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Editorial Comments

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Worldwide distribution of glomerular diseases: the role of renal biopsy registries

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Many published papers describe the frequency of histological findings from different biopsy databases all over the world. Ranging in number from hundreds to thousands, these collections sometimes report not only the frequency of the disease but the clinical and demographic correlations, too. However, the data provided are not always comparable mainly because of the lack of a common national renal biopsy registry. Polito *et al*. [1], in their paper, evaluated 9617 native renal biopsies from Brazil during the period 1993–2007 and reported the frequencies of the different histological findings. They also take into account demographic and clinical features, present several analysis and compare the results with patterns of glomerular disease distribution all over the world. It is interesting to notice that Brazil encompasses both the features of developed and developing countries and this paper allows us to better.

Overview distribution of biopsy-proven renal diseases in the world

In 2006, Nair and Walker [2] wondered if IgA nephropathy (IgAN) was the most common primary glomerulopathy in the USA, as in European and Asian areas. Analysing 5 years of renal biopsies from a referral centre serving most of the mid-western and southern states, they found that IgAN was the most common primary glomerulopathy in young adult Caucasians and the most common cause of end-stage renal disease (ESRD), while it was rare in African Americans in whom focal and segmental glomerulosclerosis (FSGS) remained more common.

The same results were found by Swaminathan *et al*. [3] evaluating the incidence of glomerular diseases in Olmest County, Minnesota. IgAN was the most frequent followed by FSGS, which was the leading cause of nephrotic syndrome in white adults, and then membranous nephropathy (MN).

In Brazil, as Polito *et al*. [1] report in their paper, FSGS is the most frequent among primary glomerulonephritides, followed by MN and IgAN. Lupus nephritis (LN) is the most common secondary form followed by post-infectious glomerulonephritis whose frequency is decreasing in most industrialized countries but remain high in some developing communities as shown by Kanjanabuch *et al*. [4]. Primary glomerulonephritides represent approximately half of all native renal biopsies, similar to almost all databases. Moreover, FSGS is the most common glomerulonephritis in children, adolescents, young adults and adults, while MN predominated in the elderly. Coppo *et al*. [5], in the Italian Registry of Renal Biopsy, described IgAN as the most frequent biopsy-proven renal disease among children.

As for Europe, IgAN is the most frequent primary glomerulonephritis in Italy [6,7], Spain [8], Czech Republic [9], France [10] and Hungary [11], while MN is the most frequent in Macedonia [12], membranoproliferative glomerulonephritis (MPGN) in Romania [13] and non-IgA mesangioproliferative glomerulonephritis in Serbia [14]. LN is the most frequent among the secondary forms (Table 1).

IgAN is the most common biopsy-proven renal disease among primary glomerulonephritides in Asia as well, as described in reports from China [15], Japan [16] and Korea [17] and LN is the most frequent among the secondary forms.

In the Middle East, FSGS is the most frequent renal disease in the Saudi Arabian Registry, followed by MPGN. IgAN accounts for only 6.5%, while LN is the most common secondary form [18].

Briganti *et al*. [19], in 2001, studied the incidence of glomerulonephritis in Australia and they found that IgAN, FSGS, LN and vasculitis were the most common renal diseases in adults with a male predominance for all glomerulonephritides except LN.

The clinical features of the different forms of glomerulonephritis do not differ much across the different countries.

The health programme of a country

The first step in a kidney disease screening programme is traditionally identified by urinalysis because it is easy to

Table 1. Worldwide distribution of biopsy-proven glomerular diseases

Country	Reference	Primary GN (%)	Secondary GN (%)
America			
USA	3	IgAN (22)[a]	LN (13)[a]
Brazil	1	FSGS (25)[b]	LN(42)[b]
Europe			
Italy	5	IgAN (37)[b]	LN (26)[b]
Spain	7	IgAN (17)[a]	LN (11)[a]
Czech Republic	8	IgAN (34)[b]	LN (23)[b]
Hungary	10	IgAN (15)[a]	LN (7)[a]
Macedonia	11	MN (13)[b]	
Romania	12	MPGN (29)[b]	LN (29)[b]
Serbia	13	Non-IgA mesangioproliferative (25)[b]	LN (76)[b]
UK	21	IgAN (39)[b]	
Asia			
China	14	IgAN (45)[b]	LN (54)[b]
Korea	16	IgAN (28)[b]	LN (9)[b]
Middle East			
Saudi Arabia	17	FSGS (21)[b]	LN (57)[b]
Australia	18	IgAN (34)[a]	LN (14)[a]

[a]Percentage of total glomerular diseases. [b]Percentage of primary or secondary glomerulonephritis.

perform, cheap and reliable. In Japan, it became part of the annual health examination programme more than 30 years ago with the aim of early detection of glomerulonephritis and early referral to a nephrologist. After adding in 1992 the measurement of serum creatinine to the programme, a core screening schedule for kidney diseases was set up. As Imai *et al*. [20] showed in their report, in adopting such a nationwide-accepted screening programme, the increase in incidence of early referral to a nephrologist and eventually the decrease of ESRD incidence is consequential. Thus, the efforts should be concentrated on implementing cost-effective first-line panels for the early detection of kidney diseases in national health programmes. Serum creatinine measurement with estimated glomerular filtration rate (Cockcroft or MDRD formula) and urinalysis with microalbuminuria should not be missing as they easily guide the nephrologist to the next diagnostic steps.

This approach is feasible and mandatory in developed countries. On the other hand, the efforts to set up a nephrological programme in developing countries such as Benin, Togo and Bolivia are much greater but still urgent as Plata *et al*. [21] show in their report. We have to take into account infections and different comorbidities influencing the development of glomerulonephritides or other kidney diseases.

Policy and registries of renal biopsy

The experience with the Italian Registry of Renal Biopsy has shown that the main reason to perform a renal biopsy is urinary abnormalities [6,7]. In the paper of Polito *et al*. [1], urinary abnormalities represent the second clinical indication to perform a biopsy after nephrotic syndrome. However, without an adequate screening programme, it would not be possible to define the effective incidence of a large proportion of glomerulonephritides characterized by asymptomatic urinary abnormalities at their early stage. The consequent renal biopsy defines the underlying disease and lets the nephrologist chose the proper clinical intervention and time follow-up. This consolidated strategy of preventive medicine is being indicated by the 'Kidney Disease: Improving Global Outcomes' initiative. The slice of chronic kidney disease burden constituted by glomerulonephritides would be lighted up by dissecting it through a thorough epidemiological approach. Developing a well-structured national registry to catalogue the histological findings by common diagnostic codes, like those suggested by the European Dialysis and Transplant Association, would provide many benefits both for developed and developing countries. Setting up a renal biopsy registry could provide highly valuable data, which are useful for several purposes ranging from the correct epidemiological description and clinical correlations to the development of protocols for preventive medicine. Moreover, combining data with renal replacement therapy registries would allow us to evaluate the long-term outcome of patients with kidney disease.

Actually, it is not easy to compare the results of the analysis of different databases across the different countries also because of the different policy in biopsy practice. Hanko *et al*. [22] has recently analysed the changing pattern of adult primary glomerular disease in a single UK region in 30 years. They noticed that the biopsy rates increased significantly from 2.02 to 7.08 per hundred thousand population per year (php/year) and reported international biopsy rates ranging from 21.5 php/year in Australia to 1.1 php/year in Romania.

These data clearly show that policy in renal biopsy practice plays an important role. However, a regional renal biopsy registry may be a modern and easy tool for programming the early referral to a nephrologist and consequently reduce the chronic kidney disease burden which is represented by ∼10% of the population in developed countries (i.e. 50 million individuals in the European Union—27 countries).

Conflict of interest statement. None declared.

(See related article by M. G. Polito *et al*. An overview on frequency of renal biopsy diagnosis in Brazil: clinical and pathological patterns based on 9617 native kidney biopsies. *Nephrol Dial Transplant* 2010; 25: 490–496.)

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IgA nephropathy—the case for a genetic basis becomes stronger

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Primary IgA nephropathy (IgAN) is a common glomerular disease with a complex genetic architecture. Ethnic differences in susceptibility to IgAN, as well as inter-individual variation in the disease course and prognosis strongly argue for the crucial role of genetic factors in its pathogenesis. For example, IgAN occurs with greatest frequency in Chinese and Japanese populations but is relatively rare in individuals of African descent [1]. A high frequency of IgAN has also been reported in biopsies of Zuni and Manitoba Native Americans and Australian aborigines [2–6]. Familial aggregation of IgAN was first reported in the 1970s, and multiple large series of familial cases have provided further evidence for genetic contribution. Two European studies demonstrated that 4–10% of patients with IgAN had a family history of kidney disease [7,8]. In other studies, urinary abnormalities were detected in over 20% of asymptomatic first degree relatives of IgAN patients [9]. Several extended kindreds with IgAN have also been reported throughout the world, including the United States [10], France [11], Italy [12], Canada [13], Australia [5] and Lebanon [14]. In all reported families, segregation of IgAN is consistent with autosomal dominant transmission with incomplete penetrance, although more complex genetic models are also compatible with the observed pedigrees. The incomplete penetrance is likely explained by the requirement of additional environmental or genetic factors for clinical manifestation of disease.

To date, three genome-wide linkage studies of familial IgAN have been reported, but no causal gene has yet been identified [13,15,16]. Unfortunately, numerous difficulties