Paulista registry of glomerulonephritis: 5-year data report

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Abstract

Background. The Paulista Registry of Glomerulopathies was created in May 1999 and comprises several centres of São Paulo, the most populous Brazilian State, that concentrates people from all regions of the country who look for health care.

Methods. This report includes data from 2086 patients from Brazil submitted to renal biopsy due to the presumed diagnosis of glomerular diseases, registered prospectively since May 1999 until January 2005. Data were collected by the integrants of the 11 centres involved, utilizing a standardized questionnaire.

Results. The mean age of the patients was 34.5 ± 14.6 years. Primary glomerular diseases were more frequent in males (55.1%) than in females; on the other hand, secondary glomerular diseases were more frequent in females (71.8%). The most common clinical presentation was nephrotic syndrome and the frequency of hypertension, at this time, was 55.5%. There was a predominance of indication of biopsies in the third, fourth and fifth decades of life. The most common primary glomerular diseases were focal and segmental glomerulosclerosis (29.7%), followed by membranous nephropathy (20.7%), IgA nephropathy (17.8%), minimal change disease (9.1%), membranoproliferative glomerulonephritis (7%), crescentic glomerulonephritis (4.1%), advanced chronic glomerulopathy (4%), non-IgA mesangial glomerulonephritis (3.8%), diffuse proliferative glomerulonephritis (2.5%), focal segmental proliferative glomerulonephritis (1%) and others (0.3%). The most frequent secondary glomerular disease was lupus nephritis, corresponding to 66.2% of the cases, followed by post-infectious glomerulonephritis (12.5%), diabetic nephropathy (6.2%), diseases associated to paraproteinaemia (4.9%), hereditary diseases (4.6%), vasculitis (3.2%), malignancies (0.9%), secondary focal segmental glomerulosclerosis (0.6%) and others (0.9%).

Conclusion. Focal segmental glomerulosclerosis was the most frequent primary glomerular disease, followed by membranous nephropathy and IgA nephropathy. Lupus nephritis predominated over all the other secondary glomerular diseases.

Keywords: Brazilian registry; epidemiology; glomerulopathy

Introduction

The study of the epidemiological aspects of glomerular diseases, both primary and secondary, has been greatly facilitated by the development of registries of these diseases in several countries. This kind of information may help to identify the frequency of glomerulopathies and their causes, the presenting symptoms, the potential regional difficulties for establishing a diagnosis, the usual local biopsy indications and other relevant clinical, laboratorial and histological features.

As far as we know, this is the first reported Brazilian multicentre registry of glomerulopathies. The collection of data was initiated in May of 1999 and involves 11 public and private centres of São Paulo, which is the...
most populous State of Brazil, situated in the southeast and which concentrates people from all regions of the country looking for health care (Figure 1). The renal biopsies were analysed by renal pathologists whose expertise in the area was recognized by the integrants of all participant centres, and this condition was considered as essential for the inclusion of the centres in the Paulista Registry of Glomerulopathies group.

Methods

This report includes data from 2086 patients from Brazil submitted to renal biopsy due to the presumed diagnosis of glomerular diseases, registered prospectively since May 1999 until January 2005. Data were collected by the integrants of the 11 centres involved utilizing a standard form, which included relevant details of light, immunofluorescence and electron microscopy, demographic information, presenting syndrome, frequency of hypertension and familial history of glomerulopathy, associated diseases, results of laboratory examinations that confirmed the diagnosis of glomerular diseases and presenting syndromes, as well as diagnostic tests for common diseases aetiologically related to glomerulopathies (i.e. blood tests for the determination of anti-nuclear antibodies, anti-HIV, anti-HCV and HBsAg, ANCA, cryoglobulins and others). Glomerular disease was defined as primary when the signs and symptoms were exclusively related to the kidney and the consequences of its disorder [1] and as secondary in the other cases.

Statistics

Descriptive statistics were used to present the distribution of the histological types of glomerulopathies, and the relative frequencies of the clinical findings were calculated for the whole group, and means ± SD are presented.

Results

During the period of May 1999 to January 2005, data were collected from 2086 patients, but only in 1844 cases did the available data point to the diagnosis of glomerulopathies.

Of all diseases, primary glomerulopathies were the most frequent (54.2%), followed by secondary glomerulopathies (34.2%), tubulointerstitial nephropathies (acute tubular necrosis and acute tubulointerstitial nephritis) (2.3%), vascular nephropathies (cortical necrosis, benign nephroangiosclerosis and malignant nephroangiosclerosis) (4%) and miscellaneous/unclassifiable (5.3%). The following analysis is exclusively based on the 1844 cases of glomerulopathies.

The mean age of the patients was 34.5 ± 14.6 years.

The population was mixed: 66.6% of the patients were

### Participating Centres

<table>
<thead>
<tr>
<th>Participating Centres</th>
<th>Renal Biopsies (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Faculdade de Ciências Médicas da Santa Casa de São Paulo</td>
<td>9.0</td>
</tr>
<tr>
<td>2. Faculdade de Medicina do ABC</td>
<td>2.7</td>
</tr>
<tr>
<td>3. Hospital da Beneficência Portuguesa de São Paulo</td>
<td>1.6</td>
</tr>
<tr>
<td>4. Pontificia Universidade Católica de São Paulo- Sorocaba</td>
<td>4.1</td>
</tr>
<tr>
<td>5. Universidade Estadual de Campinas</td>
<td>13.4</td>
</tr>
<tr>
<td>6. Universidade Estadual Paulista-Butocatu</td>
<td>5.0</td>
</tr>
<tr>
<td>7. Universidade Federal de São Paulo</td>
<td>13.9</td>
</tr>
<tr>
<td>8. Universidade do Oeste Paulista-UNOESTE</td>
<td>1.6</td>
</tr>
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<td>9. Universidade de São Paulo-Ribeirão Preto</td>
<td>10.6</td>
</tr>
<tr>
<td>10. Universidade de São Paulo-SP</td>
<td>36.7</td>
</tr>
<tr>
<td>11. Universidade de São Paulo-Hospital Universitário</td>
<td>1.4</td>
</tr>
</tbody>
</table>

Fig. 1. Distribution of the participating centres and individual contributions to the registry.
Caucasians, 10.6% of African and 2.2% of Asiatic origin; 20.6% corresponded to the combination of individuals of Caucasian and African origin. Systemic hypertension was present in 55.5% of the patients at presentation.

The distribution of renal biopsies by age can be seen in Figure 2. There was a predominance of indication of biopsies in the third, fourth and fifth decades of life, and the relative frequencies of indication were 27.5, 22.7 and 16.7%, respectively.

The period of time since the symptoms started until the renal biopsy was performed corresponded to <6 months in 44.5% of the cases, 6–12 months in 22.3% and more than 12 months in 33.2% of the cases.

The most common indication for a biopsy was the nephrotic syndrome followed by asymptomatic haematuria and/or proteinuria, chronic renal failure associated nephrotic/nephritic syndrome, rapidly progressive glomerulonephritis, nephritic syndrome, acute renal failure and macroscopic haematuria, as can be seen in Figure 3. It is worth noting that some patients presented more than one indication for biopsy, and this explains the frequencies shown in this figure.
Primary glomerular diseases were more frequent in males (55.1%) than in females (44.9%); on the other hand, secondary glomerular diseases were more frequent in females (71.8%).

Primary glomerular diseases corresponded to: focal and segmental glomerulosclerosis, membranous nephropathy, IgA nephropathy, minimal change disease, membranoproliferative glomerulonephritis, crescentic glomerulonephritis, advanced chronic glomerulopathy, non-IgA mesangial glomerulonephritis, diffuse proliferative glomerulonephritis, focal segmental proliferative glomerulonephritis and others, as can be seen in Figure 4.

Of all patients with secondary glomerular diseases, the majority of the cases corresponded to systemic lupus erythematosus, and the remainder were classified as post-infectious glomerulonephritis, diabetic nephropathy diseases associated to paraproteinaemia, hereditary diseases, vasculitis, malignancies, secondary focal segmental glomerulosclerosis and others, as shown in Figure 5. Overall, the more frequent glomerulopathies were lupus nephritis followed by focal and segmental glomerulosclerosis.

Of the primary and secondary glomerular diseases when considered altogether, the more frequent glomerulopathies were lupus nephritis followed by focal and segmental glomerulosclerosis.

Discussion

The Paulista Registry of Glomerulopathies has obtained data from 1844 patients with glomerulopathies submitted to renal biopsies between 1999 and 2005. The main objectives of the registry were, based on histopathological findings, to establish the frequency of the glomerulopathies in our country, the period of time until definite diagnosis, their most common causes, as well as the most frequent clinical and laboratory presentation. Biopsies of kidney grafts were not included. Data of all the patients with histopathological evidence of glomerulopathy seen at the 11 participating centres were collected on standard forms and stored in a computer program for further analysis.

There is no overall registry in Brazil at the moment, nor are there regional registries. It is noteworthy that São Paulo is the most populous Brazilian State and concentrates people from all regions of the country who look for health care. But, we cannot say that this

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Fig. 4. Frequency of different forms of primary glomerulopathies (n = 1131); see abbreviations (Appendix I).
sample of patients is actually representative of the nationwide frequency of glomerulopathies in the country.

We observed that there is still a considerable delay between the appearance of symptoms and the biopsy among our subjects, as 55.5% of the patients were submitted to renal biopsy after 6 months of the first evidence of renal disease, with likely bad prognostic consequences [2]. This finding is possibly related to insufficient knowledge about renal disease by the population and inappropriate basic health care structure in our country.

The ideal renal biopsy should be processed for light, immunofluorescence and electron microscopy, but in many regions of Brazil, as well as in many developing countries, an adequate structure for biopsy evaluation is not available. So our study is based predominantly on the findings of light and immunofluorescence microscopy analysed by experienced renal pathologists. In some of our nephrology services, specimens for electron microscopy are stored and utilized when these two techniques are not able to establish a diagnosis.

The frequencies of glomerulopathies according to sex are similar to those seen in other studies when primary and secondary glomerular diseases are considered separately [3].

In the evaluation of race, there was a predominance of Caucasians, as they corresponded to 66.6% of the cases. But, it is worth noting that it is very difficult to determine the race of individuals in Brazil, because the majority of the population is constituted by a mixed race [4,5]. The evaluation of racial characteristics of ancestry would be necessary to establish more precisely the race of each patient, because physical appearance is a poor predictor of genomic African ancestry, as estimated by molecular markers in the Brazilian population [6].

In our registry as in others [7,8], nephrotic syndrome, followed by asymptomatic haematuria and/or proteinuria, was the most common indication for renal biopsy. The predominance of nephrotic syndrome in an adult population submitted to renal biopsy is expected, as this biopsy indication is not an object of controversy in adult patients [9]. When the presenting manifestation of glomerular disease was

Fig. 5. Frequency of different forms of secondary glomerulopathies (n = 713); see abbreviations (Appendix I).
evaluated in a tertiary health care service of São Paulo (Brazil) over the years, it was shown that the frequency of nephrotic syndrome has been increasing recently [5]. In European studies, the frequency of nephrotic syndrome among patients submitted to renal biopsy has ranged from 17 to 36.6% [9–11], and reports from Singapore and Japan have shown frequencies of 34 and 49.5%, respectively [12,13].

We found 54.2% of primary glomerulopathies in the evaluated population. Recent studies show that primary glomerular diseases are responsible for 59.8–70.8% of the causes of glomerulopathies, as can be seen in Table 1.

The Glomerulonephritis Registry of the Spanish Society of Nephrology (involving data from 7016 patients with biopsied renal diseases between 1994 and 1999) revealed nephrotic syndrome as the most common clinical syndrome at any age, and the most common glomerular diseases were IgA nephropathy, focal and segmental glomerulosclerosis and membranous nephropathy [9]; the same profile of primary glomerular diseases was observed in the Czech Republic and Romania [8,14]. In China and Italy, IgA nephropathy was the most common, followed by membranous nephropathy and focal and segmental glomerulosclerosis, respectively, as can be seen in Table 2 [3,15]. A possible explanation for the difference between these studies and ours is the periods of time evaluated (only applicable to part of the surveys), as more recently the frequency of focal and segmental glomerulosclerosis is seen to be increasing all over the world [16,17] and also in Brazil [5]. In addition, the presumed regional differences of the prevalence of IgA nephropathy, as being the most common biopsied glomerulopathy [10,18] occurs in some places, while not in others [19].

In fact, in the afore-cited registries as in our own, the three glomerulopathies that predominated were the same, but in a different sequence; focal and segmental glomerulosclerosis was the most frequent primary glomerular disease in our study, followed by membranous nephropathy and IgA nephropathy.

Lupus nephritis predominated over all the other secondary glomerular diseases. The elevated prevalence of systemic lupus erythematosus as a cause of secondary nephritis has been observed in several studies [3,7–9,14,15,18].

Some glomerular diseases predominate in underdeveloped or developing countries, as ours, and knowing their epidemiology can lead us to focus research efforts on such glomerulopathies. Some of them are disappearing in developed countries, although still relatively common in our own, such as membranoproliferative glomerulonephritis [10,20–24].

This study is a contribution to the understanding of the epidemiology of glomerular diseases in Brazil, with possible implications on the planning of transplantation, dialysis and health politics, as glomerulopathies are among the main causes of end-stage renal failure [25,26], and until recently were the most frequent cause of renal failure in Brazil [27] and the whole of Latin America [4]. This information could also result in benefits in patient care.

### Table 1. Distribution of the major histological groups of renal disease in different countries

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<td>Primary GD</td>
<td>54.2</td>
<td>70.8</td>
<td>66.2</td>
<td>59.8</td>
<td>68.6</td>
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<tr>
<td>Secondary GD</td>
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<td>23.7</td>
<td>26.4</td>
<td>25.4</td>
<td>24.8</td>
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<tr>
<td>TIN</td>
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<td>2.3</td>
<td>1.5</td>
<td>4.4</td>
<td>3.4</td>
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<tr>
<td>VN</td>
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<td>3.4</td>
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<tr>
<td>Miscellaneous/unclassifiable</td>
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<td>–</td>
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</table>

Refer abbreviations (Appendix I).

### Table 2. Frequency of several forms of primary glomerular diseases in different countries

<table>
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<td>FSGS</td>
<td>29.7</td>
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<td>10.8</td>
<td>6.0</td>
</tr>
<tr>
<td>MGN</td>
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<td>23.4</td>
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<td>IgAN</td>
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<td>43.5</td>
<td>28.9</td>
<td>34.5</td>
<td>45.3</td>
</tr>
<tr>
<td>MCD</td>
<td>9.1</td>
<td>9.2</td>
<td>8.5</td>
<td>12.5</td>
<td>0.9</td>
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<tr>
<td>MPGN</td>
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<td>6.6</td>
<td>29.4</td>
<td>4.6</td>
<td>3.4</td>
</tr>
<tr>
<td>CrescGN</td>
<td>4.1</td>
<td>2.3</td>
<td>7.9</td>
<td>3.2</td>
<td>1.9</td>
</tr>
<tr>
<td>Non-IgAN mes GN</td>
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<td>–</td>
<td>–</td>
<td>11.3</td>
<td>25.6</td>
</tr>
<tr>
<td>Other/unclassifiable</td>
<td>7.8</td>
<td>1.9</td>
<td>2.5</td>
<td>13.8</td>
<td>7.0</td>
</tr>
</tbody>
</table>

Refer abbreviations (Appendix I).
Acknowledgements. The authors would like to thank the renal pathologists who made this study possible: Marcello F. Franco, PhD; Luiz Antônio Moura, PhD; Denise Malheiro, PhD; Luiz Baltazar Saldanha, PhD; Dino Martini Filho, PhD; Roberto Silva Costa, PhD; Rosa Marlene Viero, PhD; Athanase Billis, PhD; Maria Alice Sperito Ferreira Baptista, PhD.

Conflict of interest statement. None declared.

References


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Appendix I

Abbreviations

Hemat = macrohaematuria
Hemat/prot = asymptomatic haematuria and/or proteinuria
INS = nephritic syndrome
NS = nephrotic syndrome
ARF = acute renal failure
CRF = chronic renal failure
RPGN = rapidly progressive glomerulonephritis
NS+INS = nephrotic syndrome + nephritic syndrome
FSGS = focal and segmental glomerulosclerosis
MN = membranous nephropathy
IgAN = IgA nephropathy
MCD = minimal change disease
MPGN = membranoproliferative glomerulonephritis
ACN = advanced chronic nephropathy
CrescGN = crescentic glomerulonephritis
Non-IgA mesGN = non-IgA mesangial glomerulonephritis
ADGN = acute diffuse glomerulonephritis
DPGN = diffuse proliferative glomerulonephritis
FSGN = focal segmental proliferative glomerulonephritis
LN = lupus nephropathy
Infectious GN = infectious glomerulonephritis
Secondary FSGS = secondary focal and segmental glomerulosclerosis
TIN = tufulointerstitial nephropathy
VN = vascular nephropathy
GN = glomerulonephritis
Primary GD = primary glomerular disease
Secondary GD = secondary glomerular disease
Appendix II

Paulista Registry of Glomerulopathies Group

Participating centres and their coordinators

Faculdade de Ciências Médicas da Santa Casa de São Paulo (YAS Sens)
Faculdade de Medicina do ABC (RR Bergamo)
Hospital da Beneficência Portuguesa de São Paulo (JE Romão Jr.)
Pontifícia Universidade Católica de São Paulo-Sorocaba (RAM Cadaval)

Universidade Estadual de Campinas (MAR Alves)
Universidade Estadual Paulista-Botucatu (MF Carvalho)
Universidade Federal de São Paulo (G Mastroianni-Kirsztajn)
Universidade do Oeste Paulista-UNOESTE (GN Betônico)
Universidade de São Paulo-Ribeirão Preto (OM Vieira Neto)
Universidade de São Paulo-SP (RT Barros e V Woronik)
Universidade de São Paulo-Hospital Universitário (MSM Marrocos)