Renal Histological Findings in Adults in Jamaica

AK Soyibo[1], D Shah[2], EN Barton[1], W Williams[1], R Smith[1]

ABSTRACT

Background: *In 2006, it was reported that Focal and Segmental Glomerulosclerosis (FSGS), Minimal Change Disease (MCD) and Membranous Glomerulonephritis (MGN) were the commonest primary glomerular diseases identified from percutaneous kidney biopsies done in Jamaica for that year (*n = *76). The sample size was thought to be small and might have affected the reported findings. So a three-year review of percutaneous kidney biopsies in Jamaica was carried out.*

Methods: *Histology reports and clinical data were reviewed for percutaneous kidney biopsies performed from January 2005 to December 2007. Demographic data (age, gender), laboratory investigations such as serum urea, serum creatinine, proteinuria, haematuria, 24-hour urinary protein, and creatinine clearance, and clinical diagnosis were collected from the histology requisition form.*

Results: *There was a total of 224 native kidney biopsies performed. There were 91 males (40.6%) and 133 females (59.4%). Age distribution showed a total number of 25 paediatric cases (11.2%) and 199 adult cases (88.8%). Proteinuria was present in 171 cases (76.3%) and haematuria in 86 cases (38.4%). Of the total biopsies done, 78 cases (39.2%) had primary glomerular diseases, 110 cases (55.3%) had secondary glomerular diseases and 11 (5.5%) biopsies were reported as either normal or inadequate for histological diagnosis. The most common reasons indicated for percutaneous kidney biopsy were proteinuria, haematuria and staging of lupus nephritis. Most common histological findings for primary glomerular disease after percutaneous kidney biopsy were FSGS (n = 34), MGN (*n = *15) and MCD (*n = *12). In secondary glomerular diseases (*n = *110), there were more females (70.8%) than males. Systemic lupus erythematosus was present in 63.3%. Histology of lupus nephritis according to the International Society of Nephrologists classification shows Membranous Lupus Nephritis [MLN] (40.2%), Diffuse Lupus Nephritis [DLN] (19.5%) and Minimal Mesangial Lupus Nephritis [MMLN] (14.3%) as the common histological types.*

Conclusions: *The most common histological finding for primary glomerular disease following percutaneous kidney biopsy was FSGS, MCD and MGN. Membranous Lupus Nephritis was the commonest histological type for lupus nephritis in this series.*

Hallazgos Histológicos Renales en Adultos en Jamaica

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RESUMEN

Antecedentes: *En 2006, se reportó que la Glomeruloesclerosis Segmentaria y Focal (GESF), la Enfermedad de Cambios Mínimos (ECM) y la Glomerulonefritis Membranosa (GNM) fueron las enfermedades glomerulares primarias más comunes identificadas a partir de las biopsias renales percutáneas realizadas en Jamaica ese año (*n = *76). El tamaño de la muestra se consideró pequeño y pudo haber afectado los hallazgos reportados. De manera que se realizó un examen de tres años, de las biopsias renales percutáneas en Jamaica.*

Métodos: *Se revisaron los reportes de histología y los datos clínicos correspondientes a las biopsias renales percutáneas realizadas desde enero de 2005 a diciembre de 2007.*

Resultados: *Hubo un total de 224 biopsias de riñón nativo. Se realizaron 74, 78 y 72 biopsias renales en 2005, 2006 y 2007 respectivamente. Hubo 91 varones (40.6%) y 133 hembras (59.4%). La distri-*

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*bución por edades mostró un total de 25 casos pediátricos (11.2%) y 119 casos de adultos (88.8%). La proteinuria estuvo presente en 171 casos (76.3%) y la hematuria en 86 casos (38.4%). Del total de biopsias realizadas, 78 casos (39.2%) tenían enfermedades glomerulares primarias, 110 casos (55.3%) tenían enfermedades glomerulares secundarias y 11 (5.5%) biopsias fueron reportadas como normales, o como inadecuadas para el diagnóstico histológico. Las razones más comunes señaladas para la biopsia renal percutánea fueron la proteinuria, la hematuria y la estadificación de la nefritis por lupus o nefritis lúpica. Los hallazgos histológicos más comunes para la enfermedad glomerular primaria tras la biopsia renal percutánea fueron GESF (*n *= 34), GNM (*n *= 15) y ECM (*n *= 12). En relación con las enfermedades glomerulares secundarias (*n *= 110), hubo más hembras (70.8%) que varones. El lupus eritematoso sistémico estuvo presente en 63.3%. De acuerdo con la clasificación de la Sociedad Internacional de Nefrología, la histología de la nefritis por lupus muestra la nefritis lúpica membranosa (NLM) [40.2%], la nefritis lúpica difusa (NLD) [19.5%], y la nefritis lúpica mesangial mínima (NLMM) [14.3%], como los tipos histológicos más comunes.*

***Conclusión:** Los hallazgos histológicos más comunes para la enfermedad glomerular primaria tras la biopsia renal percutánea, fueron GESF, ECM y GNM. La nefritis lúpica membranosa fue el tipo de histología más común para la nefritis por lupus en esta serie.*

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INTRODUCTION

In 2006, it was reported that Focal and Segmental Glomerulosclerosis (FSGS), Minimal Change Disease (MCD) and Membranous Glomerulonephritis (MGN) were the commonest primary glomerular diseases on histology of percutaneous kidney biopsies done in Jamaica for 2006 (1). Lupus nephritis was the commonest secondary glomerular disease from percutaneous kidney biopsy. There were however only 78 kidney biopsies that were performed, and therefore the sample size was thought too small. So a three-year review of the histology of percutaneous kidney biopsies in Jamaica was conducted.

Review of renal biopsy data can help to give epidemiological information, determine local trends and change in disease pattern (2, 3). It can give insight to clinically significant glomerular disease and clinical manifestation and pattern of disease progression. The knowledge of these parameters can help to monitor disease pattern and response to treatment through case control and cohort studies.

Due to the emergence and changes in the trend of medical illness from communicable diseases to chronic non-communicable diseases and the consequential ageing population (4), it is important to continue surveillance and monitoring of the histological pattern of kidney biopsy specimens, not just in Jamaica but in the Caribbean.

METHODS

A retrospective analysis was carried out on percutaneous renal biopsies performed from January 2005 to December 2007. All renal biopsies done in Jamaica were sent to the University Hospital of the West Indies (UHWI) for histopathological report and diagnoses. Demographic data (age, gender), laboratory investigations such as serum urea, serum creatinine, proteinuria, haematuria, 24-hour urinary protein and creatinine clearance, and clinical and histological diagnoses were obtained from the histology requisition form sent to the Department of Pathology and the histology report issued. Missing data were supplemented from review of the patients' records.

All biopsy specimens were evaluated by light microscopy but not all underwent immunofluorescence. No electron microscopic evaluation was done but special staining was carried out.

Data were entered and analysed using the Statistical Package for the Social Sciences (SPSS) 12.0. Graphs were generated with Microsoft Excel spread sheet 2003.

RESULTS

There was a total of 224 native kidney biopsies performed. There were 74, 78 and 72 kidney biopsies performed in 2005, 2006 and 2007 respectively. There were 91 males (40.6%) and 133 females [59.4%] (Fig. 1). Age distribution showed a total number of 25 paediatric cases (11.2%) and 199 adult cases (88.8%). Age defined as paediatric was 12 years old or less. The paediatric data were not further analysed for this

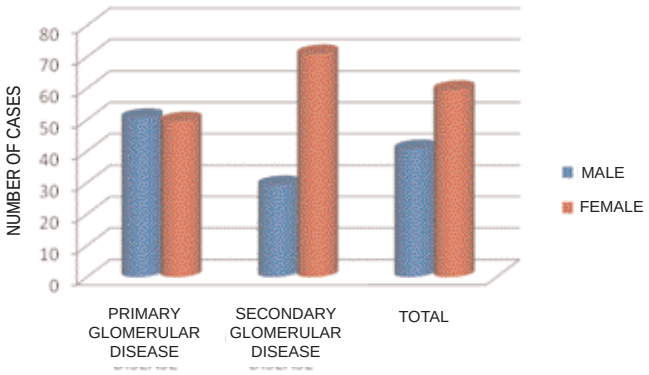

Fig. 1: Gender distribution and comparison between primary and secondary glomerular disease.

report. Proteinuria was present in 76.3% and haematuria in 38.4% of analysed data.

The average age was 34.9 (+/-15.9) years, with age range from 12 to 78 years. The average age for males was 38.9 years and females was 32.1 years. Of the total biopsies done, 78 cases (39.2%) had primary glomerular disease, 110 cases (55.3%) had secondary glomerular disease and 6 (3.0%) biopsies were reported as normal and 5 (2.5%) were inadequate for histological diagnosis. Most common reasons reported as indications for percutaneous kidney biopsy were:

* Proteinuria and/or haematuria.
* Staging of lupus nephritis.
* Abnormal urea and creatinine.
* Diagnostic work-up for secondary glomerular disease.

For those reported cases of primary glomerular disease (n = 78), 71.4% had nephrotic range proteinuria (> 3 g/24 hours), 7.1% had sub-nephrotic range proteinuria (2-3 g/ 24 hours) and 21.4% had non-nephrotic range proteinuria (Fig. 2). Overall, for primary glomerular disease, proteinuria was present in 80.6% and haematuria was detected in 44.1% of cases. Active urinary sediments were present in 71.4% of cases. Hypertension was present in 31.2% of cases with primary glomerular disease while only 2.2% had diabetes mellitus. Renal failure was present in 22.8% of these cases.

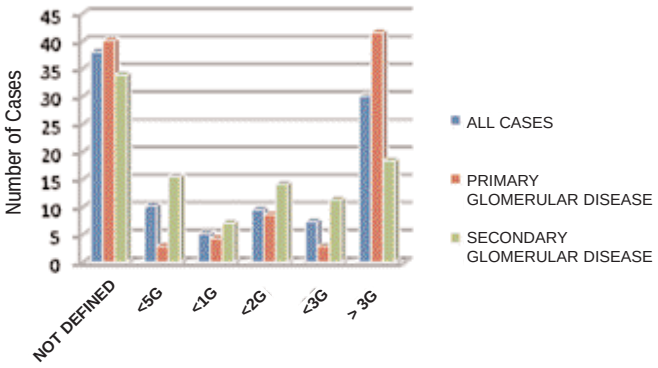

Fig. 2: 24-hour urine quantification by category.

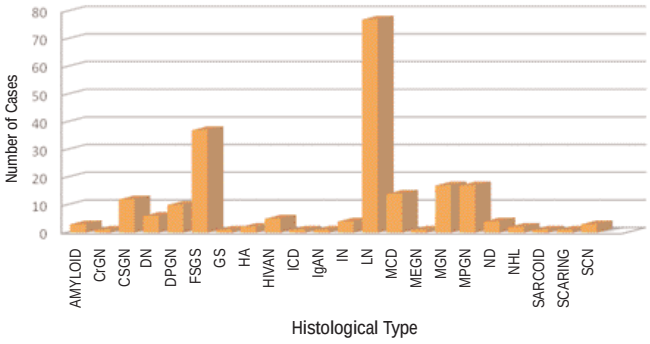

Fig. 3: Overall histological pattern between 2005 and 2007.

Key:
Amyloid = amyloidosis, CrGN = crescentic glomerulonephritis, CSGN = chronic sclerosing glomerulonephritis, DN = Diabetic Nephropathy, DPGN = diffuse proliferative glomerulonephritis, FSGS = focal and segmental glomerulosclerosis, GS = global sclerosis, HA = hypertensive arteriosclerosis, HIVAN = HIV associated glomerulonephritis, ICD = immune complex disease, IgAN = Ig A nephropathy, IN = interstitial nephritis, LN = lupus nephritis, MCD = minimal change disease, MEGN = mesangioproliferative glomerulonephritis, MGN = membranous glomerulonephritis, MPGN = membranoproliferative glomerulonephritis, ND = no structural disease, NHL = non-Hodgkin's lymphoma, SARCOID = sarcoidosis, SCN = sickle cell nephropathy.

The most common histological findings in adults with primary glomerular disease (Fig. 3) was FSGS (n = 34), MGN (n = 15) and MCD (n = 12). There was one case of crescentic glomerulonephritis in adults.

In secondary glomerular disease (n = 110), there were more females (70.8%) than males (29.2%). Proteinuria was present in 70.8% and haematuria in 33.3%, while 50.0% had active urinary sediments. Systemic Lupus Erythematosus was present in 63.3%, diabetes mellitus in 11.7% and hypertension in 25.8%. Renal failure was seen in 33.9% of cases. Indications recorded for biopsy were: lupus nephritis with proteinuria (62.5%) and diagnostic work-up (31.7%), for example multiple myeloma. Of the secondary glomerular disease in these adults, lupus nephritis was the most common. Histology of lupus nephritis according to the International Society of Nephrologists classification shows MLN, DLN and MMLN as the common histological types (Fig. 4).

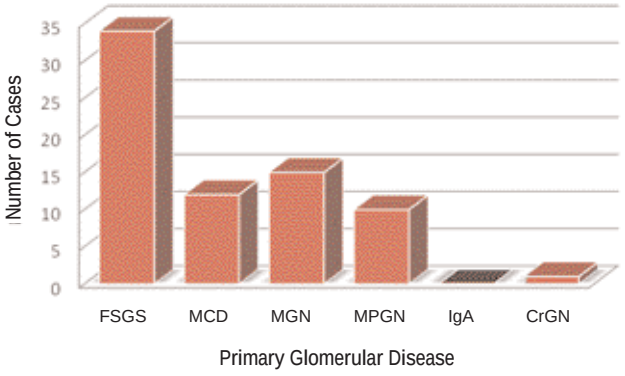

Fig. 4: Number of cases of primary glomerular disease.

DISCUSSION

Percutaneous renal biopsy, based on the use of an aspiration needle and the patient in the sitting position, was first described by Iversen and Brun in 1951 (5). It provided useful clinical details about glomerular, tubulo-interstitial and vascular renal disease. The information helped to plan treatment, prognosticate and determine follow-up cohort studies. The number of kidney biopsies performed in each year was roughly the same. In general, the number of kidney biopsies performed is dependent on the availability of technical support and a nephrology service. There was however no

change in the pattern over the study period, this pattern was also seen in the Danish biopsy registry (2).

Gender distribution showed a slight predominance of females (54.9%) in the overall histological report, however when looking at secondary glomerular disease, there were more females (70.8%) than males (29.2%). This reflects the prevalence of SLE in the female population.

In this histological series, paediatric age cut-off was at 12 years, as compared to other series which used an older cut-off for paediatrics (5). This accounted for 11.2% of the cases. This is smaller than the percentages reported in other series (3, 6).

Proteinuria is a common manifestation and the most common clinical presentation of renal disease, and is of prognostic value (7); haematuria is less common and so is elevated urea and creatinine (7, 8). In the present study, proteinuria was present in 76.3% of cases; haematuria in 38.4% and renal failure in 33.9% of cases. There were no significant changes between primary and secondary glomerular disease with respect to these parameters.

In the population with secondary glomerular disease, SLE was present in almost two-thirds of the cases (63.3%), hypertension in 25.8% and diabetes mellitus in 11.7%. Although diabetes mellitus, hypertension and chronic glomerulonephritis were reported in the Caribbean renal registry as the common causes of chronic kidney disease (8), renal biopsy is usually not performed in patients with diabetes mellitus and hypertension unless there are atypical presentations. Such instances are the diabetic with significant haematuria and/or significant proteinuria with no other microvascular complication or the hypertensive with nephrotic or sub-nephrotic range proteinuria.

Common indications for renal biopsy include: nephrotic syndrome (except in children (9) and in diabetics (10) unless there are special indications); renal manifestation in systemic disease/disorder *eg*, SLE and vasculitis, multiple myeloma or amyloidosis); suspected glomerular disease and abnormalities in renal function in renal transplant recipients (rejection or recurrence of *de novo* glomerular disease). Some patients with non-nephrotic proteinuria, haematuria and chronic renal failure may also benefit from a renal biopsy for diagnostic and prognostic purposes. Indication for renal biopsy found in this series was similar to those reported in the literature (11–13).

In this biopsy series, LN was the commonest histological finding overall (Fig. 5). In primary glomerular disease, FSGS was the most common histological finding (n = 34), followed by MGN (n = 15) and MCD (n = 12). Focal Segmental Glomerulosclerosis has been an important aetiology of glomerular disease and an important cause of ESRD due to glomerular damage (14). In the Caribbean, chronic glomerular disease is the third leading cause of ESRD (8). In a 10-year review of idiopathic FSGS by Barton *et al*, it was reported that 30% developed end-stage renal failure in 10 years (15). Factors predictive of rapid progression of idiopathic FSGS to renal failure included heavy proteinuria, serum creatinine elevation, histological subtype, advanced interstitial fibrosis on histology (> 20% of biopsy surface areas) and collapsing lesions (16). Recurrence of FSGS in the transplanted kidney remains a significant problem. Rapid progression of FSGS in the native kidney is predictive of recurrence in transplanted kidneys (17, 18). Also recurrence of primary disease in allograft is a strong predictor of recurrence in subsequent kidney transplants. This has impact on the social health and economy of a country.

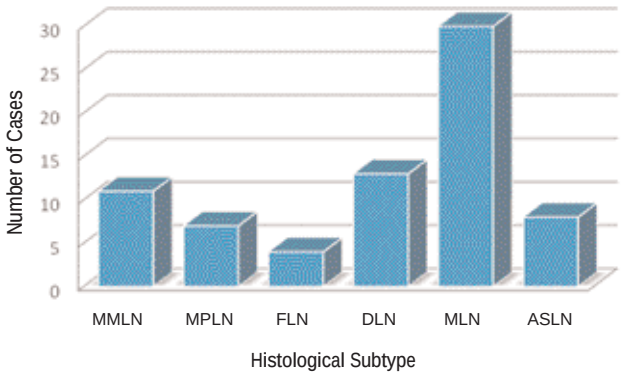

Fig. 5: Number of cases of lupus nephritis by histological subtype.

Key:
MMLN = minimal mesangial lupus nephritis, MPLN = mesangial proliferative LN, FLN = focal LN, DLN = diffuse LN, MLN = membranous LN, ASLN = advanced sclerosis LN.

Common causes of primary nephrotic syndrome are FSGS, MCD, MGN and membranoproliferative glomerulonephritis (MPGN). Membranoproliferative glomerulonephritis when seen should trigger the search for secondary causes such as SLE, dysproteinaemias and hepatitis C infection. Like other primary glomerular diseases, the incidence of MGN is increasing (Toronto Glomerulonephritis Registry). The course of MGN is such that 20 – 30% will have spontaneous remission, 30 – 40% will have persistent proteinuria while the others (20 – 30%) will progress to renal failure. The group with persistent proteinuria is of relevance, and predicting progression to renal failure is an area of ongoing research (19).

There was only one report of crescentic glomerulonephritis in a 65-year old female. It may appear as a limited disease of the kidney or as part of a multi-systemic disease. In the Italian Registry of Renal Biopsy it was commoner in the older age group > 65 years (20).

IgA nephropathy, the most common primary glomerular disease in the world (21), was not seen in the adult kidney biopsy histology. There was only one case of IgA nephropathy (IgAN) and it was in the paediatric population. There have been case reports from the Caribbean on IgA nephropathy as a cause of renal failure and, in some instances, leading to end-stage renal failure (22). IgA nephropathy is a form of glomerulonephritis that was first described by Berger and

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Hinglais in 1968 (21). The mildest form of IgAN is usually referred to as Berger's disease. As it represents a spectrum of severity, it is possible that the mildest form is not detected. It is commoner in persons of European and Asian ancestry than African descent (21, 23). There are however no report of the incidence in the Caribbean. It is usually seen in the age group between 16 and 35 years and rare below age 10 years (23). However these trends were not observed in this histological series. This can be explained since most cases of IgAN will present with haematuria and upper respiratory symptoms (40 – 50%) and another 30 – 40% have no symptoms except active urinary sediments. In these cases, a percutaneous kidney biopsy would not have been performed, especially as the majority resolve spontaneously. Another possible explanation was the relative absence of immunofluorescence during the study period.

In secondary glomerular disease, LN was the commonest. The most common subtype according to the International Society of Nephrologist classification (Fig. 4) was membranous LN (class 5) followed by diffuse LN (class 4) and minimal mesangial LN (class 1). Williams W *et al* in a 20-year review of renal histological reports found that lupus nephritis, class IV (according to the World Health Organization) was the commonest histological subtype (25). Most series also report class IV as the predominant glomerular lesion in LN (9). The reason for the pattern observed in the present study is unclear.

CONCLUSION

The pattern of glomerular disease observed internationally is confirmed in this series. There is a change in the trend of the histological pattern in biopsy series reported worldwide and this was also seen in this series. This represents a change from what Morgan *et al* reported in 1984 (12). In Jamaica, membranous lupus nephritis was the most common histology found in lupus nephritis and this has not been reported elsewhere. The reason for this is uncertain. Further data collation and analysis will continue to elucidate the histological pattern in renal biopsies in Jamaica.

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