Renal Biopsy Findings in Jamaican Children

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ABSTRACT

Objective: *To document the histological findings in Jamaican children undergoing renal biopsy in order to determine the relative prevalence of varying types of glomerular disease in the island.*

Methods: *This study analyses retrospectively the renal histology in all Jamaican children less than age 12 years undergoing their first adequate renal biopsy between January 1985 and December 2008. Clinicopathological data were obtained solely from the histology reports from the University Hospital of the West Indies where all paediatric renal biopsies are processed.*

Results: *Of the 270 children, aged 1 month to 11 years (mean 7.58 years), 147 [58.1%] were males. The commonest indications for renal biopsy were nephrotic syndrome (57.4%) and glomerulonephritis (30%). Most biopsied children (260/270) had glomerular disease.*

The predominant glomerulonephritides were diffuse proliferative glomerulonephritis (DPGN) (27.7%) and mesangial proliferative glomerulonephritis (MesGN) (25.5%). Glomerular disease was idiopathic in 136/260 (53%) but was infection-associated in 32.3% (84 cases) of which Poststreptococcal glomerulonephritis (PSGN) was the commonest (75%) – predominantly DPGN (74.6%). Hepatitis B followed at 15.5% (13/84) manifested as membranous nephropathy in 83.3% (10/12). In patients with SS disease, DPGN was the commonest histology (47.4%). Systemic lupus erythematosus accounted for 5% of all renal biopsies. Over time, PSGN occurred less frequently, with a parallel reduction in DPGN and MesGN.

Conclusion: *In Jamaican children, DPGN is the commonest nephritis. Membranous nephropathy is primarily due to Hepatitis B. The commonest histology in SS disease is DPGN. The role of infection in the pathogenesis of renal disease in Jamaican children is probably underestimated.*

Key words: glomerulonephritis, haematuria, renal histology

Hallazgos en las Biopsias Renales en Niños Jamaicanos

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RESUMEN

Objetivo: *Documentar los hallazgos histológicos en niños jamaicanos a los que se les ha realizado biopsias renales para determinar la prevalencia relativa de los diversos tipos de enfermedad glomerular en la isla.*

Métodos: *Este estudio analiza retrospectivamente la histología renal en todos los niños jamaicanos menores de 12 años sometidos a su primera biopsia renal adecuada entre enero de 1985 y diciembre de 2008. Los datos clinicopatológicos fueron obtenidos exclusivamente de los reportes de histología del Hospital Universitario de West Indies, dónde se procesan todas las biopsias renales.*

Resultados: *De 270 niños, cuyas edades fluctuaban de 1 mes a 11 años (media 7.58 años), 147 [58.1%] eran varones. Las indicaciones más comunes para la biopsia renal fueron el síndrome nefrótico (57.4%) y la glomerulonefritis (30%). La mayoría de los niños sometidos a biopsia (260/270) tenían la enfermedad del glomerular. Las glomerulonefritis predominantes fueron la glomerulonefritis proliferativa difusa (GNPD) (27.7%) y glomerulonefritis proliferativa mesangial (GNMes) (25.5%). La enfermedad glomerular fue idiomática en 136/260 (53%) pero estuvo asociada con infecciones en*

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32.3% (84 casos) en los cuales la glomerulonefritis poststreptocóccica (GNPS) fue la más común (75%) – predominantemente GNDP (74.6%). La hepatitis B siguió con 15.5% (13/84), manifestada como nefropatía membranosa en 83.3% (10/12). En los pacientes con la enfermedad de la hemoglobina SS, la GNDP fue la histología más común (47.4%). El lupus eritematoso sistémico representó el 5% de todas las biopsias renales. Al pasar el tiempo, la GNPS ocurrió menos frecuentemente, con una reducción paralela en GNPD y GNMes.

***Conclusión:** En los niños jamaicanos, la GNPD es la nefritis más común. La nefropatía membranosa se debe principalmente a la Hepatitis B. La histología más común en el caso de la enfermedad de hemoglobina SS es la GNPD. Probablemente se subestima el papel que las infecciones desempeñan en la patogénesis de la enfermedad renal en los niños jamaicanos.*

Palabras claves: glomerulonefritis, hematuria, histología renal

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INTRODUCTION

There are no comprehensive reviews of renal histology in Caribbean children. Earlier studies of renal biopsy findings in Jamaican children with nephrotic syndrome (1,2) found mesangial proliferative glomerulonephritis (MesGN) to be more common than minimal change disease (MCD) while in Trinidadian children MCD predominated (3).

Isolated reports (1, 2, 4–6) attest to the contribution of post-infectious nephritis to the spectrum of renal disease – more specifically nephrotic syndrome – in Jamaican children. In Jamaica, Paediatric Nephrology services are offered at the University Hospital of the West Indies (UHWI) and Bustamante Children's Hospital (BCH) and all renal biopsies are processed by the Pathology Department of the UHWI. The data presented in this paper therefore completely represent the histological pattern of renal disease in Jamaican children. The purpose of this study was to document the histological appearances in all first adequate renal biopsies performed in Jamaican children less than < age 12 years old between January 1985 and December 2008 in order to determine the relative prevalence of varying types of glomerular disease in the island. Where possible, clinicopathological correlations were made to enable reasonable predictions of pathology when immediate renal biopsy is unfeasible and empiric therapy necessary.

SUBJECTS AND METHODS

The study was a retrospective review of the histology reports of all renal biopsies performed in Jamaican children < less than 12 years of age, between January 1985 and December 2008. The study was approved by the University Hospital of the West Indies, University of the West Indies, Faculty of Medical Sciences (UHWI/UWI/FMS) Ethics committee. Clinical data were obtained solely from the information provided on the pathology request forms. The primary indications recorded for renal biopsy were: nephrotic syndrome, glomerulonephritis, prolonged acute, severe or chronic renal failure, autoimmune disease, heavy proteinuria and recurrent gross haematuria.

Children with the nephrotic syndrome were biopsied if at the onset they had the following features: age < 12 months, sustained hypertension, renal impairment, gross haematuria, secondary nephropathy: sickle haemoglobinopathy, positive serology (ANF, VDRL, ASOT, Hepatitis B surface antigen and HTLV-1 antibody) and hypocomplementaemia. Children with HIV infection were not biopsied. Late biopsies were performed for steroid resistance, progressive disease, hypertension and renal failure. From 1985 to 1992, frequent relapsers were also biopsied. Children with glomerulonephritis of uncertain aetiology or with serologically confirmed Poststreptococcal Glomerulonephritis (PSGN) but atypical presentation (gross haematuria or hypertension > 4 weeks, severe persistent or progressive renal failure, hypocomplementaemia > 6 weeks, nephrotic syndrome or nephrotic range proteinuria) were biopsied.

Renal biopsy was percutaneous using Tru-Cut ® or Quick – Core® disposable biopsy needles in all cases except in patients with a single kidney or those who weighed < 10 kg in which case an open wedge biopsy under general anaesthesia was performed. All renal tissue was examined by light microscopy, but immunofluorescence (IF) and electron microscopy (EM) could only be performed when these facilities were available. An adequate biopsy was defined as one containing a minimum of five glomeruli, however if the process appeared to be diffuse the diagnosis was made on as few as 2 glomeruli. All renal histology was examined at the UHWI. Only the information on the first adequate renal biopsy of each child was considered.

Data were analysed using the Statistical Package for the Social Sciences (SSPS) – Version 14. The data on nephrotic syndrome will be evaluated separately.

RESULTS

Between January 1985 and December 2008, 270 children had adequate first renal biopsies. In the 264 children in whom age-related data were available, the ages ranged between 1 month and 11 years (mean 7.58 ± 3.24 years). All biopsies had light microscopy but only 99 (36.7%) were subjected to electron microscopy EM) and 57 (21.1%) to immuno-

fluorescence. There were 147 males (58.1%) and 123 females (M: F 1.2:1). The commonest indication for renal biopsy was the nephrotic syndrome (NS) [57.4%] followed by glomerulonephritis (GN) [30%] (Table 1).

Table 1: Indications for renal biopsy in Jamaican children

Indication	Number	%
Nephrotic syndrome	157	58.1
Glomerulonephritis	81	30
Recurrent gross haematuria	11	4
Autoimmune for staging (no clinical nephritis)	7	2.6
Acute renal failure	5	1.8
Chronic renal failure	4	1.5
Hypertension	2	0.7
Other	3	1.3
Total	**270**	**100**

Renal histology (Table 2). Glomerular disease (260 cases) accounted for the majority of renal pathology (96.3 %). Non-glomerular disease (3.7 %) consisted of interstitial nephritis in 4 children (one of whom had systemic lupus erythematosus), acute tubular necrosis (2 cases) and one case each of Wilms tumour, autosomal recessive polycystic kidney disease, amyloidosis and cortical scarring. The two commonest histological patterns in the study were diffuse proliferative glomerulonephritis (DPGN) [27.7%] and mesangial proliferative glomerulonephritis (MesGN) [25.5%] (Table 2). Membranoproliferative glomerulonephritis (MPGN) was seen in 13 cases (4.8%): [Type I (10 cases) and Type III (three cases)]. There was no Type II MPGN. Twelve patients had membranous nephropathy (MN) which was secondary to Hepatitis B infection in 10 cases (83.3%). Thirteen children had systemic lupus erythematosus (SLE) nephritis of which the commonest histology was Class 1 (36%) followed by Classes II and IV (22% and 21% respectively). Of the 157 children biopsied because of nephrotic syndrome, the commonest histology overall was MesGN 49/157 (31%). The data on nephrotic syndrome are presented separately.

Table 2: Renal histology in Jamaican children

Histology	Number	%
Nonglomerular	10	3.7
Glomerular		
Diffuse proliferative GN	75	27.7
Mesangial proliferative GN	69	25.5
Minimal change disease	36	13.3
Focal sclerosis	23	8.5
Membranoproliferative GN	13	4.8
SLE nephritis	13	4.8
Membranous GN	12	4.4
Normal histology	6	2.2
IgA/ HSP nephropathy	4	1.5
Crescentic GN	4	1.5
Chronic sclerosis	3	1.3
Amyloidosis/ sickle nephropathy	2	0.7
Total	**270**	**100**

Histology in infection: The commonest histology in infection was DPGN seen in 50 /84 (59.5%) cases. In PSGN, DPGN accounted for 74.6% (47/63), followed by MesGN in 11.1% (7/63). Minimal change, focal sclerosis, chronic sclerosis, sickle nephropathy and MPGN1 were also seen. Most patients with Hepatitis B renal disease had membranous nephropathy (83.3%), but MCNS, MPGN III were also noted. One patient with SLE Class IV was also Hepatitis B positive. Histology in 25 cases of AGN of uncertain cause again showed a predominance of DPGN (44% – 11/25) followed by MesGN (36%). Crescentic nephropathy was seen in 2 patients and MPGN I, MPGN III and FSGS in one patient each.

Aetiology of glomerulonephritis: Of the 260 patients with glomerular disease, nephritis was idiopathic in 53% (136 patients). In the remaining 122 children, glomerular disease was associated with infection in 84 (32.4%), sickle haemoglobinopathy in 25 (9.6%) and SLE in 13 (5%). Poststreptococcal glomerulonephritis was the commonest infection-related GN, 75% (63/84) followed by Hepatitis B, 15.4% (13 cases), HTLV 1 (3 cases), CMV and parvovirus infection (2 cases each) and mumps (1 case). Parvovirus testing was only performed in two sicklers whose nephrotic syndrome followed an aplastic crisis. Over the 24-year period of observation, the frequency of PSGN peaked in 1985–1988 and again in 1993–1995 with a corresponding trend in the frequency of DPGN and MesGN (Fig. 1).

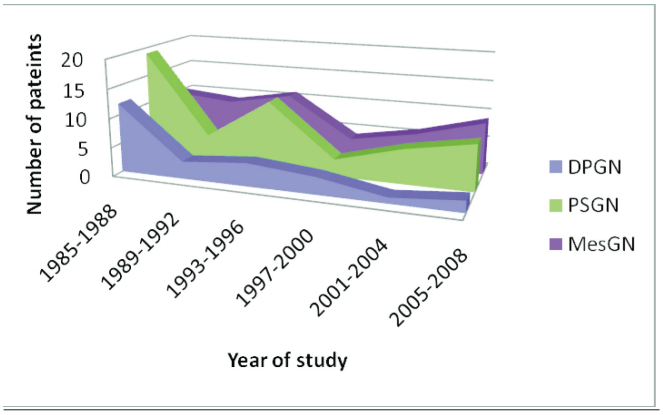

Figure: Changing patterns of childhood glomerular disease with time

DPGN – diffuse proliferative glomerulonephritis; MesGN – mesangial proliferative glomerulonephritis; PSGN – Poststreptococcal glomerulonephritis

Histology in sickle haemoglobinopathy: 25 patients had sickle haemoglobinopathy of whom 19 had homozygous sickle cell (SS) disease, 2 had $S\beta^0$ Thalassaemia and 4 had sickle cell trait (AS). All patients with sickle haemoglobinopathy presented with either atypical glomerulonephritis or nephrotic syndrome. In SS disease, DPGN was the commonest histology seen (47.4%), followed by MPGN 1 (hypocomplementaemic) and MesGN (3 cases each), FSGS and minimal change (2 cases each). There was no statistically significant difference between the frequency of DPGN, PSGN and MesGN in the children with SS disease and the overall study group.

Recurrent gross haematuria: Eleven patients were biopsied because of recurrent unexplained gross haematuria in the absence of clinical features of glomerulonephritis. MesGN was the commonest histology observed (5/11). IgA nephropathy was only confirmed in 2 cases, the remainder were normal (2) or had focal global sclerosis or resolving DPGN (1 each).

DISCUSSION

Meaningful comparison between studies of paediatric renal disease is complicated by differences in the definition of childhood. It was considered less than age 12 years in the present series but up to 19 years in others (7–9). Nephrotic syndrome was the commonest reason for renal biopsy in children from Jamaica as was also observed in Saudi Arabia [77%] (8). Glomerular disease was more frequently an indication for renal biopsy than non-glomerular disease in the present study as it was in Saudi Arabia (8) and Korea (7).

Overall, the most prevalent histology in biopsy specimens was DPGN (27.7%) followed by MesGN (25.5%). This is unusual and the frequency of these histological appearances parallels the overall frequency of PSGN (23.3%). It is known that PSGN follows a path from an acute diffuse proliferative phase to mesangial proliferation and either resolution or focal sclerosis (10). All such patterns were seen in this reported population with DPGN being the commonest histology observed in PSGN (74.6%). It is uncertain how many of those children presenting with MesGN or focal sclerosis may have had previous PSGN, which by the time of referral after a failed course of steroids would have no acute serological parameters for confirmation. DPGN is rarely documented in international paediatric series – 0.6% in Chinese children (9) – and was not mentioned at all in the series from Korea (7).

In the present series, lupus nephritis accounted for only 5.2% of glomerular disease, but in Hong Kong where patients up to age 19 years were included (9), it is the predominant nephritis (23%) followed by MCD (14%) while in Korea (7) MCD is the commonest (24.8%). IgA and Henoch Schonlein Purpura nephropathy are common in Hong Kong (9) and Korea (7) [10–13%] but were confirmed only in 1.5% of Jamaican cases. A contributory factor to this is likely to be the limited availability of immunofluorescence, as children presenting clinically with IgA nephropathy demonstrated, by light microscopy, mesangial changes which could have been compatible with the diagnosis.

Glomerulonephritis was secondary in 47% of children. It was associated with infection in 32.3%, sickle haemoglobinopathy in 9.6%, SLE in 5% and amyloidosis in one case. The commonest infections were streptococcal (75%) and Hepatitis B (15.4%), although other viruses were represented. Infection as a cause of renal disease is more a feature of developing than developed countries – for example in Nigeria (1977–1981) Hepatitis B and malarial nephropathy accounted for about 51% of cases of nephrotic syndrome (11).

The literature on glomerular pathology in sickle cell disease in childhood is sparse. Tejani *et al* (12) and Elfenbein *et al* (13) describe focal sclerosis, diffuse proliferative nephritis, mesangial proliferation and glomerular basement membrane splitting in children with sickle haemoglobinopathy, proteinuria and nephrotic syndrome. In the present series, Jamaican children with sickle haemoglobinopathy had predominantly DPGN and the pattern of glomerular disease in sicklers was similar to that in non-sicklers. We suggest that in Jamaican children less than 12 years old with sickle haemoglobinopathy, glomerular disease is likely secondary to the renal pathology common to the island's population – *ie* either infection mediated or idiopathic rather than due to sickle related pathology. Further study is required.

In summary, in Jamaican children, DPGN is the commonest nephritis and may be largely infection related. Membranous nephropathy is primarily due to Hepatitis B. IgA nephropathy is seen and may be under-diagnosed. The commonest histology in SS disease is DPGN. The role of infection in the pathogenesis of renal disease in Jamaican children is probably underestimated.

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