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Editorial

Spanish Registry of glomerulonephritis 2020 revisited: past, current data and new challenges☆

Registro de glomerulonefritis de la Sociedad Española de Nefrología en 2019: pasado, presente y nuevos retos

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Past

In our country, there is a long tradition of designing and maintaining records of the most prevalent kidney diseases such as glomerulonephritis (GN) and pathologies diagnosed by kidney biopsy. The studies on the epidemiology of biopsy kidney diseases in Spain, especially glomerular pathologies, was started in 1986 when the decrease in the incidence of membranoproliferative GN (MPGN) was independently described in two hospitals in Madrid.[1,2] At that time, a publication in the journal Nefrología insisted on the need to join efforts to create study groups with the purpose of obtaining consistent and reliable multicenter data.[3] Shortly after, in 1987, the first reports were published, both in the child population (1364 cases)[4] and in the adult population (8545 cases),[5,6] including kidney biopsies performed between 1970 and 1986. These publications, made by the SEN Study Group, mark the beginning of continued and productive work at the national level, a fact that was favorably commented on and encouraged by the then Director of the Nephrology Journal.[7] A few years later, in 1990, a multicenter study was published, including 2123 kidney biopsies, carried out in 1987 and 1988, which consolidated the so-called Spanish Registry of Glomerulonephritis (REGN).[8] Based on this registry there were several publications in the 90 s, reporting the results of kidney biopsies nationwide, with a significant percentage of participation by the Nephrology Services or Units of the entire country.[9–15] In 1994, there were two new features introduced

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in data collection: a) filling individualized information of each patient to facilitate statistical processing and b) inclusion of non-glomerular pathology. With the information collected with a record for each renal biopsy, the first publication was made in *Nephrology Dialysis and Transplantation* in 2002,[16] which had a high impact. In summary, 23 manuscripts have been published[4,8–27]: 12 in Nefrologia[4,8,10–15,25] and 11 in other international journals[16,26,27] (el numero de publicaciones no se corresponde con el numero de referencias). The reliability of the registry was demonstrated by the publication of detailed information about the incidence and prevalence of the different renal histological forms,[6,8,10–13,15,16,25] as well as its correlations with the clinical expression,[18] both in the child[4] and in the elderly.[14,20] In addition, certain clinical syndromes such as: acute renal failure,[19] hematuria[26] and nephrotic syndrome[9] have been studied in depth. Various renal entities have been analyzed, such as IgA nephropathy,[27] extracapillary GN,[24] membranoproliferative GN,[4,5,17] lupus nephritis,[21] amyloidosis[23] and acute tubulointerstitial nephritis.[22] Since 1988 these data have been presented in the session of Registries at the annual congresses of the SEN, downloadable from the SEN website.[28] To facilitate participation, for about 15 years, data has been sent electronically through the SEN website. As a last novelty, there has been stablished a link to send biopsy material to the SEN Biobank (https://www.senefro.org/modules.php?name=webstructure&idwebstructure=30) with the objective to collaborate with applied research using techniques of molecular biology and precision medicine.

With these information, it is confirmed that REGN is one of the largest and most reliable registries worldwide, since the mentioned manuscripts are included among the references of the research dealing with the epidemiology of the kidney biopsy diseases.

It is well known that kidney disease registries provide key information to be applied in clinical practice since it provides knowledge of the most frequent pathologies with real data on their incidence and prevalence,[29] it facilitates the implementation of prevention and treatment protocols, as well as serving as the basis for multicenter clinical studies and trials. One of the fundamental points in of a registry is collaboration nationwide, with a form of data entry previously agreed,[31] and a uniform policy of indication of renal biopsy[32,33]; the information obtained helps to answer unresolved questions about prevention and treatment of kidney diseases.[34] As discussed in a previous publication, these were the reasons for the generation and development of the REGN.[35] Another reason for having a registry of biopsied kidney diseases is that many pathologies, especially glomerular diseases, can only be diagnosed with certainty by doing a renal biopsy.[30] A good example of this is the value of renal biopsy in acute renal failure[36] or the study of glomerular pathology in elderly patients.[37–39] Finally, the information provided with the registry may contribute to assess the overload that these diseases have on the health system due to the number of hospitalizations, progression towards advanced renal failure and deaths.[40,41]

Studies from a single center give relevant but insufficient information. However, a number of studies carried out in a single reference center have been published, such as studies from in Springfield and Minnesota in the US,[42,43] Colombia,[44] Ireland,[45] Helsinki,[46] Belgium,[47] Germany,[48,49] Porto (Portugal),[50] Macedonia,[51] Serbia,[52] Poland,[53] India,[54] Japan,[55] China,[56] Korea,[57] Thailand,[58,59] Egypt,[60,61] South Africa,[62] South Asia[63], Pakistan.[64] In addition, local data have been published about certain renal syndromes, such as nephrotic syndrome in Chicago,[65] China[66] and Pakistan,[67] acute kidney failure in Chicago[68] and India[69] and urinary disorders in Serbia.[70] And also about specific entities as referents about the IgA N in Kentucky and in 24 states of the South and Midwest of USA,[71,72] Focal Segmental glomerulosclerosis (FSG) in USA[73,74] and Brazil,[75] primary GN in Sao Paulo (Brazil)[76] and UK,[77] membranous nephropathy in UK,[78] renal vasculitis in Norfolk (UK),[79] extracapillary GN-pauci immune in Stockholm[80] and Estonia,[81] and thin basement membrane in Limburg (Netherlands).[82] Finally, some studies have focused on certain age groups such as the child population in China[83]

Table 1 – Multicenter publications on biopsied kidney disease.

Authors	Country	No. biopsies	Comments
Johnston et al.[88]		599	IgAN data
Johnston et al.[90]	UK	255	NS data in the elderly
Hedger et al.[89]		241	Renal vasculitis data
McQuarrie et al.[91]		2480	Incidence variations in Scotland
Simon et al.[92]		942	IgAN as the most frequent
Simon et al.[93]	France	1742	IgAN as the most frequent
Painter et al.[94]	New Caledonia	275	IgAN and FGS as the most frequent
Stratta et al.[95]		1926	IgAN as the most frequent
Schena et al.[96]		15,461	IgAN and MN as the most frequent
Coppo et al.[97]	Italy	432	IgAN and Henoch – Schönlein purpura nephropathy in children
Vendemia et al.[98]		2511	MN and proliferative extracapillary GN in ≥ 65 years
Gesualdo et al.[34]		14,607	IgAN and nephroangiosclerosis as the most frequent
Lupo et al.[99]		816	IgAN as the most frequent in primary GN
Zaza et al.[100]		2680	IgAN as the most frequent
Zaza et al.[101]		1185	IgAN, FSG and MN in patients with advanced renal failure
Chugh et al.[102]	India	2947	High prevalence of nephrotic syndrome: minimal changes, amyloidosis (leprosy and other infections)
Yahya et al., [103]	United Arab Emirates	490	Predominance of proliferative GN and MN

– Table 1 (*Continued*)

Authors	Country	No. biopsies	Comments
Research Group on Progressive Chronic Renal Disease.[149]			
Iseki et al.[105]		1850	High prevalence of IgAN
Imai et al.[106]	Japan	2832	Renal survival according to renal biopsy results
Sugiyama et al.[107]		281	Amyloidosis review
Yokoyama et al.[108]	Japan	2400	IgAN and MN prevalence
Yokoyama et al.[109]		2082	Data from patients ≥ 65–83 years (prevalence of vasculitis ANCA +)
Kawamura et al [110]		3073	Data in the elderly
Sugiyama et al.[111]		79	MN data
Yokoyama et al.[112]		4016	MPGN data
Yokoyama et al.[113]		438	IgAN and MN prevalence
Nakashima et al.[114]		328	Data on Nephrotic syndrome in patients ≥65 years
Hiromura et al.[115]		47	Data on drug induced nephropathy
Nishi et al.[116]		331	Data on IgG-4 associated disease
Komatsu et al.[117]		281	LN data
Nakaga wa et al.[118]		152	Amyloidosis data
		593	Data from Henoch-Schönlein nephritis in ≥ 65 years MPGN data
Heaf et al.[119,120]	Denmark	2380	High prevalence of proliferative mesangial GN and MC
Woo et al.[121]	Singapore	2102	High prevalence of proliferative mesangial GN and MC. Role of environmental antigens
Hurtado et al.[122]	Peru	1263	Prevalence of LN and MPGN
Briganti et al.[123]	Australia	2030	Prevalence of IgAN and FSG
Choi et al.[124]	Korea	4514	Prevalence of MC and IgAN
Li et al.[125]	China	13,519	Prevalence of IgAN and LN
Rychlik et al.[126]	Czech Republic	4004	Prevalence of IgAN and MC
Maixnerova et al.[127]		10,472	Prevalence of IgAN, MN, LN and MC
Horvatic et al.[129]	Croatia	922	Prevalence of IgAN, FSG and MN
Sipiczki et al.[128]	hungr ed	798	Prevalence of IgAN and MN
Mazzuchi et al.[130]	Uruguay	2058	Prevalence of FSG and LN GSF and NL prevalence
Covic et al.[131]	Romania	635	Prevalence of MPGN and mesangioproliferative
Gusbeth-Tatomir et al.[132]		336	Prevalence of MPGN and mesangioproliferative
Malafont e et al.[133]		2086	Prevalence FSG and MN
Polito et al.[134]	Brazil	9617	Prevalence FSG and MN
Costa et al.[135]		1151	Prevalence FSG and GNMP
Machado et al.[136]	Brazil	582	Prevalence of FSG, MC and IgAN
Karnib et al.[137]	Lebanon	1327	Prevalence of mesangioproliferative GN and FSG
Layton et al [138]	U.S	217	Difficulty classifying results of kidney biopsy
Brazdziute et al.[139]	Lithuania	5368	Prevalence IgAN and FSG
Fidan et al.[140]	Turkey	3982	Child population data: prevalence of FSG and Henoch-Schönlein purpura
Barrera et al.[141]	Colombia	12,613	Prevalence of Glomerulosclerosis, IgAN and LN
Norby et al.[142]		178	LN data
Bjorneklett et al.[143]	Norway	81	Renal Vasculitis ANCA + in the elderly
Bjorneklett et al.[144]		357	Evolution of Renal Vasculitis ANCA + according to gender
Perkowska-Ptasinska et al.[145]	Poland	3934	Prevalence of IgAN and FSG

MC: minimal changes; GN: glomerulonephritis; MPGN: membranoproliferative glomerulonephritis, FSG: focal segmental glomerulosclerosis; IgAN: IgA nephropathy; LN: lupus nephropathy; MN: membranous nephropathy; NS: nephrotic syndrome.

and South Asia[63] or in patients ≥ 60 years in Chicago,[68] ≥ 65 in Ireland,[45] Japan[84] and Turkey[85] and in ≥ 80 years in Japan[86] and USA[87].

National or multicenter registries are the most reliable to know the epidemiology of biopsied kidney diseases and allow comparisons; in Table 1, are indicated most of these studies, including those made in the UK,[88–91] France,[92,93] New Caledonia,[94] Italy,[95–101] India,[102] United Arab Emirates,[103] Japan,[104–118] Denmark,[119,129] Singapore,[121] Peru,[122] Australia,[123] Korea,[124] China,[125] Czech Republic,[126,127] Hungary,[128] Croatia,[129] Uruguay,[130] Romania,[131,132] Brazil,[133–136] Lebanon,[137] States States,[138] Lithuania,[139] Turkey,[140] Colombia,[141] Norway[142–144] and Poland,[145] among the most important. IgA Nephropathy is the most frequent nephropathy in Europe and Asia, while in the USA the FSG could be increasing.[42,73,74,146]

The REGN, which has more than 28,000 kidney biopsies in 2018, is only comparable to the registries of Italy[34] and Japan[118] that have collected, at least until their latest publications, between 15,000 and 26,000 biopsies, respectively.

In the present publication we want to summarize in broad terms the results of our REGN registry, think about the future, examine the current data in 2019, as well as the innovations necessary to maintain it updated and useful.

Table 2 – Number and proportion of kidney biopsies by time periods.

Age (years)	1994–1998 n (%) *	1999–2003 n (%) *	2004–2008 n (%) *	2009–2013 n (%) *	2014–2019 n (%) *	Total N (%) *
< 15	487 (8.5)	292 (6.1)	188 (3.2)	116 (2.2)	148 (2.9)	1231 (4.6%)
15–65	4107 (71.8)	3355 (70.5)	4236 (73.0)	3683 (70.6)	3471 (67.1)	18,852 (70.7)
65–80	1058 (18.5)	1012 (21.3)	1252 (21.6)	1232 (23.6)	1331 (25.7)	5885 (22.1)
> 80	70 (1.2)	100 (2.1)	124 (2.1)	185 (3.5)	224 (4.3)	703 (2.6)
Total	5722	4759	5800	5216	5174	26,671 **

*Percentage with respect to total in each period of time.
**Total number of cases in groups of age documented in the registry.

Table 3 – Age, gender, hypertension and renal function according to age groups.

Age group (years)	Age (years) (median) *	Quotient Male/ Female	Hypertension (%)	Serum creatinine (median, mg / dl) *
< 15 (n = 1.231)	10	1.3	19	0.6
15–65 (n = 18,852)	44	1.5	52	1.4
65–80 n = 5.885)	72	1.6	69	2.5
> 80 (n = 703)	83	1.3	69	3.2
Total (n ° = 26.671)	50	1.5	55	1.6

* Non-Gaussian distribution.

Present, updated data

During the last 26 years (from 1994 to 2019), 27,116 kidney biopsies have been collected (92% first biopsy), with an average of 1042 biopsies per year. A total of 157 Nephrology Units have participated, the list is shown in the Appendix A.

The years of study have been grouped into 5 periods of 5 years each (except the last one that includes 6 years): 1994–1998, 1999–2003, 2004–2008, 2009–2013 and 2014–2019. The ages at the time of the biopsy they have been separated into 4 intervals: < 15 years, 15–65 years, 65–80 years and> 80 years. Histological diagnoses have been grouped into 5 sections: primary GN, secondary GN, tubulointerstitial nephropathy and vascular nephropathies. The rest (hereditary or difficult to classify) have been labeled asöther:

Table 2 indicates the number and percentage of biopsies performed in each time interval according to the age group.

The median ages and creatinine at the time of the renal biopsy of the entire population are 50 years and 1.6 mg / dl, respectively (neither one have a Gaussian distribution). Males predominate over females, with a ratio of 1.5. The prevalence of hypertension is 55%. In Table 3 these values are given for each age group.

Regarding the study method, 74.7% of the biopsies had a simultaneous study with an optical microscope and immunofluorescence, 17.8% also had electron microscopy, while 7% only had a study with optical microscopy and 0.5% only immunofluorescence.

The proportions of the renal syndromes at the time of the renal biopsy are indicated in Fig. 1.

Figs. 2 and 3 show the overall prevalence of all grouped kidney biopsies and for specific diagnoses, respectively.

Figs. 4–7 summarize the prevalence in the different age ranges.

Figs. 8 and 9 show the trend of the most frequent kidney pathologies, grouped and by histological diagnoses, respectively.

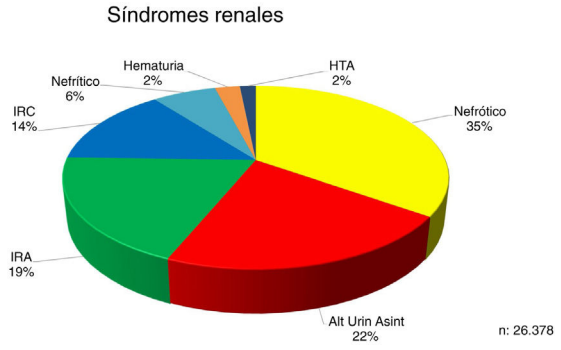

Fig. 1 – Distribution of renal syndromes at the time of renal biopsy.

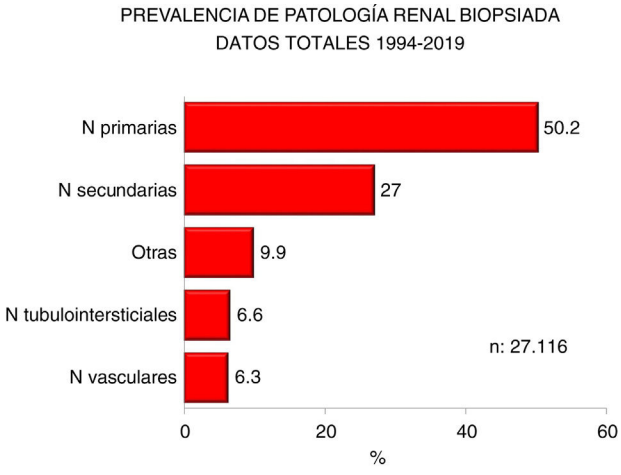

Fig. 2 – Prevalence of nephropathies by groups.

Figs. 10–13 show the trends of the biopsied pathologies in each age interval, <15 years, 15-65 years, 65-80 years and > 80 years, respectively.

Table 4 – Summary of data from the Glomerulonephritis Registry (1994-2019). General data.

Prevalence of males in all age groups
The median age is 50 years old
High presence of hypertension and kidney failure in adults and the elderly
Nephrotic syndrome is the most frequent indication for kidney biopsy, followed by asymptomatic urinary abnormalities.
Half of all diagnoses are primary kidney diseases
IgA, membranous and lupus nephropathy are the most frequent diagnosis (1/3 of the total)
There are changes in the temporal trends of diagnoses in general:
-Increase of secondary GN and tubulointerstitial nephropathies and decrease of primary GN
-Increased prevalence of IgA nephropathy and decreased of glomerulosclerosis, minimal changes, membranous and lupus nephropathy.
Steadiness of vasculitis, amyloidosis and membranoproliferative GN

Table 5 – Summary of data from the Glomerulonephritis Registry (1994-2019). Data and trends according to age groups.

<15 years:
Predominance of minimal change nephropathy, IgA nephropathy and focal glomerulosclerosis.
Increased in IgA nephropathy, membranoproliferative GN and decreased prevalence of minimal changes and glomerulosclerosis.
15–65 years :
Predominance of IgA, lupus and membranous nephropathy.
Increasing IgA nephropathy and decreasing glomerulosclerosis and lupus.
65–80 years :
Predominance of vasculitis, diabetic and membranous nephropathy.
Increasing IgA nephropathy, diabetic nephropathy, and acute interstitial nephritis, with a decrease in vasculitis, membranouse GN, amyloidosis, and glomerulosclerosis; nephroangiosclerosis unchanged.
> 80 years :
Predominance of vasculitis, amyloidosis, and acute tubulointerstitial nephritis.
Increase in acute interstitial nephritis, minimal changes and IgA nephropathy, with a decrease in vasculitis and membranous GN and without changes in nephroangiosclerosis and diabetic nephropathy.

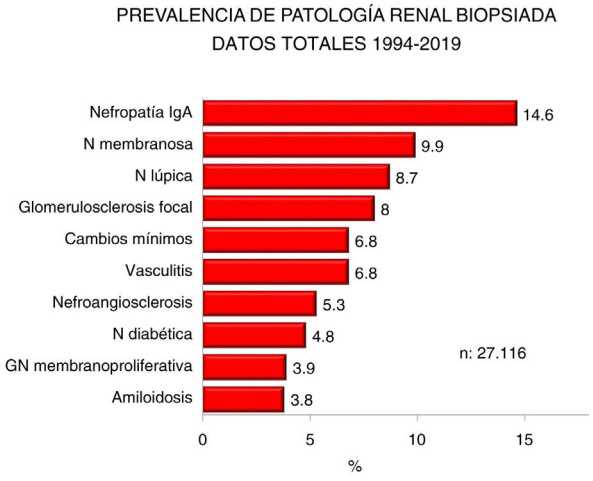

Fig. 3 – Prevalence of specific nephropathies biopsied.

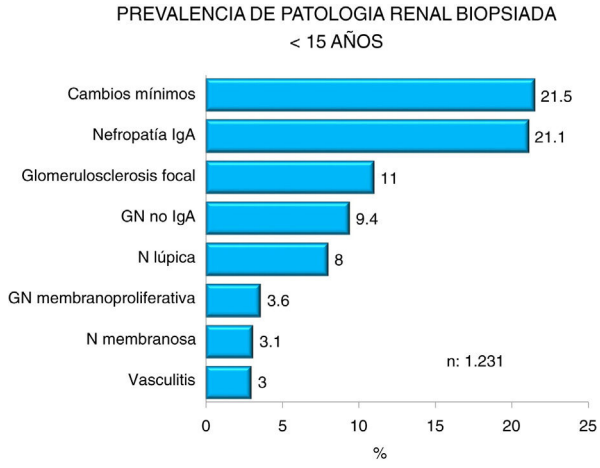

Fig. 4 – Prevalence of biopsied kidney disease in patients <15 years.

Tables 4 and 5 summarize the conclusions of all these results.

Future and new challenges

Nephrology has undergone numerous changes in recent years and kidney diseases that require biopsy have not been unaffected by these modifications. The emergence of new entities (C3 GN, among others) stands out, as well as a new approach for the classification and reporting GN.[147,148] Therefore, the registries must adapt to these changes in order to collect the data in a uniform and modern manner. Without a doubt, the REGN needs some changes such as:

a) Modification of the data completion sheet, with an extension of the clinical syndromes that indicate the reason to perform the renal biopsy (eg: nephrotic syndrome + acute renal failure; urinary alterations + hypertension).
b) Possibility of selecting various pathologies detected in the renal biopsy (eg: IgA N + nephroangiosclerosis; diabetic nephropathy + extracapillary GN).
c) Improve data collection to find out the incidence of the different pathologies "p.m.p". according to the reference population of the center performing the kidney biopsies.
d) Adapt the classification of kidney disease according to the new system proposed at the Mayo Clinic.[147]

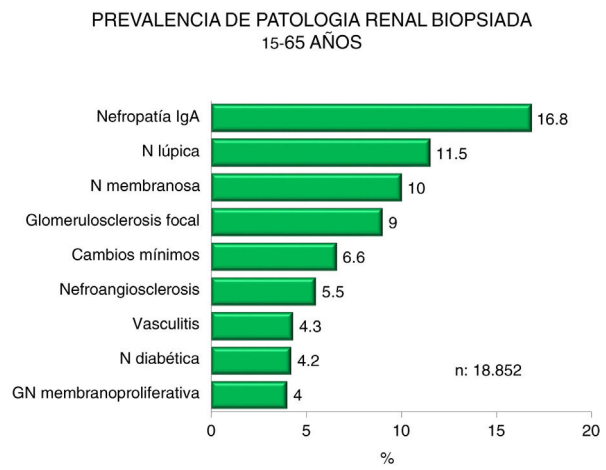

Fig. 5 – Prevalence of biopsied kidney diseases in patients 15-65 years.

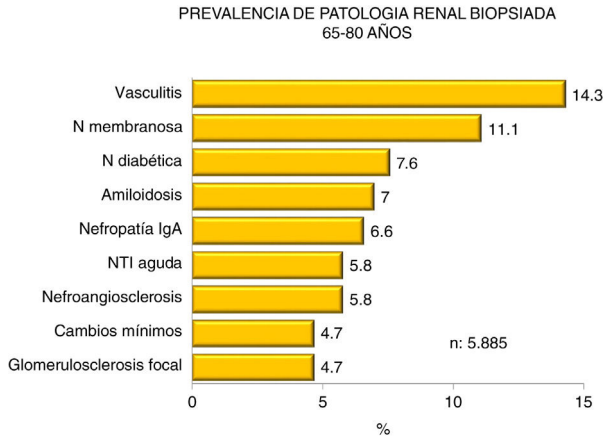

Fig. 6 – Prevalence of biopsied kidney diseases in patients 65-80 years.

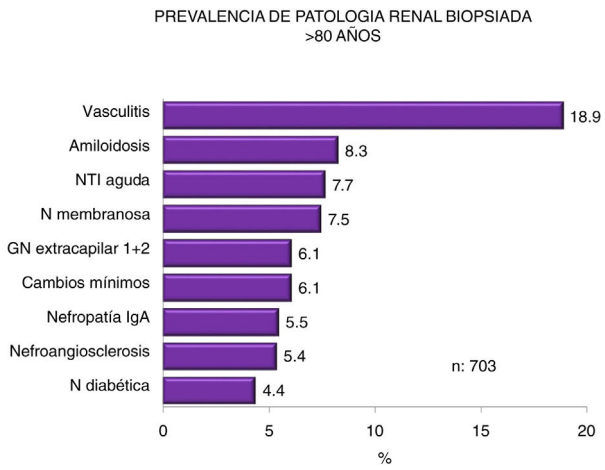

Fig. 7 – Prevalence of biopsied kidney diseases in patients > 80 years.

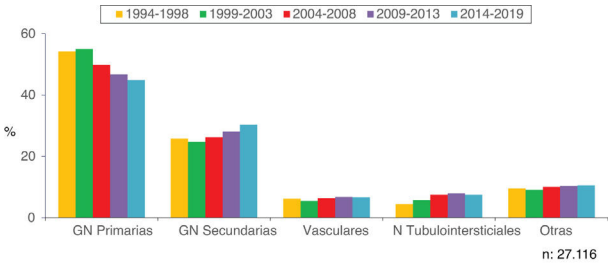

Fig. 8 – Evolution of the most frequent biopsied pathologies by groups.

e) Increase participation, especially in Child Nephrology Centers.
f) Promote multicenter studies and perform studies or clinical trials based on the data obtained.
g) Maintain the analysis of the data and its subsequent publication, to determine changes in prevalence and incidence, as well as to evaluate correlations between clinical syndromes and the histological substrate.
h) Incorporate information on associated morbidity, in order to establish the diagnosis of secondary forms (eg, viral or other infections, tumors, among others), given the availability of new biomarkers.[78]

Finally, the REGN must remain active to maintain the achievements, accumulated experience and number of biopsies. Since it is one of the largest and most reliable registries in the world, it must continue to provide data for the improvement of clinical practice and for the development of clinical research. Knowing the quality and quantity of participating

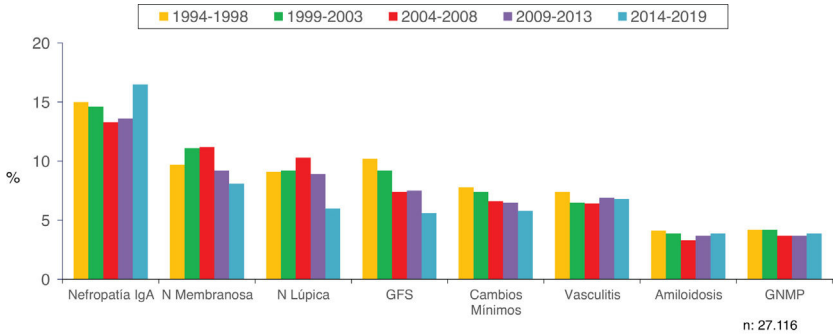

Fig. 9 – Evolution of the most frequent specific pathologies.

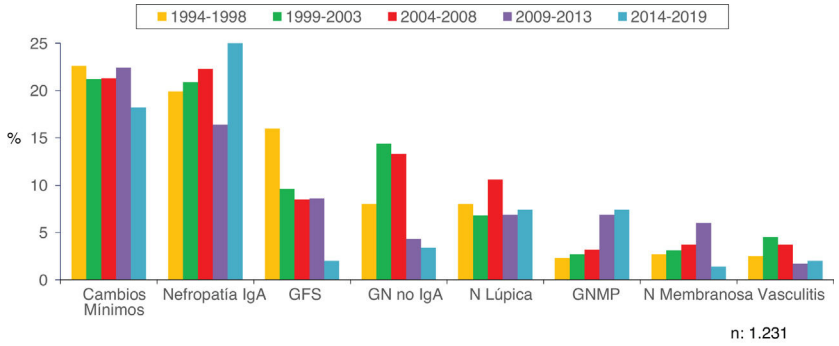

Fig. 10 – Evolution of the most frequent biopsied pathologies in patients <15 years.

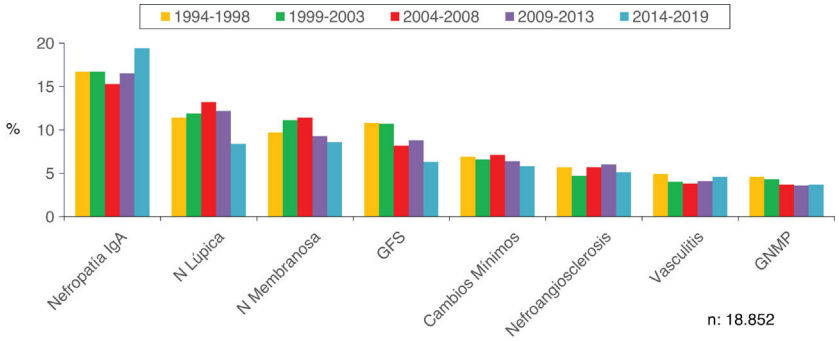

Fig. 11 – Evolution of the most frequent biopsied pathologies in patients 15-65 years.

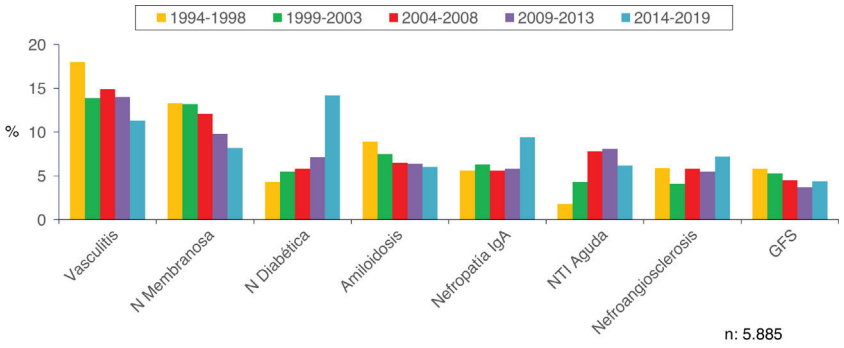

Fig. 12 – Evolution of the most frequent biopsied pathologies in patients 65-80 years.

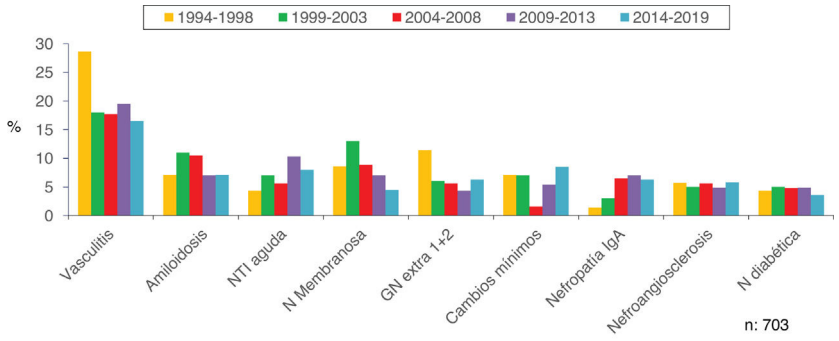

Fig. 13 – Evolution of the most frequent biopsied pathologies in patients > 80 years.

centers - despite the absence of some of them - it is predictable that the activity will not decline in the coming years.

Appendix A.

Participating Hospitals and the City (in alphabetical order).

Ciudad Sanitaria Virgen de la Nieves (Granada)
Clínica Quirón (Madrid)
Clínica Ruber (Madrid)
Clínica Universidad de Navarra (Navarra)
Clínica Vistahermosa (Alicante)
Complejo Asistencial de Palencia (Palencia)
Complejo Asistencial Universitario de Burgos (Burgos)
Complejo Asistencial Universitario de León (León)
Complejo Asistencial Universitario de Salamanca (Salamanca)
Complejo Hospitalario Arquitecto Marcide Novoa Santos Ferrol (A Coruña)
Complejo Hospitalario de Navarra (Pamplona)
Complejo Hospitalario Nuestra Sra. de la Candelaria (Tenerife)
Complejo Hospitalario Princesa de España (Jaén)
Complejo Hospitalario San Millán y San Pedro (La Rioja)
Complejo Hospitalario San Pedro de Alcántara (Cáceres)
Complejo Hospitalario Universitario A Coruña (A Coruña)
Complejo Hospitalario Universitario de Santiago (A Coruña)
Complejo Hospitalario Universitario Reina Sofía (Córdoba)
Complejo Universitario San Carlos (Madrid)
Consorci Corporació Sanitaria Parc Taulí de Sabadell (Barcelona)
Consorci Hospitalari de Terrassa (Barcelona)
Consorcio Hospital General Universitario de Valencia (Valencia)
Fundació Althaia Manresa (Barcelona)
Fundación Hospital Alcorcón (Madrid)
Fundación Hospital Manacor (Mallorca)
Fundación Puigvert (Barcelona)
Hospital 12 de Octubre Infantil (Madrid)
Hospital Arnau de Vilanova (Valencia)
Hospital Central de Asturias Infantil (Asturias)
Hospital Clinic i Provincial (Barcelona)
Hospital Clínico Universitario de Valencia (Valencia)
Hospital Clínico Universitario de Valladolid (Valladolid)
Hospital Clínico Universitario de Zaragoza (Zaragoza)
Hospital Clínico Universitario Virgen de la Victoria (Málaga)
Hospital Comarcal de Melilla (Melilla)
Hospital Comarcal Francesc De Borja (Valencia)
Hospital Costa del Sol Marbella (Málaga)
Hospital Cristal Piñor (Orense)
Hospital de Basurto (Bilbao)
Hospital de Bellvitge (Barcelona)
Hospital de Cruces (Bilbao)
Hospital de Cruces Infantil (Bilbao)
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