Epidemiology of IgA Nephropathy: A Global Perspective

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Summary: IgA nephropathy (IgAN), or Berger's disease, is the most common primary glomerular disease worldwide, but varies largely in its geographic distribution. A systematic review of 1,619 publications from the five continental regions of the world was performed to assess the prevalence of IgAN in different worldwide regions and analyze factors responsible for geographic differences. All observational studies that described the prevalence and incidence data on glomerulonephritis were considered. IgAN is more frequent in Asian populations (45 cases per million population/y in Japan) than in Caucasians (31 cases per million population/y in France). These differences are owing to some relevant aspects: (1) systematic mass screening of urine in populations, as occurring in some Asian countries (Hong Kong, Japan, Korea, and Singapore), is not common in Western countries; (2) general practitioners and health care professionals in Western countries underestimate persistent microscopic hematuria and/or mild proteinuria in apparently healthy individuals causing late referral to a nephrologist; and (3) nephrologists adopt different indications for kidney biopsy in individuals with persistent urinary abnormalities. In addition, differences also are owing to the source of data, because the frequency of IgAN observed in a nephrology center with a high incidence of kidney biopsies is higher than in a regional renal biopsy registry that receives data from many centers. In conclusion, greater efforts should be made to diagnose IgAN earlier in individuals who manifest persistent microhematuria and/or mild proteinuria and to introduce less stringent indications for kidney biopsies. This preventive approach, followed by early therapy, may reduce the global burden of end-stage kidney disease caused by IgAN.
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IgA nephropathy (IgAN), or Berger's disease, was described in 1968.[1] It is a very common kidney disease characterizedby persistent urinary abnormalities (microscopic hematuria and/or mild proteinuria) or recurrent episodes of gross hematuria in concomitance of upper respiratory tract infections. IgAN is diagnosed by the presence of diffuse mesangial IgA deposits, especially the subset of IgA1, in glomeruli. Data from the literature[2] show that IgAN is the most frequent biopsy-proven primary glomerular disease (PGD), but the geographic distribution varies widely.[3] Therefore, racial and ethnic variations in IgAN frequency have been questioned, as well as the precise indications for early referral to nephrologists and indications for performing a kidney biopsy in individuals with persistent microscopic hematuria and/or mild proteinuria.

In this review, we discuss the strengths and weaknesses of the current data available on the epidemiology of IgAN in the five continents and recommendations that the medical community not underestimate the occurrence of persistent microscopic hematuria and/or mild proteinuria.

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METHODS

Medline, Embase, and Science Direct databases (1968 to February 2017) were searched for publications on epidemiologic data regarding IgAN using the following terms: IgA nephropathy, Berger's disease, IgA nephritis, IgA glomerulonephritis, kidney biopsy registry, incidence, prevalence, and frequency. No language restriction filter was applied. All articles obtained by the search were reviewed and, when accepted, were included in the review.

Publications on the frequency of IgAN were obtained from Asia (21 countries), Europe (23 countries), North America (3 countries), South America (4 countries), Africa (4 countries), and Oceania (2 countries).

Rates of IgAN frequency reported in Table 1, 2, and 3 are shown as the percentage of patients with a biopsy-proven diagnosis of PGD. The incidence rate is expressed as the number of cases per million population per year (pmp) per year.

Asian and European countries were divided into five groups based on the range of IgAN frequency expressed as a percentage of PGD: level 1 (31%-50%), level 2 (21%-30%), level 3 (10%-20%), and level 4 (<10%).

Tables 1 and 2 summarize data shown more extensively in Supplementary Tables 1 and 2.

The distribution of countries in the five continents of the world was extracted from One World Nations Online.[4]

Table 1. Frequency of IgAN in Asian Countries

Country	PGD, %*	Study
Level 1	(31-50)	
China	54.3	Zhou et al,[55] 2009
	45.2	Li et al,[56] 2004
	36.6	Pan et al,[57] 2013
Japan	47.4	Research Group on Progressive Chronic Renal Disease,[7] 1999
	31.0	Sugiyama et al,[8] 2013
Singapore	43.2	Woo et al,[5] 2010
Level 2	(21-30)	
Korea	28.2	Chang et al,[58] 2009
Taiwan	22.4	Chou et al,[41] 2012
Level 3	(10-20)	
Bahrain	14.8	Al Arrayed et al,[59] 2007
Iran	14.7	Ossareh et al,[60] 2010
Saudi Arabia	10.8	Mitwalli et al,[61] 1996
Thailand	17.9	Parichatikanond et al,[62] 2006
Level 4	(<10)	
Bangladesh	6.9	Habib et al,[63] 2012
India	6.3	Das et al,[64] 2011
United Arab Emirates	6.3	Yahya et al,[65] 1998

*The frequency is expressed as the percentage of patients with a biopsy-proven diagnosis of PGD. The numbers in parentheses indicate the range of percentages.

RESULTS

Systematic Review

Figure 1 shows the results of the database search. We collected 1,619 publications through database searching and 59 additional records were identified by other sources (conference proceedings and current awareness alerts).

In the screening phase, 1,281 reports were excluded, then among the 397 full-text articles assessed for eligibility 278 were further excluded for other reasons. Thus, 119 articles were included in the study. Details on the prevalence of the disease in each country are shown in Supplementary Tables 1 to 5.

Table 2. Frequency of IgAN in European Countries

Country	PGD, %*	Study
Level 1	(31-50)	
Czech Republic	37.4	Maixnerova et al,[9] 2015
Estonia	35.4	Riispere et al,[66] 2012
France	52.7	Moranne et al,[67] 2008
Germany	50.7	Braun et al,[68] 2011
Italy	35.2	Schena et al,[10] 1997
Lithuania	35.0	Beitnaraite et al,[69] 2007
Sweden	40.6	Peters et al,[70] 2015
United Kingdom	39.0	McQuarrie et al,[18] 2014
Level 2	(21-30)	
Belgium	21.2	Mesquita et al,[71] 2011
Croatia	18.1	Batinić et al,[72] 2007
Poland	29.8	Kurnatowska et al,[73] 2012
Romania	28.9†	Covic et al,[74] 2006
The Netherlands	27.8	van Passen et al,[75] 2004
Level 3	(10-20)	
Macedonia	11.8	Polenakovic et al,[76] 2003
Level 4	(<10)	
Serbia and Montenegro	8.5	Naumovic et al,[77] 2009

*The frequency is expressed as the percentage of patients with a biopsy-proven diagnosis of PGD. The numbers in parentheses indicate the range of percentages.

†Includes mesangial proliferative glomerulonephritis.

Table 3. Incidence of IgAN in the World

Country	pmp/y	Study
Australia	105	Briganti et al,[29] 2001
Japan	39-45	Sugiyama et al,[8] 2013
France	25-31	Moranne et al,[67] 2008
United States, Minnesota	21	Swaminathan et al,[27] 2006
The Netherlands	19	van Passen et al,[75] 2004
Singapore	18	Woo et al,[5] 2010
Germany	17.2	Braun et al,[68] 2011
Estonia	14	Riispere et al,[66] 2012
Czech Republic	11.6	Maixnerova et al,[9] 2015
United States, New Mexico	10.2	Smith et al,[24] 1985
United Kingdom	9.9	McQuarry et al,[18] 2014
Italy	8.4	Schena et al,[10] 1997
Spain	7.9	Registro Espanol de Glomerulonefritis,[12] 1994
United States, Kentucky	5.4-12.4	Wyatt et al,[23] 1998

Asia

Table 1 shows the frequency of IgAN, allotted into 4 levels, in Asian countries.

For level 1, three reports from different provinces in China were analyzed (Table 1). IgAN was the most frequent PGD, confirming the high prevalence of the disease. Some of these reports show that when the number of renal biopsies increased, the percentage of IgAN diagnoses also increased. Interestingly, in 1999, the Dialysis and Transplantation Registry Group reported that IgAN was the most common cause of chronic kidney disease (CKD) in China. These findings were confirmed by Xie and Chen 10 years later.[5]

In Singapore, Woo et al[6] reported that the percentage of IgAN diagnoses increased from 42% of PGD (1975-1986) to 45% (1987-1997) and was confirmed in the third decade (1998-2008). This high percentage of IgAN was attributed to the indications for renal biopsy that included individuals with urinary red blood cells persistently greater than 100 per high-power-field, and proteinuria less than 1 g/d.

In 1999 in Japan, the Research Group on Progressive Chronic Renal Disease[7] found a frequency of IgAN of 47.4% among 1,045 kidney biopsy specimens studied using an immunofluorescence technique. Later, the Committee for Standardization of Renal Pathological Diagnosis and the Working Group for Renal Biopsy database published two reports in which Sugiyama et al[8] confirmed the high percentage of IgAN during the periods from 2007 to 2008 (32.9%) and 2009 to 2010 (31%). There was no difference in the proportion of patients based on sex, and the peak of distribution was the same in 20- and 30-year-old individuals of both sexes. Stage 2