ORIGINAL ARTICLE

Port J Nephrol Hypert 2010; 24(3): 215-221
Advance Access publication 24 March 2010

Renal biopsies in children. A twelve-year review

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Received for publication: 10/11/2009
Accepted in revised form: 27/01/2010

ABSTRACT

Introduction: Renal biopsy is a well-established method for the diagnostic management of children with renal disease. While data describing the spectrum of renal disease in Portuguese children are scarce, it is known there are important differences in the relative frequencies of specific renal pathological conditions in children and adults. The aim of this study was to review all the cases that underwent renal biopsy in a paediatric hospital from 1997 to 2008 and to report the relative frequency of nephropathies according to clinical presentation, based on histological diagnoses.

Patients and Methods: Records of renal biopsies performed on children at our institution from 1st January 1997 to 31st December 2008 were retrospectively examined. The total set of renal biopsies under study was divided into three different time periods (A, B and C) and the indications for renal biopsy were categorised into five clinical syndromes.

Results: 142 renal biopsies were performed during the study period. The median patient age was 10 years old. The main reasons for biopsy were nephrotic syndrome (46%) and urinary abnormalities (35%). Primary glomerulonephritis accounted for sixty-two percent of the biopsies performed. The most prevalent secondary glomerulonephritis was lupus nephropathy (43%).

Overall, the three most common renal diseases were IgA nephropathy (15.7%), mesangioproliferative non-IgA nephropathy with IgM deposits (11.9%) and lupus nephropathy (11.2%). Over the years the frequency of each disorder remained stable, although in the latter period we noted a relative increase of mesangioproliferative non-IgA nephropathy with IgM deposit.

Discussion: Renal biopsy in children is a safe method, with a low frequency of complications. The commonest indication for renal biopsy was nephrotic syndrome, as in other series. This study also revealed the predominance of IgA nephropathy as the most common type of renal disease, which is in agreement with earlier reports.

Key-Words:
Children; glomerulopathy; renal biopsy.

INTRODUCTION

Renal biopsy is a well-established method for the diagnostic management of children with renal disease. It can provide diagnostic precision, especially in glomerular diseases, and also important information of prognostic value and for treatment options. The introduction of automated biopsy devices and ultrasound location of the kidney were aimed at optimising the efficacy and safety of the percutaneous renal biopsy procedure, and nowadays it appears to be a safe method, with a low frequency (<1%) of serious complications[1-3]. Although

the majority of entities seen in the adult population can be observed in the paediatric population there can be important differences in the relative frequencies of specific renal pathological conditions in children. Analyses of various registries indicate that the epidemiology and spectrum of renal diseases in the paediatric age group differ from one geographic location to another[3-5].

Several studies have reported on the relative distribution of various diagnostic categories in large series of paediatric renal biopsies. As they all differ in the protocol and indications for biopsy across centres or countries, the results may not be directly comparable, but they do provide an overview of the most commonly encountered entities[3]. Data describing the spectrum of renal disease in Portuguese children are scarce. Analysis of kidney biopsies performed in one single centre can, however, provide some insight into the frequencies and most significant types of glomerulonephritis encountered in the Portuguese paediatric population.

The aim of this study was to review all the cases that underwent renal biopsy in a paediatric hospital from 1997 to 2008 and to report the relative frequency of nephropathies according to clinical presentation, based on histological diagnoses.

PATIENTS AND METHODS

Records of renal biopsies performed on children (≤18 years old) at our institution from 1st January 1997 to 31st December 2008 (12 years) were retrospectively examined. We considered all biopsies performed in native kidneys.

In order to disclose any bleeding diathesis, blood samples were drawn for determination of the haemoglobin level, platelet count, prothrombin level and partial thromboplastin time prior to biopsy. The procedure was conducted using an automated technique, and only one type of needle was used (Bardbiopsygun®). Continuous ultrasonographic guidance was used with the children under sedation or short-acting general anaesthesia. Postbiopsy observations of the patients included bed rest for 24 hrs and regular checking of blood pressure and pulse rate.

We recorded the following data from each patient: age, gender, indication for renal biopsy (clinical syndrome) and histological diagnosis. Renal biopsy specimens were stained and analysed by light microscopy and almost all were analysed by immunofluorescence. Electron microscopy was not systematically used; only 17% renal biopsy specimens were analysed using this method.

Published biopsy series have shown temporal variations in the patterns of glomerulonephritis (GN) over the years. Based on that, the total set of renal biopsies under study was divided into three 4-year time periods: Period A, 1997-2000; Period B, 2001-2004 and Period C, 2005-2008 and trends in the diagnosis of glomerular disease were considered.

The indications for renal biopsy were categorised into five clinical syndromes[4,7,10]: nephrotic syndrome (NS) was considered as proteinuria greater than 50 mg/kg/day and serum albumin <2.5 g/dl; acute nephritic syndrome (ANS) was defined as haematuria, hypertension (TA≥P95 for age), oliguria, oedema and reduced glomerular filtration rate; acute renal failure (ARF) was defined as a sudden and rapid deterioration of renal function; chronic renal failure (CRF) was considered when persistent creatinine clearance was less than 75 ml/min/1.73 m^2 and urinary abnormalities (UA) was defined as persistent nonnephrotic proteinuria with or without microscopic haematuria.

The global evaluation of each patient (integrating clinical, pathological and laboratory data) allowed a classification of renal diseases into three categories[4,7]: primary glomerulonephritis (PGN), when the disease primary involved the kidney; secondary glomerulonephritis (SGN), as part of systemic disorders and vascular/tubulointerstitial diseases (VTD). The remaining causes were classified as "others" (sclerotic kidney, "difficult classification biopsy" and "failed biopsy"). Primary glomerulonephritis encompassed eleven pathologies: minimal change disease (MCD); IgA nephropathy (IgAN); mesangioproliferative nephropathy with IgM deposits (MesGN-IgM); mesangioproliferative non-IgA nephropathy (MesGN-nonIgA); focal segmental glomerulosclerosis (FSGS); proliferative diffuse acute endocapillary glomerulonephritis (PEGN); thin membrane disease (TMD); membranous glomerulonephritis (MGN); membranoproliferative glomerulonephritis (MPGN); diffuse

mesangial sclerosis (DMS) and crescentic glomerulonephritis (CGN). Lupus nephritis (LN), Henoch-Schonlein purpura (HSP), Alport syndrome (AS), haemolytic-uraemic syndrome (HUS) and Finnish nephrotic syndrome (FNS) were considered as secondary glomerulonephritis. Vascular/tubulointerstitial diseases included acute interstitial nephritis (AIN) and acute tubular necrosis (ATN).

RESULTS

We analysed records from 142 consecutive native renal biopsies (RB) performed during the study period. Eight cases were excluded for lack of data and only included in the demographic analysis of the sample.

When analysing gender distribution there was a slight predominance of females in the total number of cases (56%). Primary glomerulonephritis were more frequent in males (51.2%) while secondary glomerulonephritis were more frequent in females (68.6%).

The age at which renal biopsy was performed ranged from 1 month to 18 years, with a median of 10 years. The most represented age group was that of children aged between 7 and 11 years old (41.5%). Three cases (2%) had less than 12 months old.

The distribution of renal biopsies performed each year is illustrated in Fig. 1. There was a gradual decrease in the number of biopsies performed between 2000 and 2006 and an increase in the last two years.

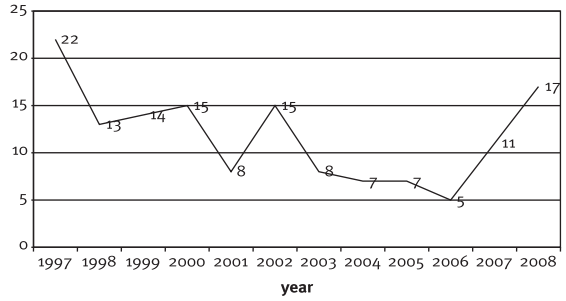


Figure 1

Number of cases of renal biopsy performed each year (n: 142)

The main reasons for performing a renal biopsy were grouped by clinical syndromes and are shown in Fig. 2. Overall, over 12 years, nephrotic syndrome was the most common clinical indication, comprising 46% of cases, followed by urinary abnormalities with 35% of cases. Acute nephritic syndrome accounted for 10% of biopsies and acute renal failure 8% of cases. Only two children (1% of the sample) had chronic renal failure. Analysing the data by the three different periods under study (Fig. 2), we found that although in period A urinary abnormalities were slightly prevalent (44% of cases), in the last two periods (B and C) the predominance of nephrotic syndrome was stable; 49% and 52% of cases, respectively. Note also an increase in the proportion of acute renal failure cases in period C; 12.5%, as compared with 7% and 5% in periods A and B.

Globally, primary glomerulonephritis was predominant and accounted for 62.7% of the renal biopsies performed, 26.1% cases were secondary glomerulonephritis and 1.5% vascular/tubulointerstitial disease. This predominance of primary glomerulonephritis prevailed when we analyse data by different time intervals (Table I).

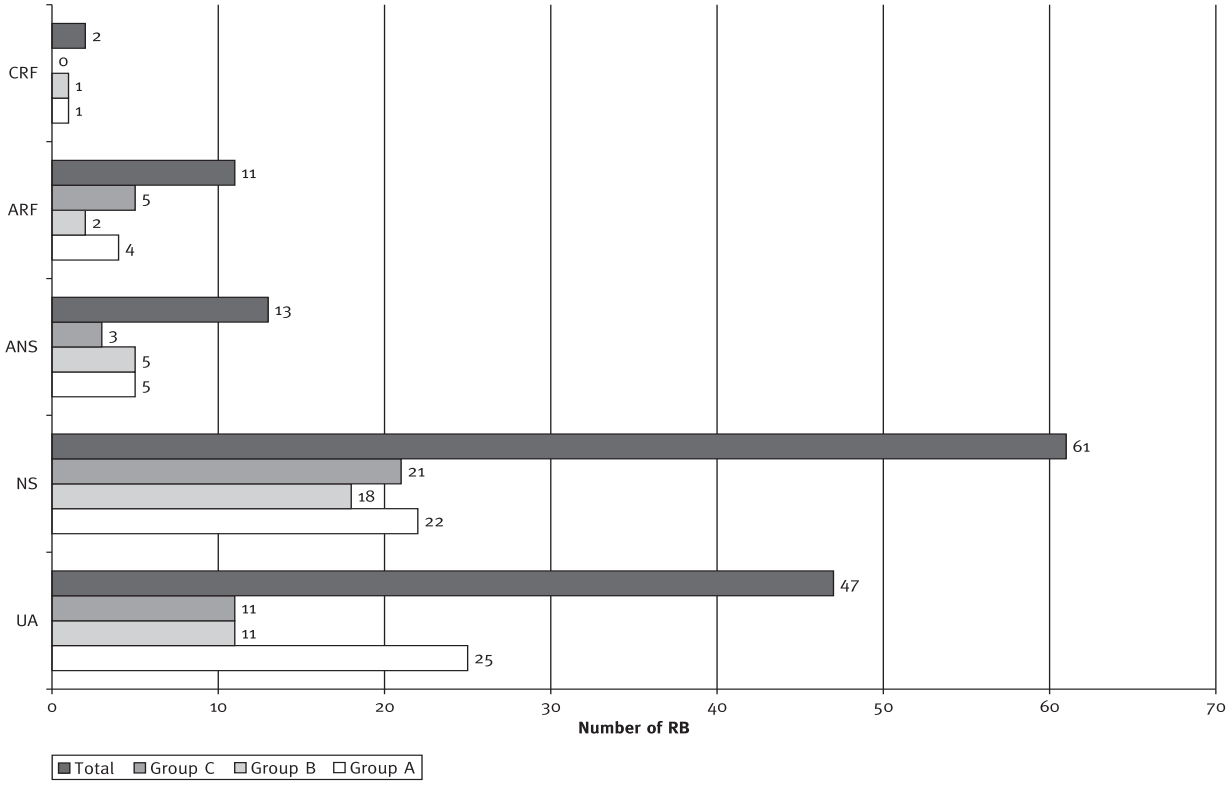
Among primary glomerulonephritis, IgAN was the more frequent pathology, representing 25% of cases, followed by MesGN-IgM (19%) and MCD (14%). IgAN remained the main primary glomerulonephritis in groups A and B, but in Group C was exceeded by MesGN-IgM (6 cases *vs.* 5 cases). The most prevalent disease in secondary glomerulonephritis was LN (43%), followed by AS (31%) and HSP (17%).

Analysing the results of biopsies by clinical syndrome (Table II) we found that in patients with

Table I

Distribution of renal biopsies by most important categories (Primary glomerulonephritis-PGN, Secondary glomerulonephritis-SGN, Vascular/tubulointerstitial diseases-VTD, others) according to time period

	PGN	SGN	VTD	Others
Period A (1997-2000)	35 (61.4%)	15 (26.3%)	0	7 (12.3%)
Period B (2001-2004)	22 (59.5%)	11 (29.7%)	0	4 (10.8%)
Period C (2005-2008)	27 (69.2%)	9 (23.1%)	2 (5.1%)	1 (2.6%)
Total (1997-2008)	84 (62.7%)	35 (26.1%)	2 (1.5%)	13 (9.7%)



UA: urinary abnormalities; NS: nephrotic syndrome; ANS: acute nephritic syndrome; ARF: acute renal failure; CRF: chronic renal failure.

Figure 2

Renal syndromes as indication for renal biopsy (n: 134)

Table II

Frequency of most common renal pathology in children with Urinary Abnormalities (UA), Nephrotic Syndrome (NS), and Acute Nephritic Syndrome

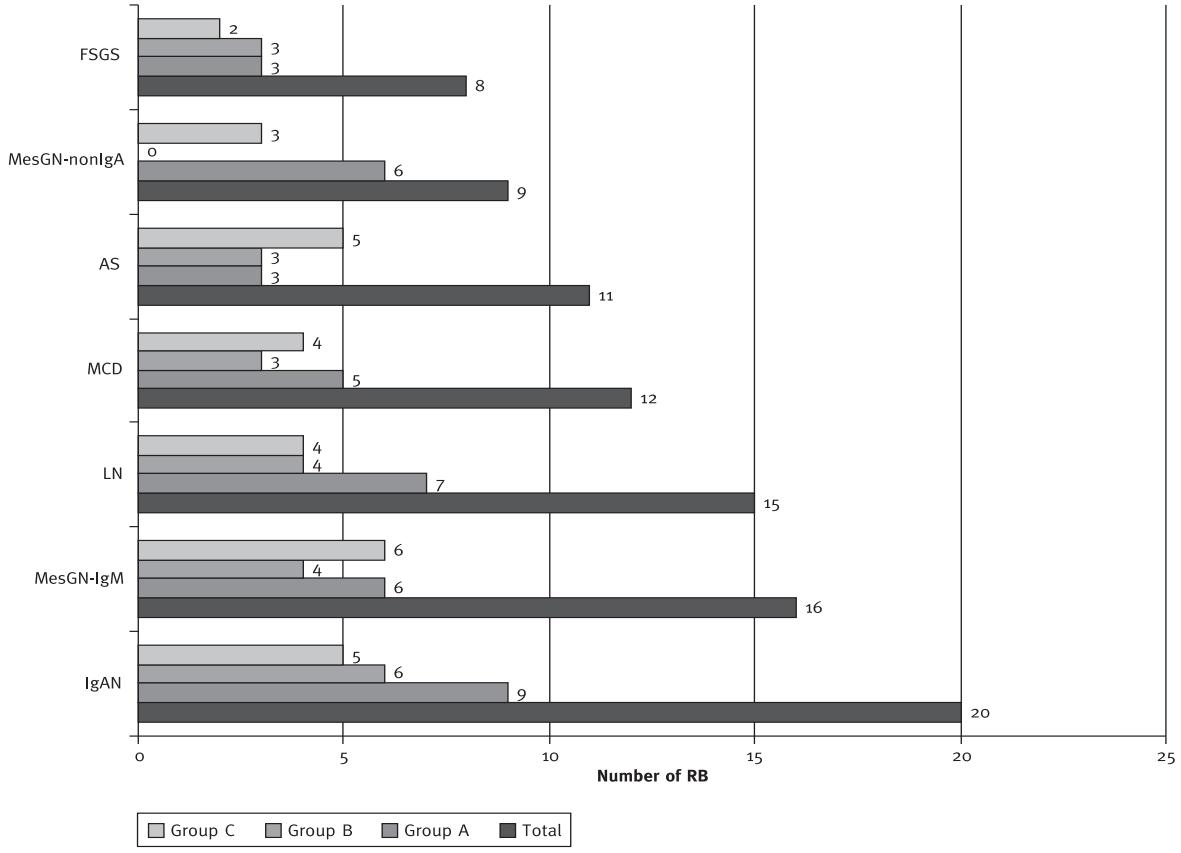
Pathology	UA	NS	ANS	ARF
IgAN	14 (30%)	4 (6.6%)	2 (15.4%)	1 (9%)
MesGN-IgM	–	15 (24.5%)	–	–
MCD	–	12 (19.7%)	–	–
FSGS	2 (4.2%)	6 (9.8%)	–	–
PEGN	–	–	3 (23%)	–
TMD	4 (8.5%)	–	–	–
AS	6 (12.8%)	4 (6.6%)	1 (7.7%)	–
LN	5 (10.6%)	5 (8.2%)	5 (38.5%)	–
HSP	3 (6.4%)	2 (3.2%)	1 (7.7%)	–
CGN	–	–	1 (7.7%)	5 (45.5%)
ATN	–	–	–	1 (9%)

IgAN: IgA nephropathy; MesGN-IgM: mesangioproliferative non-IgA nephropathy with IgM deposits; LN: lupus nephritis; MCD: minimal change disease; AS: Alport syndrome; MesGN-nonIgA: mesangioproliferative non-IgA nephropathy non-classified; FSGS: focal segmental glomerulosclerosis; TMD: thin membrane disease; HSP: Henoch-Schonlein púrpura; CGN: crescentic glomerulonephritis; PEGN: proliferative diffuse acute endocapillary glomerulonephritis

nephrotic syndrome the most frequent glomerulopathy was MesGN-IgM, accounting for 24.5% of cases, followed by MCD (19.7%) and FSGS (9.8%). In the two children presenting with NS in the first year of life we found Finnish-type congenital NS on RB.

In patients with urinary abnormalities, the most frequent pathology was IgAN (30%), followed by AS in 12.8% and LN in 10.6%. In acute nephritic syndrome, LN was found in 38.5% of cases, followed by PEGN in 23% and IgAN in 15.4%. In acute renal failure, 45.5% of cases corresponded to CGN, and the remaining corresponded to one MPGN, IgAN, AIN, ATN, HUS and SK. The two cases of chronic renal failure derived from a DMS and a case of MesGN-IgM.

Overall, the three most common renal diseases were IgAN (15.7%), IgM MesGN (11.9%) and LN



IgAN: IgA nephropathy; MesGN-IgM: mesangioproliferative non-IgA nephropathy with IgM deposits; LN: lupus nephritis; MCD: minimal change disease; AS: Alport syndrome; MesGN-nonIgA: mesangioproliferative non-IgA nephropathy non-classified; FSGS: focal segmental glomerulosclerosis

Figure 3

Most frequent renal pathology in the 12 year period and by group (n: 134)

(11.2%) (Fig. 3). Over the years the frequency of each disorder has remained stable, although in the later period a relative increase of MesGN-IgM was noted, which became the most frequent pathology, overtaking IgAN.

DISCUSSION

Renal biopsy is an important technique used in nephrology to clarify the clinical diagnosis, management, and monitoring of many kidney diseases. Although it is generally considered to be more difficult in children than in adults due to the smaller size of the kidney and unwillingness of the patients to co-operate, it is currently considered a routine safe procedure in children.

Several studies have reported on the relative distributions of various diagnostic categories in series of paediatric renal biopsies. As there may be differences in the indication for biopsy across centres, the results may not be directly comparable. Worldwide the most common indication for renal biopsy in childhood is nephrotic syndrome, but in some countries, such as Italy, the most frequent reason is urinary abnormalities (microscopic haematuria and non nephrotic proteinuria)[3-9]. In general, IgA nephropathy is the most common glomerular disease in most of the series, followed by minimal change disease and Henoch-

Schonlein nephritis[3-9]. In addition, it has been reported that the frequency of focal segmental glomerulosclerosis is increasing[3,5,6], although it remains uncertain whether this represents a true increase in prevalence or is simply a consequence of changing indications for biopsy.

Our results provide some insight into the frequency of biopsy-proven renal disease in the paediatric age group in the north of Portugal. We observed a slight predominance of females; 56% of cases. The higher relative frequency of secondary glomerulonephritis in females may be explained by the fact that systemic lupus erythematosus was the most common secondary glomerulonephritis and it occurs more frequently in women.

The commonest indication for renal biopsy was nephrotic syndrome, accounting for about half of the cases, in accordance with other studies[3,6,7,10] followed by urinary abnormalities. In a series of adult patients from the north of Portugal a predominance of nephrotic syndrome as indication for renal biopsy was found[3]. Similarly to other reports primary glomerulonephritis accounted for 62.7% of all biopsies performed, followed by secondary glomerulonephritis. This study also revealed the predominance of IgA nephropathy as the most common type of primary glomerular disease, which is in agreement with previous reports from Italy[4], Spain[11] and Japan[12].

When taking into consideration nephrotic syndrome, the most prevailing indication for renal biopsy in our population, MesGN-IgM was the most common glomerulopathy, followed by MCD, with FSGE representing only a small proportion of nephrotic syndrome cases.

Although MCD is by far the most common cause of idiopathic nephrotic syndrome in the paediatric population, in our study MCD was not the most frequent histological pattern in children with NS; MesGN-IgM was. This is probably as cases of NS that go under biopsy are selected and most of the children with NS due to MCD do not present any criteria for undergoing a renal biopsy.

In most centres, empiric steroid therapy is given in patients with a high probability of having MCD without confirmation of the diagnostic by renal biopsy. It is consensual not to perform renal biopsy in children with a recent diagnosis of nephrotic syndrome who meet all the following criteria: age between 1 and 10 years old; children without the following findings: arterial hypertension, gross haematuria, and/or a marked elevation in serum creatinine; normal complement levels, and no extrarenal symptoms or signs suggestive of secondary glomerular disease. Accordingly, we only perform renal biopsy in children with nephrotic syndrome that are not included in the group suggestive of MCD, in steroid-resistant NS and in frequently relapsing or steroid dependent NS before beginning other therapies such as calcineurin-inhibitors or mycophenolate mofetil or rituximab. This could explain why in our study MCD is not the most common cause of nephrotic syndrome.

In fact, MesGN-IgM was a pathology with rising prevalence in this study. We did not find an increase in FSGE during the periods analysed. However, we cannot rule out that the true incidence of FSGS may have been underestimated in that FSGS can be missed on renal biopsy due to sampling error, since, by definition, the disease is focal.

In conclusion, we showed that primary and secondary glomerulonephritis have a similar incidence and a similar distribution by major histological groups as in other European countries.

This study was important to our institution not only for providing us with detailed information about glomerulonephritis in our paediatric population but also for assuring us that we are using correct criteria for selecting cases for biopsy. We think that, in the future, genetic analysis of podocyte-specific genes should be more commonly offered as a diagnostic and prognostic aid in patients presenting with nephrotic syndrome especially concerning the likelihood of corticosteroid sensitivity, and this will decrease the need for renal biopsy in some patients.

This study may represent significant data in the understanding of paediatric kidney disease in Portuguese children.

Conflict of interest statement. None declared.

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