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Real-World Analysis of Patients with Immunoglobulin A Nephropathy – Diagnosis and Disease Monitoring

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CONCLUSIONS

- Despite KDIGO guideline recommendations, 14% of patients did not undergo kidney biopsy to confirm their diagnosis of IgAN.
- In many patients who did not undergo biopsy, diagnosis was based on non-invasive methods such as blood tests (61%).
- Diagnostic delay experienced by biopsied IgAN patients was driven by waiting for tests to be conducted and referral to a specialist.
- Future research focusing on idenitifying current non-invasive diagnostic tests, as well as biomarkers of IgAN that may allow non-invasive diagnosis, should be encouraged.

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INTRODUCTION

- Immunoglobulin A Nephropathy (IgAN) is the most common form of primary glomerulonephritis worldwide, with an estimated annual incidence of 25 cases per million.[1]
- IgAN diagnosis can only be confirmed by kidney biopsy as recommended by the Kidney Disease Improving Global Outcomes (KDIGO) 2021 guidelines.[2] There are no validated diagnostic serum or urine biomarkers for IgAN.
- Limited data are available on the diagnostic journey of patients with IgAN in large real-world settings.

OBJECTIVE

- This retrospective analysis of real-world data aimed to provide a better understanding of the diagnostic journey and disease monitoring for patients with IgAN.

METHODS

- Data were drawn from the Adelphi IgAN Disease Specific Programme (DSP™), a cross-sectional survey with retrospective data collection of IgAN-treating nephrologists and their consecutively consulting patients, across the United States (US), Europe (France, Germany, Italy, Spain, and the United Kingdom), China, and Japan, conducted between June – October 2021.
- The DSP methodology has been previously described,[3,4] validated,[5] and demonstrated to be representative and consistent over time.[6]
- Ethics exemption was obtained where required, from the Pearl Institutional Review Board and Hospital Clínic de Barcelona.
- Nephrologists completed structured online records for their next 10 patients presenting with IgAN. Records included data regarding patients' demographics, tests conducted and disease monitoring.
- Patients were invited to voluntarily fill out a form reporting data on the reasons for delay in IgAN diagnosis.
- All analyses were descriptive.

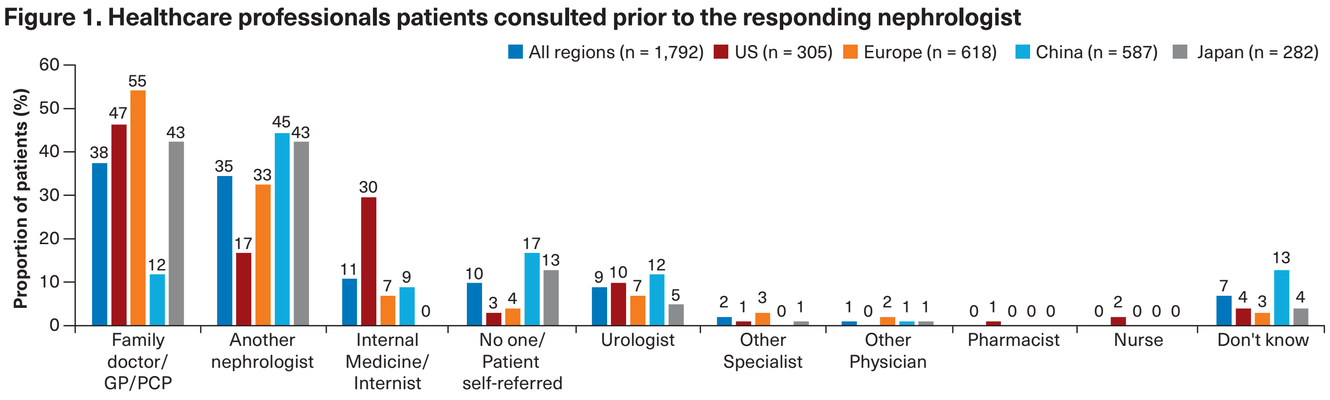
RESULTS

- A total of 295 nephrologists completed records for 1,792 patients. Overall, the mean (standard deviation; SD) patient age was 43.6 (15.0) years and 59% were male.

Diagnosis pathway

- Prior to visiting the responding nephrologist, IgAN patients primarily consulted with a family doctor/general physician (GP)/primary care physician (PCP) for their symptoms (38%) (**Figure 1**).
  - In Europe, 55% of IgAN patients consulted a family doctor/GP/PCP as compared with only 12% in China.
  - In China, 45% of IgAN patients consulted another nephrologist, compared with 17% in the US.
- The majority of IgAN patients were diagnosed by nephrologists (other than the responding physician) (All regions: 1,722 [96%], US: 285 [93%], Europe: 591 [96%], China: 567 [97%], and Japan: 279 [99%]).

Figure 1. Healthcare professionals patients consulted prior to the responding nephrologist



Europe: France, Germany, Italy, Spain and the United Kingdom; GP, general physician; PCP, primary care physician; US, United States.

Tests for diagnosis of IgAN

- Kidney biopsy was used to diagnose 85% (n = 1,515) of patients, 14% had not undergone a biopsy, and for 1% their biopsy status was unknown.
- Across all regions, biopsy was performed mostly by nephrologists (All regions: 84%, US: 59%, Europe: 81%, China: 95%, and Japan: 95%) followed by radiologists (All regions: 12%, US: 38%, Europe: 13%, China: 3%, and Japan: 0%).
- Amongst the patients who did not undergo confirmatory kidney biopsy for IgAN diagnosis (n = 251, 14%), 41% refused biopsy (US: 53%, Europe: 43%, China: 32%, and Japan: 80%), 8% could not undergo biopsy due to medical reasons (US: 0%, Europe: 12%, China: 5%, and Japan: 0%), and other reasons were cited for 2% of IgAN patients (US: 6%, Europe: 2%, China: 0%, and Japan: 0%). The majority of non-biopsied patients (61%) were diagnosed via non-invasive methods e.g., blood tests (US: 50%, Europe: 57%, China: 72%, and Japan: 80%).
- To aid the diagnosis of IgAN, a mean (SD) of 4.1 (3.0) tests, in addition to biopsy were conducted (**Table 1**).
- Other than biopsy, serum creatinine (SCr) test (All regions: 61%, US: 61%, Europe: 73%, China: 65%, and Japan: 30%), urinalysis of red blood cells (All regions: 60%, US: 66%, Europe: 68%, China: 63%, and Japan: 30%) and measurement of blood pressure (All regions: 59%, US: 58%, Europe: 68%, China: 62%, and Japan: 31%) aided the diagnosis of IgAN.

Table 1. Number of tests conducted to aid diagnosis of IgAN

Countries	Overall		Biopsied patients		Non-biopsied patients		Biopsy status unknown	
	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD
All regions	1,792	4.1 ± 3.0	1,515	4.1 ± 3.1	251	4.2 ± 2.8	26	3.7 ± 3.5
US	305	3.6 ± 2.3	265	3.6 ± 2.2	36	3.6 ± 2.6	*	4.5 ± 4.2
Europe	618	4.6 ± 2.7	484	4.9 ± 2.6	122	3.9 ± 2.6	12	2.1 ± 3.2
China	587	4.8 ± 3.3	489	4.8 ± 3.4	88	4.9 ± 2.9	10	5.4 ± 3.0
Japan	282	1.8 ± 2.5	277	1.8 ± 2.5	5	4.0 ± 2.2	*	0.0 ± 0.0

Europe: France, Germany, Italy, Spain, and the United Kingdom; IgAN, Immunoglobulin A Nephropathy; SD, Standard Deviation; US, United States. *represents patient numbers <5.

- The levels of proteinuria and estimated glomerular filtration rate (eGFR) are reported in **Table 2**. Amongst all regions, the eGFR was lowest in the US and level of proteinuria was highest in Europe.

Table 2. Proteinuria and eGFR levels among IgAN patients by biopsy status

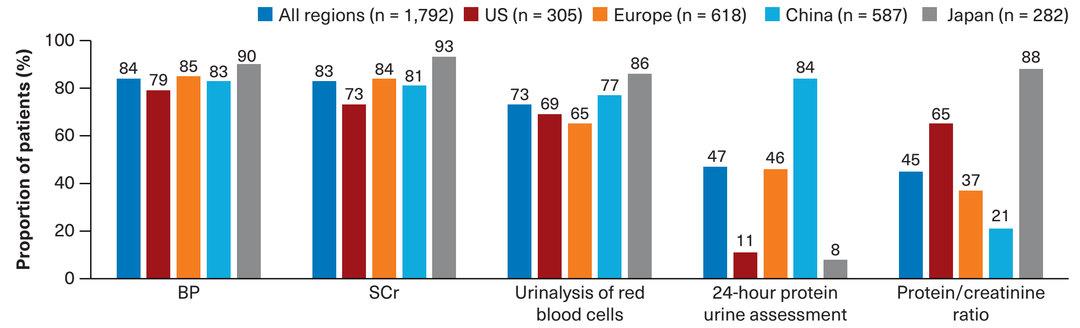
At diagnosis (at biopsy for biopsied patients)		Proteinuria (g/day)					eGFR/GFR (ml/min/1.73m²)				
		All regions	US	Europe	China	Japan	All regions	US	Europe	China	Japan
Overall	n	1,369	233	465	459	212	1,356	240	465	438	213
	Mean ± SD	2.3 ± 2.5	2.3 ± 1.8	2.9 ± 3.5	2.3 ± 1.9	1.1 ± 0.9	69.8 ± 29.5	58.1 ± 25.7	63.9 ± 30.2	83.9 ± 28.9	66.8 ± 21.4
Biopsied patients	n	1,219	210	390	411	208	1,200	213	390	388	209
	Mean ± SD	2.2 ± 2.3	2.4 ± 1.8	2.7 ± 3.2	2.3 ± 1.9	1.1 ± 0.9	69.9 ± 28.3	56.8 ± 24.8	66.3 ± 28.4	82.4 ± 28.4	66.9 ± 21.5
Non-biopsied patients	n	145	21	74	46	*	152	25	74	49	*
	Mean ± SD	3.2 ± 3.7	1.0 ± 0.9	4.4 ± 4.5	2.4 ± 2.1	1.2 ± 1.2	68.6 ± 37.6	67.2 ± 24.1	51.5 ± 36.2	95.9 ± 30.4	58.8 ± 11.7
Biopsy status unknown	n	*	*	*	*	*	*	*	*	*	*
	Mean ± SD	2.5 ± 1.3	3.5 ± 0.7	1.0 ± 0.0	2.4 ± 1.2	0.0 ± 0.0	65.8 ± 60.4	76.5 ± 101.1	44.0 ± 0.0	66.0 ± 0.0	0.0 ± 0.0

Note: data presented here is for patients in whom the proteinuria and eGFR values were available. eGFR, Estimated Glomerular Filtration Rate; Europe: France, Germany, Italy, Spain, and the United Kingdom; GFR, Glomerular Filtration Rate; IgAN, Immunoglobulin A Nephropathy; SD, Standard Deviation; US, United States. *represents patient numbers <5.

Monitoring of IgAN patients

- The two most commonly conducted measurement/test within three months prior to the survey were SCr and blood pressure (**Figure 2**).
- Within three months prior to survey, a mean (SD) of 4.9 (2.1) tests were conducted for IgAN patients (US: 4.1 [2.1], Europe: 4.8 [1.9], China: 5.6 [2.3], and Japan: 4.8 [1.3]).
- Within three and twelve months prior to survey, a mean (SD) of 4.2 (2.3) tests were conducted for patients across all regions (US: 3.3 [2.1], Europe: 4.3 [2.2], China: 4.6 [2.5], and Japan: 4.4 [1.9]).

Figure 2. The most common measurement/tests conducted within 3 months prior to the survey for monitoring IgAN patients

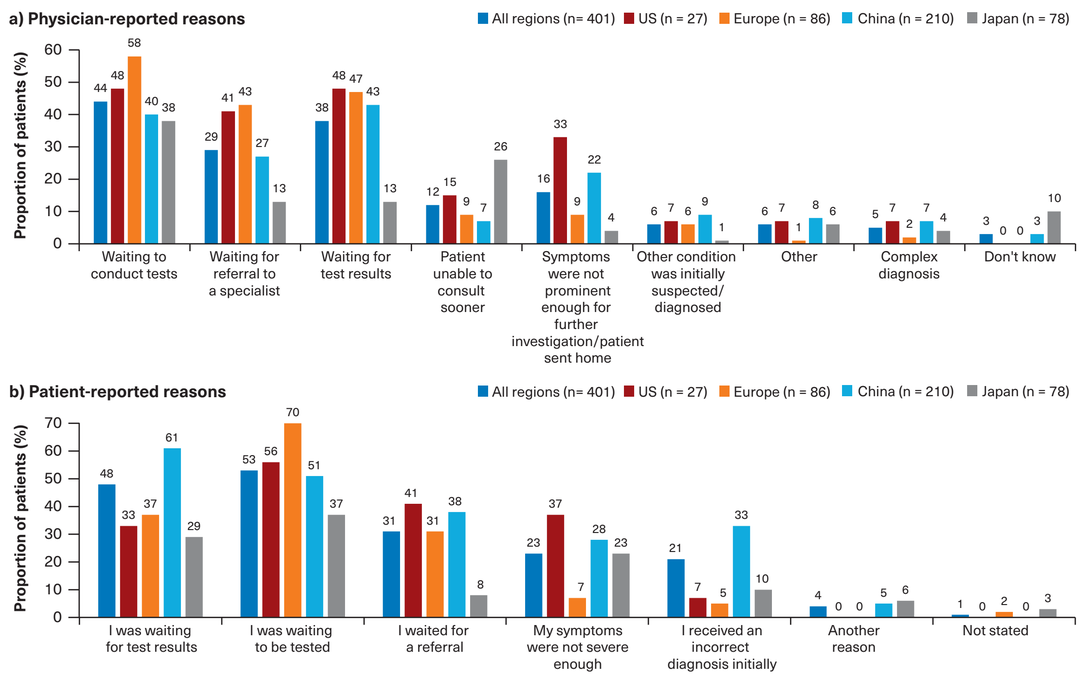


BP, blood pressure; Europe: France, Germany, Italy, Spain and the United Kingdom; IgAN, Immunoglobulin A Nephropathy; SCr, serum creatinine; US, United States.

Reasons for diagnostic delay

- The data regarding the delay between initial consultation and IgAN diagnosis (defined as >4 weeks) is reported for patients who also self-reported reasons for diagnostic delay.
- In biopsy-diagnosed patients, the main reason for a delay from initial consultation to diagnosis of >4 weeks, was a wait for the tests to be conducted, reported by 44% physicians and 53% patients (**Figure 3**).
- For physician-reported and patient-reported reasons for a delay in diagnosis, waiting for test results and referral to a specialist were amongst the leading factors (**Figure 3**).

Figure 3. Reasons for diagnostic delay* in biopsied patients, a) physician-reported and b) patient-reported



*Defined as >4 weeks between initial consultation to diagnosis. Europe: France, Germany, Italy, Spain, and the United Kingdom; US, United States.

LIMITATIONS

- Participating patients may not reflect the general IgAN population since the DSP only includes patients who are consulting with their physician. This means that patients who consult more frequently have a higher likelihood of being included.
- Patients completed the survey on a voluntary basis and this may have contributed to a selection bias.
- Recall bias (not being able to recollect accurate and complete information), a common limitation of surveys, might also have affected responses of both physicians and patients. However, physicians did have the ability to refer to the patients' records, thus minimizing the possibility of recall bias.

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Disclosures

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