetic glomerulosclerosis	5 (10.9)	48.4 ± 17 (28–70)	3 (60)	2 (40)	CRF, proteinuria, RI
Amyloidosis	3 (6.5)	42 ± 21.2 (28–50)	1 (33.3)	2 (36.7)	NS, CLD (HBV), hepatomegaly
Alport syndrome	2 (4.3)	22 ± 5.6 (18–26)	1 (50)	1 (50)	Alport syndrome
Wegener's granulomatosis	1 (2.2)	(46)	1	0	Hematuria
Henoch-Schönlein purpura nephritis	1 (2.2)	(10)	0	1	Henoch-Schönlein purpura
Hypertensive nephrosclerosis	1 (2.2)	(65)	1	0	Acute/CRF, CAD, HTN, DM

SD = standard deviation; GN = glomerulonephritis; NS = nephrotic syndrome; HTN = hypertension; SCD = sickle cell disease; CRF = chronic renal failure; FSGS = focal/segmental glomerulosclerosis; NF1 = neurofibromatosis type 1; ESRD = end-stage renal disease; RI = renal impairment; RPGN = rapidly progressive glomerulonephritis; CLD = chronic liver disease; HBV = hepatitis B virus; CAD = coronary artery disease; DM = diabetes mellitus.

the most frequently diagnosed disease (33 cases, equivalent to 71.7% of secondary glomerulonephritides). Diabetic glomerulosclerosis was found in five cases (10.9%), amyloidosis in three cases (6.5%), and Alport syndrome in two cases (4.3%). There was one case (2.2%) each of Wegener's granulomatosis, Henoch-Schönlein purpura nephritis, and hypertensive nephrosclerosis.

The frequency distribution and the clinical and epidemiologic data of the various primary and secondary glomerular diseases encountered are shown in Table 1.

Lupus nephritis was the most common secondary glomerulopathy seen in the pediatric age group (Figure 1), encountered in three out of four cases (75%), followed by Henoch-Schönlein purpura nephritis in one case (25%). No other secondary glomerulonephritides were encountered in this age group. Lupus nephritis was also the most frequently found secondary glomerulopathy in adults, seen in 31 out of 46 cases (67.4%), and in males (8 out of 14 cases, 57.1%). It was also by far the most common secondary glomerulopathy encountered in females (Figure 2), seen in 25 out of 32 cases (78.1%), followed by diabetic glomerulosclerosis and amyloidosis (2 patients each, 6.3%), and finally Alport syndrome, Henoch-Schönlein purpura nephritis and hypertensive nephrosclerosis in one patient each (3.1%).

Minimal change glomerulopathy

Patients with minimal change glomerulopathy had an age range between 7 and 61 years, with a mean age of 27.2 ± 12.9 years; 25 (45.5%) were male and 30 (54.5%) were female. The majority of cases (85.5%, 47 patients) presented with nephrotic syndrome, which was steroid dependant/resistant in 18.2% of cases (10 patients) and associated with bilharzial liver disease in one case (1.8%), and type II diabetes mellitus in another (1.8%). Proteinuria was the presenting manifestation in 14.5% of cases (8 patients), associated with hematuria in 5.5% of cases (3 patients), hypertension in 3.6% (2 patients), and recurrent urinary tract infection in 1.8% (1 patient). All glomeruli appeared to be essentially normal on light

microscopy, and immunofluorescence yielded negative results. Diffuse fusion and loss of foot processes of podocytes was the only abnormality seen on electron microscopy.

Mesangioproliferative glomerulonephritis

Patients with mesangioproliferative glomerulonephritis ranged between 7 and 70 years old, with a mean age of 31.5 ± 13.8 years; 19 (51.4%) were male and 18 (48.6%) were female. The most common clinical presentation was nephrotic syndrome (in 23 patients, equivalent to 62.2% of cases), which was steroid dependant/resistant in 8.1% (3 patients), and accompanied by hypertension in 10.8% (4 patients), hematuria in 8.1% (3 cases), sickle cell disease in 5.4% (2 patients) and chronic renal failure in 2.7% (1 case). Proteinuria was the second most common presenting manifestation (seen in 4 patients, equivalent to 10.8% of cases). Light microscopy revealed variable increase of mesangial cells and matrix in all glomeruli. Immunofluorescence showed glomerular deposits of IgG, IgM, IgA and C3, singly and in various combinations, mainly in a mesangial location. Electron microscopy was not available in any of the cases.

Focal/segmental glomerulosclerosis

Patients with focal/segmental glomerulosclerosis ranged between 7 and 53 years of age, with a mean age of 32 ± 11.8 years; 21 (72.4%) were male and eight (27.6%) were female. The most common clinical presentation was nephrotic syndrome (in 18 patients, equivalent to 62.1% of cases), followed by proteinuria (in 9 patients, 31.0%). Associated hypertension was present in 6.9% of cases (2 patients). Light microscopy revealed a variable number of sclerotic segments in a variable number of glomeruli. In most cases, the sclerotic segments were few, sometimes so few as to be identified only after serial sectioning of the specimen. Mild-to-moderate tubular atrophy and interstitial fibrosis were observed in two cases (6.9%). Immunofluorescence, available in 19 cases, yielded negative results in 10 cases (34.5%) while positive fluorescence was seen in nine (31.0%). The commonest protein identified was IgM. However, the staining was weak, and segmental and focal in distribution.

Membranoproliferative glomerulonephritis

Patients in this group ranged between 13 and 54 years of age, with a mean age of 28.9 ± 10.3 years; nine (50%) were male and nine (50%) were female. The most common clinical presentation was nephrotic syndrome (in 13 patients, equivalent to 72.2% of cases). Proteinuria was the second most common presenting manifestation, seen in 11.1% (2 patients). Hypertension was also present in 11.1% (2 patients). An associated sickle cell disease and neurofibromatosis type 1 were present in one case each (5.6%). Light microscopy revealed irregular, patchy thickening of glomerular capillary walls accompanied by variable increase of mesangial cells and matrix with accentuated glomerular lobulation. Immunofluorescence (available in 13 cases) revealed IgG and C3 deposits in 10 cases (76.9%), IgM in five cases (38.5%), and IgA in only one case (7.7%). The pattern of fluorescence was diffuse and granular, mainly along the glomerular capillary loops. Electron microscopy was available in two cases. It showed interposition of mesangial cell cytoplasm between the glomerular basement membrane and the endothelial cell cytoplasm with duplication of the basement membrane. There were also subendothelial, subepithelial and intramembranous electron dense deposits (membranoproliferative type I, Figure 3).

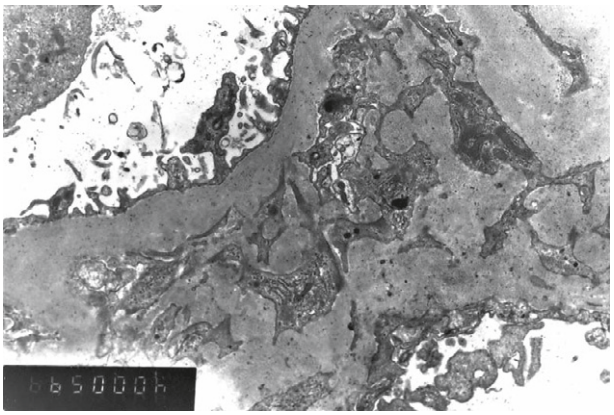

Figure 3. Membranoproliferative glomerulonephritis type I. Electron photomicrograph shows "interposition" of mesangial cell cytoplasm between endothelial cell and glomerular basement membrane, and duplication (splitting) of basement membrane.

Membranous glomerulopathy

The age range in this group was 23–62 years, with a mean of 38.4 ± 10.3 years; 10 patients (62.5%) were male and six (37.5%) were female. The commonest clinical presentation was nephrotic syndrome (in 11 patients, constituting 68.8% of cases), followed by proteinuria (in 4 patients, 25.0%) with or without microscopic hematuria, and finally end-stage renal disease (in only 1 case, 6.3%). Sickle cell disease was present in one of the patients who presented with proteinuria. None of the patients had hepatitis, malignancy or evidence of parasitic infestation. Light microscopy revealed variable, uniform, diffuse thickening of glomerular capillary walls. Immunofluorescence was available in 12 cases and showed diffuse granular deposits of IgG along the glomerular capillary loops. IgM was also present in four cases, IgA in four and C3 in four. Electron microscopy, available in four cases, showed subepithelial electron dense deposits separated by "spikes" or incorporated within the glomerular basement membrane in two cases, and marked irregular thickening of the basement membrane in the other two cases (consistent with stage IV membranous glomerulopathy). There was also diffuse fusion of epithelial foot processes.

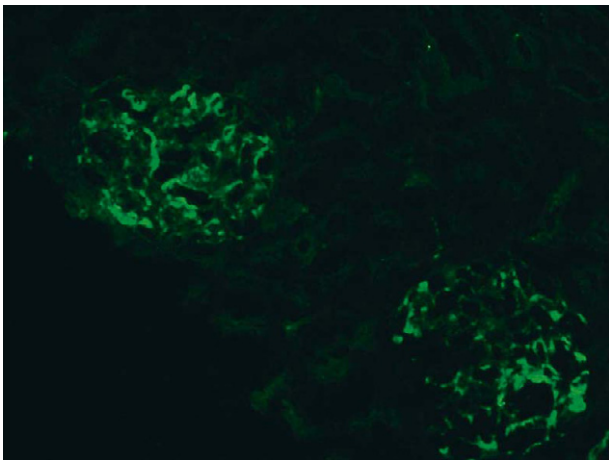

Figure 4. IgA nephropathy. Note mesangial fluorescence for IgA. Direct immunofluorescence (50×).

IgA nephropathy

Patients with IgA nephropathy had an age range between 7 and 46 years, with a mean age of 31.5±14.6 years; eight (66.7%) were male and four (33.3%) were female. The most common clinical presentation was proteinuria (in 6 patients, 50% of cases), followed by nephrotic syndrome (in 2 patients, 16.7%), and finally gross hematuria (in 1 patient, 8.3%). Associated microscopic hematuria was present in three patients (25% of cases) and hypertension or renal impairment in two patients (16.7%). Immunofluorescence revealed the diagnostic finding in all cases of the presence of mesangial IgA deposits in all glomeruli (Figure 4). Associated C3 deposits were found in seven patients (58.3%), IgM in four patients (33.3%) and IgG in one patient (8.3%). Light microscopic findings ranged from essentially normal glomeruli to variable increase of mesangial cells and matrix with or without focal, segmental or global glomerular sclerosis. Electron microscopy was available in four cases. It showed increased mesangial cells and matrix accompanied by mesangial electron dense deposits and focal fusion of foot processes in one case.

End-stage glomerulopathy (chronic glomerulonephritis)

Patients in this group ranged between 21 and 51 years old, with a mean age of 36.5±10.4 years; seven (63.6%) were male and four (36.4%) were female. Five patients (45.5%) presented with chronic renal failure, three (27.3%) with nephrotic syndrome, one (9.1%) with hypertension, and one (9.1%) with proteinuria. Light microscopy revealed global glomerular sclerosis/hyalinosis involving 50% or more of the glomeruli accompanied by variable tubular atrophy and interstitial fibrosis and inflammation, and hypertensive vascular changes. Immunofluorescence, available in four cases, revealed segmental and focal deposits of C3, accompanied by IgM deposition in one. Electron microscopy was available in two cases, showing focal periglomerular fibrosis with no electron dense deposits.

Crescentic glomerulonephritis

Patients in this group ranged between 17 and 43 years old, with a mean age of 28±8.6 years; four (66.7%) were male and two (33.3%) were female. Four patients (66.7%) presented with rapidly progressive glomerulonephritis, one (16.7%) with chronic renal failure, and one (16.7%) with vasculitis. The main light microscopic feature was the presence of large epithelial crescents in more than 50% of glomeruli. Immunofluorescence was available in two cases, and showed granular deposits of IgG, IgA and C3 along the glomerular capillary loops and in the mesangium. Electron microscopy was not available in any of the cases.

IgM nephropathy

All three patients in this group were 12 years old; one patient was male and two were female. Light microscopy revealed unremarkable glomeruli or a mild, focal and segmental increase of mesangial cells. The clinical presentation was a relapsing or steroid-dependant nephrotic syndrome. Immunofluorescence (available in all cases) revealed mesangial IgM deposits, and electron microscopy (available in 1 case) revealed focal fusion of epithelial foot processes.

Lupus nephritis

Patients with lupus nephritis ranged between 13 and 52 years of age, with a mean of 23.8±9.2 years; eight (24.2%) were male and 25 (75.8%) were female. Clinical manifestations included nephrotic syndrome, proteinuria, hematuria, hypertension and impairment of renal function. One patient also had sickle cell disease. Light microscopy, immunofluorescence (available in 20 cases) and electron microscopy (available in 4 cases) revealed World Health Organization Class IV disease in 12 patients (36.4%), Class III disease in 11 patients (33.3%), Class III progressing to Class IV disease in four (12.1%), Class V disease in three (9.1%), and Classes I, II, and VI in one patient (3.0%) each.

Diabetic glomerulosclerosis

Of the five patients in this group, three were male (60%) and two were female (40%); age ranged from 28 to 70 years, with a mean of 48.4±17 years. One patient presented with chronic renal failure, and another with proteinuria and chronic renal impairment. The remaining three patients were diabetics with a clinical diagnosis of diabetic nephropathy. Light microscopy showed nodular glomerulosclerosis in one patient, and mixed diffuse and nodular glomerulosclerosis in the other four. Hyaline sclerosis of both afferent and efferent glomerular arterioles (a finding seen exclusively in diabetic

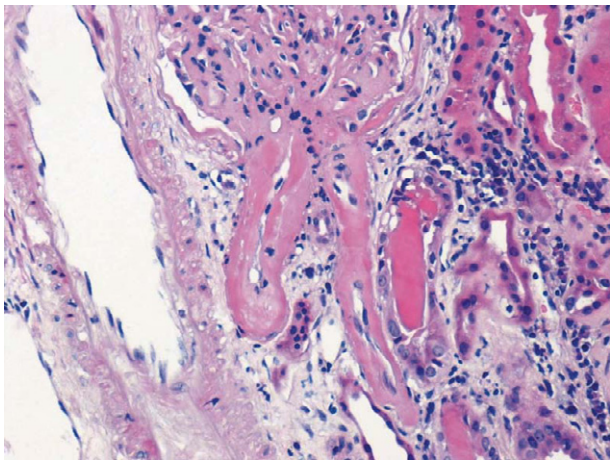

Figure 5. Diabetic glomerulosclerosis. Note hyaline sclerosis of both afferent and efferent arterioles (hematoxylin & eosin, 100×).

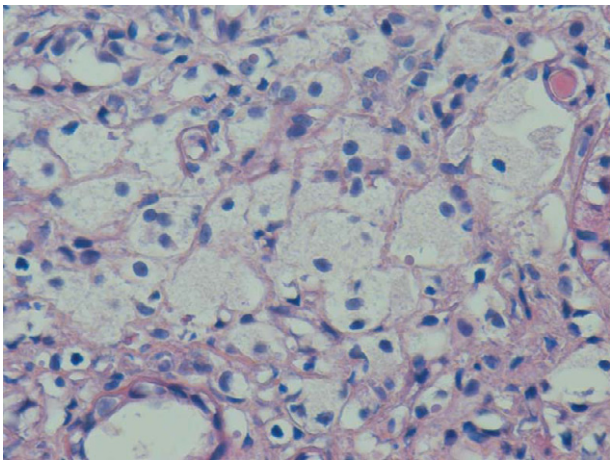

Figure 6. Alport syndrome. Note prominent interstitial foam cells (hematoxylin & eosin, 200×).

glomerulosclerosis) could also be demonstrated in one of these four cases (Figure 5). Immunofluorescence, available in one case, showed faint glomerular staining for IgA. Electron microscopy, available in another case, showed increased mesangial matrix and glomerular basement membrane thickening.

Amyloidosis

This was seen in three cases, who all presented with nephrotic syndrome, which was associated with chronic liver disease due to hepatitis B virus in one patient and hepatomegaly in another. Age ranged between 28 and 50 years, with a mean of 42±21.2 years. One patient was male and two were female. Light microscopy revealed amyloid deposits in glomeruli and blood vessel walls that stained positively for Congo red with apple green birefringence elicited by polarized light. Immunofluorescence and electron microscopy were not performed.

Alport syndrome

This was seen in two cases, a 26-year-old male and an 18-year-old female with a provisional clinical diagnosis of Alport syndrome based on the association of hematuria, mild proteinuria and renal impairment with deafness and a positive family history. Light microscopy revealed focal and segmental glomerulosclerosis with variable thickening of glomerular capillary walls and prominent foam cells in the interstitium and also within the tubules and glomerular tufts (Figure 6). Immunofluorescence and electron microscopy were not available. The presence of prominent interstitial foam cells in the absence of nephrotic range proteinuria strongly supported the clinical impression of Alport syndrome.

Wegener's granulomatosis

This was seen in a 46-year-old male who presented with hematuria. Light microscopy revealed a focal and segmental proliferative glomerulonephritis with prominent epithelial crescents and few necrotic or sclerotic glomerular segments. Immunofluorescence and electron microscopy were not available.

Henoch-Schönlein purpura nephritis

This was seen in a 10-year-old female with a provisional clinical diagnosis of Henoch-Schönlein purpura. Light microscopy revealed a mesangial proliferative glomerulonephritis. Immunofluorescence revealed mesangial IgA and C3 deposits. Electron microscopy was not available.

Hypertensive nephrosclerosis

This was seen in a 65-year-old female with diabetes mellitus, hypertension and coronary artery disease who presented with acute on top of chronic renal failure. Light microscopy revealed hyaline arteriolosclerosis, arteriolar myointimal hyperplasia, focal glomerular sclerosis and interstitial fibrosis. Immunofluorescence and electron microscopy were not available.

Discussion

Identification of the pattern of glomerular disease in a particular geographic location is of fundamental importance. It may help recognition of specific risk factors for glomerular disease and aid subsequent planning for possible prevention.

Studies published so far from different countries as well as from a number of centers in Saudi Arabia have reported conflicting results with regard to the prevalence of the different types of glomerular lesions. Possible reasons for the discrepancies include environmental or racial (genetic) factors, the small number of patients in some of the studies, differences in the indications for renal biopsies, and the non-availability of all necessary diagnostic

Table 2. Prevalence of glomerular diseases compared to that reported by other centers in Saudi Arabia

	Present study	Saudi Registry [2]	Alkhunaizi [3]	Bernieh et al [4]	Mousa et al [5]	Mitwalli et al [6]	Al-Homrany [7]	Akhtar et al [8]	Huraib et al [9]
Place of study	KFHU Al-Khobar	Six referral hospitals	DHC, Aramco Dhahran	Madinah region	AFH Riyadh	KKUH Riyadh	ACH Abha	KFSH Riyadh	KKUH Riyadh
Period of study	1986–2008	–	1998–2005	–	1 year	1994–1999	1989–1997	1983–1988	1980–1988
Primary GN (%)									
MCG	**29.4**	11.5	10	**29**	–	8.6	9.9	5.8	21.8
MsPGN	19.8	16.3	6	15.3	**20.4**	25.1	4.5	29	8
FSGS	15.5	**21.3**	**35**	15.3	31	**34.6**	17.1	**34.9**	11.4
MPGN	9.6	20.7	4	8.2	2	15.7	**38.7**	–	**26.4**
MG	8.6	10.6	4	3.2	–	3.9	9	6.5	21.8
IgAN	6.4	6.5	14	–	14.5	10.2	18.9	5.8	
Secondary GN (%)									
LN	**71.7**	**57**	**36**	**15.3**	–	**55**	**61.5**	**46.7**	**53.6**
DGS	10.9	7.5	14	–	–	5.6	–	5.1	7.3
AMD	6.5	3.2	–	2.4	–	–	–	–	
HSP	2.2	2.3	–	–	–	1.1		9	4.8
HTNS	2.2	5.9	11	–	–	3.3	–	9	17.6

KFHU = King Fahd Hospital of the University; DHC = Dhahran Health Center; AFH = Armed Forces Hospital; KKUH = King Khaled University Hospital; ACH = Abha Central Hospital; KFSH = King Faisal Specialist Hospital; GN = glomerulonephritis; MCG = minimal change glomerulopathy; MsPGN = mesangioproliferative glomerulonephritis; FSGS = focal segmental glomerulosclerosis; MPGN = membranoproliferative glomerulonephritis; MG = membranous glomerulonephritis; IgAN = IgA nephropathy; LN = lupus nephritis; DGS = diabetic glomerulosclerosis; AMD = amyloidosis; HSP = Henoch-Schönlein purpura; HTNS = hypertensive nephrosclerosis.

Table 3. Prevalence of glomerular diseases compared to that reported in countries other than Saudi Arabia

	Present study, 2010	Narasimhan et al, 2006 [10]	Al Arrayed et al, 2004 [11]	Rychlík et al, 2004 [12]	Shaker et al, 2002 [13]	Barsoum & Francis, 2000 [14]	Said et al, 2000 [15]	Chan et al, 1999 [16]	Stratta et al, 1996 [17]
Place of study	KFHU Al-Khobar	India	Bahrain	Czech Republic	Iraq	Egypt	Jordan	Hong Kong	Italy
Primary GN (%)									
MCG	29.4	11.6	30.0	12.4	17.1	–	–	8.8	5.9
MsPGN	19.8	20.2	–	11.3	22.5	–	–	–	–
FSGS	15.5	17.0	23.8	10.8	26.3	22.6	27.1	–	7.8
MPGN	9.6	3.7	14.3	–	16.2	–	35.0	–	7.3
MG	8.6	9.8	–	9.3	14.5	–	–	–	20.0
IgAN	6.4	8.6	–	34.5	0	9.8	–	23.9	26.0
Secondary GN (%)									
LN	**71.7**	**6.5**	**38.9**	**23.0**	**45.5**	–	38.8	–	–
DGS	10.9	2.5	31.9		14.5	–	–	–	–
AMD	6.5	–	–	9.9	27.3	–	**40.7**	–	–
HSP	2.2	–	–	5.7	–	–	–	–	–
HTNS	2.2	2.2	20.4	–	1.8	–	–	–	–

KFHU = King Fahd Hospital of the University; GN = glomerulonephritis; MCG = minimal change glomerulopathy; MsPGN = mesangioproliferative glomerulonephritis; FSGS = focal segmental glomerulosclerosis; MPGN = membranoproliferative glomerulonephritis; MG = membranous glomerulonephritis; IgAN = IgA nephropathy; LN = lupus nephritis; DGS = diabetic glomerulosclerosis; AMD = amyloidosis; HSP = Henoch-Schönlein purpura; HTNS = hypertensive nephrosclerosis.

facilities in some of the reporting centers [2]. Tables 2 and 3 and Figures 7–10 show the prevalence of the more common glomerular diseases encountered in the present study as compared to the prevalence reported by other centers in Saudi Arabia as well as in some other parts of the world, including neighboring countries [2–17].

Other than a significantly higher incidence of minimal change glomerulopathy (29.4% of primary glomerular

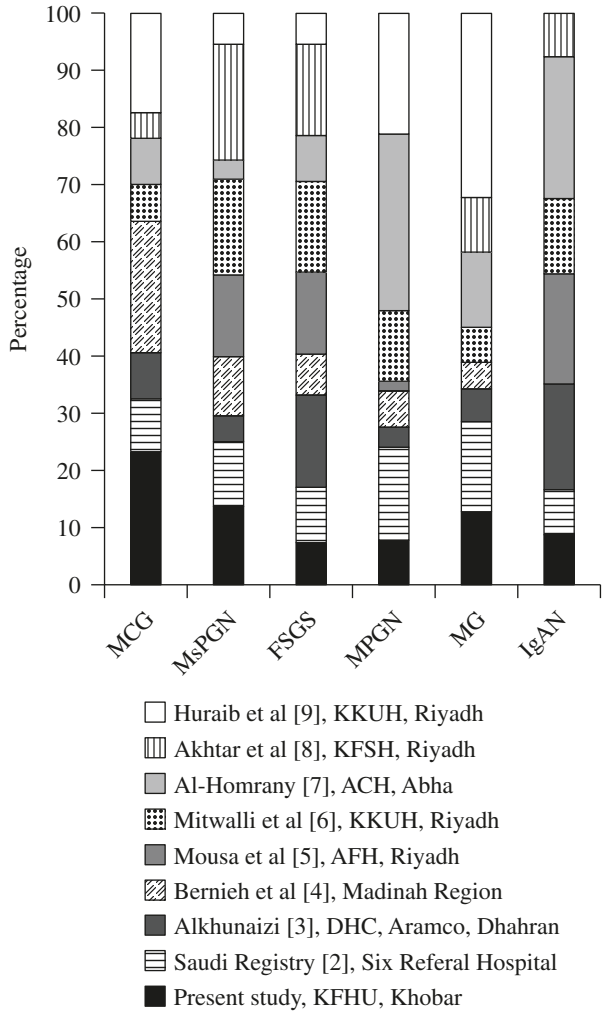

Figure 7. Prevalence of primary glomerular diseases compared to that reported by other centers in Saudi Arabia. A 100% stacked column chart comparing the prevalence of each type of primary glomerulonephritis to a total across various centers in Saudi Arabia. MCG = minimal change glomerulopathy; MsPGN = mesangioproliferative glomerulonephritis; FSGS = focal segmental glomerulosclerosis; MPGN = membranoproliferative glomerulonephritis; MG = membranous glomerulonephritis; IgAN = IgA nephropathy; KFHU = King Fahd Hospital of the University; DHC = Dhahran Health Center; AFH = Armed Forces Hospital; KKUH = King Khaled University Hospital; ACH = Abha Central Hospital; KFSH = King Faisal Specialist Hospital.

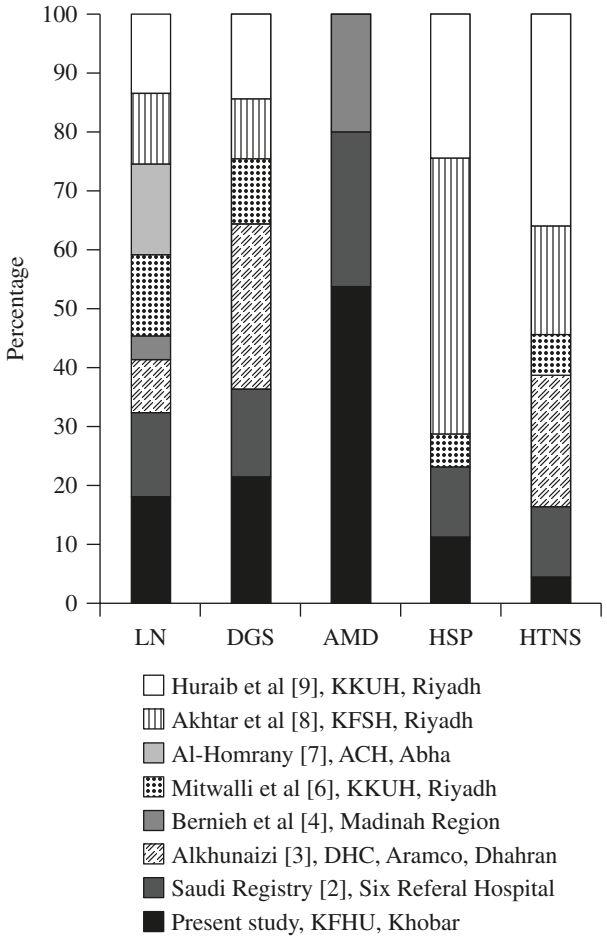

Figure 8. Prevalence of secondary glomerular diseases compared to that reported by other centers in Saudi Arabia. A 100% stacked column chart comparing the prevalence of each type of secondary glomerulonephritis to a total across various centers in Saudi Arabia. LN = lupus nephritis; DGS = diabetic glomerulosclerosis; AMD = amyloidosis; HSP = Henoch-Schönlein purpura; HTNS = hypertensive nephrosclerosis; KFHU = King Fahd Hospital of the University; DHC = Dhahran Health Center; KKUH = King Khaled University Hospital; ACH = Abha Central Hospital; KFSH = King Faisal Specialist Hospital.

disease in the present study *vs.* 11.5% reported by the registry, $p<0.001$) and lupus nephritis (71.7% of secondary glomerular disease *vs.* 57%, $p<0.001$), and a significantly lower prevalence of membranoproliferative glomerulonephritis (9.6% of primary glomerular disease *vs.* 20.7%, $p=0.029$), our results are generally comparable to those reported by the Saudi registry for glomerulopathy [2] and in neighboring countries [11,13–16]. It should be noted that the study of the Saudi registry published in the year 2000 included 131 of the glomerulonephritis cases included in the present study.

Age- and sex-adjusted analyses revealed that minimal change glomerulopathy and lupus nephritis were also the most prevalent primary and secondary glomerulopathies in the pediatric age group as well as in adults, females and males.

In agreement with the present study, minimal change glomerulopathy was reported to be the leading primary glomerular disease in the Madinah region of Saudi Arabia [4] and also in Bahrain [11], amounting to 29% and 30% of cases, respectively. It is interesting to note that Bahrain is the closest country to Eastern Saudi Arabia and that the people of both regions have the same ethnic roots and are strongly tied by tribal and family kinship. Could genetic factors underlie the prevalence of minimal change glomerulopathy in both regions?

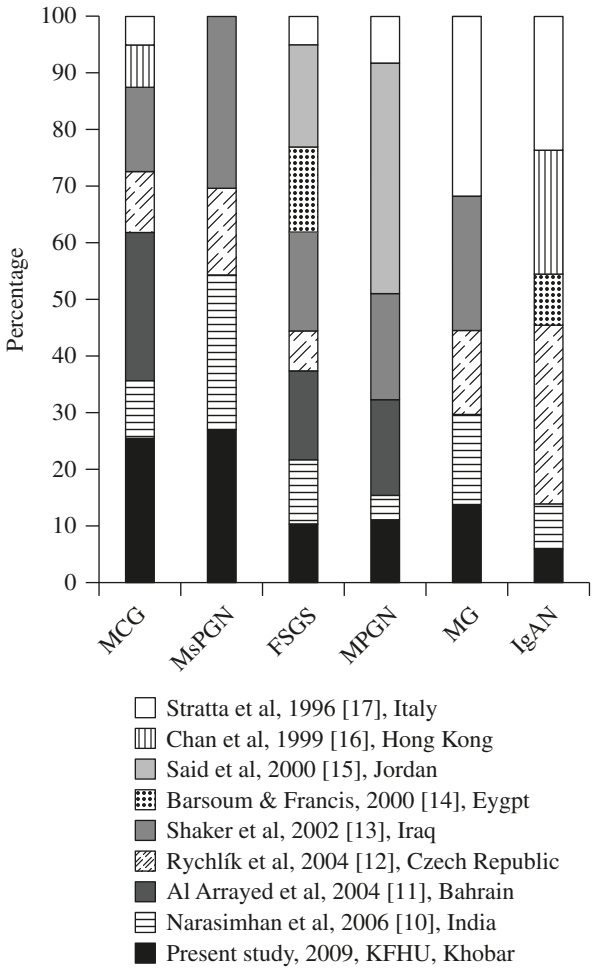

Figure 9. Prevalence of primary glomerular diseases compared to that reported in countries other than Saudi Arabia. A 100% stacked column chart comparing the prevalence of each type of primary glomerulonephritis to a total across various countries. MCG = minimal change glomerulopathy; MsPGN = mesangioproliferative glomerulonephritis; FSGS = focal segmental glomerulosclerosis; MPGN = membranoproliferative glomerulonephritis; MG = membranous glomerulonephritis; IgAN = IgA nephropathy; KFHU = King Fahd Hospital of the University.

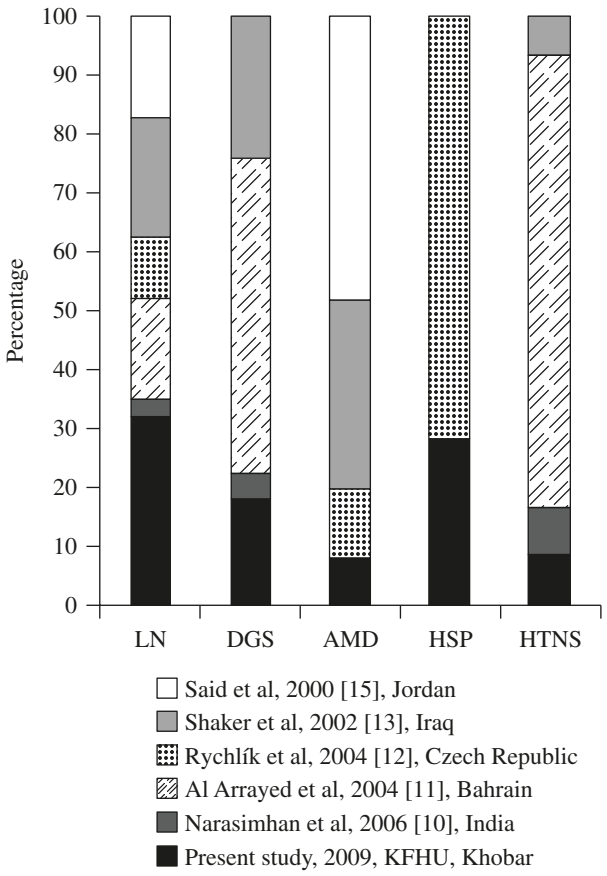

Figure 10. Prevalence of secondary glomerular diseases compared to that reported in countries other than Saudi Arabia. A 100% stacked column chart comparing the prevalence of each type of secondary glomerulonephritis to a total across various countries. LN = lupus nephritis; DGS = diabetic glomerulosclerosis; AMD = amyloidosis; HSP = Henoch-Schönlein purpura; HTNS = hypertensive nephrosclerosis; KFHU = King Fahd Hospital of the University.

Lupus nephritis was frequent in the present study (75% of secondary glomerular diseases), probably because all the cases studied were known cases of systemic lupus erythematosus biopsied for the purpose of establishing a diagnosis of lupus nephritis or grading and staging of an already diagnosed lupus nephritis.

The lower prevalence of membranoproliferative glomerulonephritis in the present study and also in most of the studies reported from the Kingdom [3–5] (Table 3) may be attributed to the non-availability of immunofluorescence and electron microscopy in a number of the cases studied, so that early cases (where mesangial hypercellularity and glomerular capillary wall thickening may be too slight to be recognized by light microscopy) could have been misinterpreted as minimal change glomerulopathy or mild mesangioproliferative glomerulonephritis [18].

Finally, a markedly lower incidence of IgA nephropathy has been noted in the present study as well as in most of the studies reported from Saudi Arabia [2,6,8] and from neighboring countries [13,14], as compared to its incidence in other parts of the world where IgA nephropathy has generally been the leading primary glomerular disease [12,16,17] (Tables 2 & 3). This again may be attributed to the non-availability of immunofluorescence in all of the glomerular biopsies studied. Without immunofluorescence, IgA nephropathy can be mistaken morphologically as well as clinically for almost any type of glomerulonephritis.

It is clear from the above discussion that without performing immunofluorescence and electron microscopy on every renal biopsy evaluated for suspected glomerular disease, a precise typing of the glomerular disease may not be possible on the basis of light microscopy alone.

This may be the main reason for the discrepancies in the prevalence of the different types of glomerular lesions in different reports, particularly those from Saudi Arabia and other countries in the region where these facilities are not available in all laboratories.

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