Title

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

Authors: Richard Lafayette[1], Sydney Tang[2], Serge Smeets[3], Carolina Aldworth[4], Raymond Przybysz[3], Aneesh Thomas George[5], Jade Garratt-Wheeldon[6]

Affiliations: [1]Stanford University Medical Center, United States; [2]The University of Hong Kong, Hong Kong SAR, China; [3]Novartis Pharma AG, Basel, Switzerland; [4]Novartis Pharmaceuticals Corporation, East Hanover, United States; [5]Novartis Healthcare Private Limited, Hyderabad, India; [6]Adelphi Real World, Bollington, England, United Kingdom

Introduction

Immunoglobulin A nephropathy (IgAN) is the most common form of primary glomerulonephritis worldwide, with an estimated annual incidence of 25 per million. IgAN diagnosis can only be confirmed by kidney biopsy as recommended by Kidney Disease Improving Global Outcomes (KDIGO) guidelines. Limited data are available on diagnosis of patients with IgAN. This retrospective analysis of real world data aimed to better understand the diagnostic journey and disease monitoring for patients with IgAN.

Methods

Data were drawn from the Adelphi IgAN Disease Specific Programme, a cross-sectional survey with retrospective data collection from IgAN-treating nephrologists and their patients, in the United States (US), EU5 (France, Germany, Italy, Spain, United Kingdom), China and Japan, June-October 2021. Nephrologists completed structured online records for successive patients presenting with IgAN, including patients' demographics, tests for diagnosis, and disease monitoring. Patients self-completed forms included questions regarding reasons for delay in IgAN diagnosis.

Results

A total of 295 nephrologists completed records for 1792 patients. Overall, the mean patient age was 43.6 years and 59% were male. Prior to visiting the responding nephrologists, IgAN patients consulted family doctor/general physician/primary care physician on their disease (38%, EU5: 55%, China: 12%, Japan: 43% and US: 47%) closely followed by another nephrologist (35%, EU5: 55%, China: 45%, Japan: 43% and US: 17%). The mean duration from diagnosis to point of survey (biopsy or other methods: e.g., blood serum results) was 3.8 years.

Of the biopsy diagnosed IgAN patients (85%), most were performed by nephrologists (84%, EU5: 81%, China and Japan: 95%, US: 59%) or radiologists (12%, EU5: 13%, China: 3%, Japan: 0%, US: 38%). The mean duration from diagnosis to point of survey was 3.9 years. Of patients that did not undergo biopsy (14%), 61% were diagnosed by non-invasive methods (e.g., blood serum tests), 41% refused biopsy, 8% were not biopsied due to medical reasons and 2% had other reasons. Biopsy status for 1% of patients was unknown. Levels of proteinuria and estimated glomerular filtration rate observed in patients are provided in Table 1.

In biopsy diagnosed patients, the main factor leading to time delay from initial consultation (>4 weeks) to diagnosis was waiting for the tests to be conducted, reported by 44% physicians and 53% patients (Figure 1).

The mean number of tests used to diagnose IgAN patients are provided in Table 2. Serum creatinine (SCr) test, urinalysis of red blood cells and measurement of systolic blood pressure (BP) were top tests aiding diagnosis, where measurement of BP and SCr were most conducted to monitor IgAN patients, ≤12 months of consultation.

Conclusion

Despite the recommendation of kidney biopsy for IgAN diagnosis in KDIGO guidelines, 14% patients did not undergo biopsy, of whom 61% were diagnosed by non-invasive methods. In such patients, diagnosis may have been based on the physician's clinical judgement. Diagnostic delay in biopsied IgAN patients was driven by waiting for tests to be conducted. Future research on non-invasive diagnostic tests and biomarkers may be considered to enable earlier diagnosis of IgAN.

Total characters (with spaces): 3,332/3,400 (includes title, introduction, methods, results and conclusion)

Table 1: Clinical characteristics in IgAN patients by GFR and proteinuria levels and by diagnosis test

At diagnosis (at biopsy for biopsied patients)		Proteinuria (g/day)					eGFR/GFR (ml/min/1.73m^2)				
		Total	EU5	China	Japan	US	Total	EU5	China	Japan	US
Overall	n	**1,369**	**465**	**459**	**212**	**233**	**1,356**	**465**	**438**	**213**	**240**
	Mean ± SD	2.3 ± 2.5	2.9 ± 3.5	2.3 ± 1.9	1.1 ± 0.9	2.3 ± 1.8	69.8 ± 29.52	63.9 ± 30.2	83.9 ± 28.9	66.8 ± 21.4	58.1 ± 25.7
Biopsied patients	n	**1,219**	**390**	**411**	**208**	**210**	**1,200**	**390**	**388**	**209**	**213**
	Mean ± SD	2.2 ± 2.3	2.7 ± 3.2	2.3 ± 1.9	1.1 ± 0.9	2.4 ± 1.8	69.9 ± 28.3	66.3 ± 28.4	82.4 ± 28.4	66.9 ± 21.5	56.8 ± 24.8
Non-biopsied patients	n	**145**	**74**	**46**	**4**	**21**	**152**	**74**	**49**	**4**	**25**
	Mean ± SD	3.2 ± 3.7	4.4 ± 4.5	2.4 ± 2.1	1.2 ± 1.2	1.0 ± 0.9	68.6 ± 37.6	51.5 ± 36.2	95.9 ± 30.4	58.8 ± 11.2	67.2 ± 24.1
Biopsy status unknown	n	**5**	**1**	**1**	**2**	**2**	**4**	**1**	**1**	**0**	**2**
	Mean ± SD	2.5 ± 1.3	1.0 ± 0.0	2.4 ± 1.2	0.0 ± 0.0	3.5 ± 0.7	65.8 ± 60.4	44.0 ± 0.0	66.0 ± 0.0	0.0 ± 0.0	76.5 ± 101.1

Abbreviations: eGFR: estimated glomerular filtration rate; EU5: France, Germany, Italy, Spain and United Kingdom, GFR: glomerular filtration rate; IgAN: immunoglobulin A nephropathy; SD: standard deviation

Table 2: Tests conducted in IgAN patients for aid diagnosis

Countries	Overall		Biopsied patients		Non-biopsied patients		Biopsy status unknown	
	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD
Total	1,792	4.1 ± 3.0	1,515	4.1 ± 3.1	251	4.2 ± 2.8	26	3.7 ± 3.5
EU5	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 ± 0.0
US	305	3.6 ± 2.3	265	3.6 ± 2.2	36	3.6 ± 2.6	4	4.5 ± 4.2

Abbreviations: IgAN: immunoglobulin A nephropathy; SD: standard deviation

Figure 1: Reasons for diagnostic delay in biopsy patients, a) physician reported and b) patient reported