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Natural History of IgA Nephropathy: Analysis of a UK National RaDaR IgA Nephropathy Cohort

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Introduction

Background

- IgA nephropathy (IgAN) is the most prevalent primary glomerulonephritis worldwide and remains a leading global cause of chronic kidney disease (CKD) and end-stage kidney disease (ESKD)[1]
- The natural history of IgAN varies considerably across populations as does the risk of development of ESKD[2]
- It is therefore important to understand the natural history of IgAN with respect to risk of progression and to inform the associated psychosocial impact for specific patient populations

Objective

- To describe the natural history of IgAN in adult and paediatric patients living in the United Kingdom (UK) with a focus on time from diagnosis to ESKD

Methods

Data Source

- The National Registry of Rare Kidney Diseases (RaDaR) is a UK Kidney Association (UKKA) initiative that collects retrospective and prospective data from patients with rare kidney diseases in the UK
- The IgAN Rare Disease Group (RaDaR-IgAN) includes patients with biopsy-proven primary IgAN and estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m^2 or proteinuria ≥1 g/24h (or equivalent protein-to-creatinine ratio value). Patients with IgA vasculitis are separately recruited into the Vasculitis Rare Disease Group.
- Recruitment began in 2013 to RaDaR-IgAN and is ongoing in 107 adult and paediatric kidney units across the UK

Definitions and Clinical Measures

- Disease onset defined as first occurrence of positive diagnostic renal biopsy, primary renal diagnosis, or symptom presentation
- eGFR calculated via the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula (adults) and the modified Schwartz formula (paediatric)
- ESKD defined as CKD stage 5 (confirmed eGFR <15 mL/min/1.73m^2 or CKD stage 5 recorded in RaDaR) or receiving chronic dialysis or kidney transplant

Eligibility Criteria

- Patients with ≥12 months observation from disease onset were included
- Patients with ESKD at or prior to disease onset as defined were excluded

Statistical Analyses

- Comparisons across groups evaluated via Chi-square test, a two-sample t-test, Wilcoxon-Mann-Whitney test, or Fisher's exact test, as appropriate
- eGFR slope calculated as an annualised value from disease onset to ESKD onset date/death date or last follow up date. Linear mixed model was used to estimate each patient's intercept and slope of eGFR.
- Renal survival defined as absence of ESKD or death with survival time calculated from disease onset to ESKD onset date/death date or last follow-up

RaDaR, the UK Rare Renal Disease Registry (www.rarerenal.org), was established by the UK Kidney Association (https://ukkidney.org) in 2010 and now includes more than 26,000 patients at over 100 UK hospitals who have been diagnosed with one of 30 categories of rare kidney disease and who have provided written informed consent to participate. It is hosted by the UK Renal Registry (https://ukkidney.org/about-us/who-we-are/uk-renal-registry) and incorporates links to other national databases and, for the majority of participants, automated upload of biochemical and other hospital medical record data.

Results

Table 1. Disease onset characteristics and outcomes of paediatric and adult patients with IgAN

		Overall (N=2,168)	Paediatrics (<18 years) (n=140)	Adults (≥18 years) (n=2,028)	P-Value*
Age, Median (IQR)		39.0 (28.5-50.7)	13.8 (9.2-16.3)	40.7 (30.4-51.6)	
Sex (F), %		30.0	35.7	29.6	0.13**
Race/Ethnicity, %					0.26**
White		74.3	75.0	74.2	
Asian		9.2	6.4	9.4	
Black		1.3	0.7	1.3	
Multiple Races		0.3	0.0	0.3	
Other		1.3	0.7	1.3	
Not stated / Missing		13.7	17.1	13.5	
PCR (g/g)	n (%)	424 (19.6)	10 (7.1)	414 (20.4)	
	Median (IQR)	1.52 (0.57-3.27)	2.77 (0.09-4.06)	1.52 (0.58-3.18)	0.81‡
	≥3.0 g/g, %	26.7	50.0	26.1	0.09**
eGFR (mL/min/1.73m^2)	n (%)	553 (25.5)	8 (5.7)	545 (26.9)	
	Median (IQR)	46.3 (28.8-74.3)	86.1 (51.7-104.3)	46.1 (28.6-73.8)	0.02‡
Duration of Follow-up (years), Median (IQR)		9.5 (5.4 – 16.6)	15.8 (7.1 -26.2)	9.3 (5.3-16.0)	<0.01‡
ESKD or Death Events, n (%)		1,087 (50.1)	48 (34.3)	1,039 (51.2)	
First ESKD or Death Event, %					<0.01**
CKD Stage 5		58.5	31.3	59.8	
Chronic Dialysis		32.8	52.1	32.0	
Kidney Transplant		8.0	16.7	7.6	
Death		0.6	0.0	0.7	
Time to First ESKD Event (years), Median (IQR)		3.8 (1.4 – 9.6)	10.2 (4.9-16.6)	3.7 (1.4-9.1)	<0.01‡
Median (95% CI) Renal Survival Time (years)#		11.4 (10.5 – 12.6)	28.3 (19.0 – ¥)	10.7 (9.9 – 11.8)	
Age at First ESKD Event (years), Median (IQR)		47.3 (35.2-58.1)	23.9 (19.4-29.6)	48.1 (36.5-58.5)	
Rate of Loss of eGFR (mL/min/1.73m^2/year)	n (%)	1,529 (70.5)	36 (25.7)	1,493 (73.6)	
	Median (IQR)	2.4 (5.8, 0.5)	3.6 (10.2, -0.1)	2.4 (5.7, 0.5)	0.24‡

Abbreviations: CI, confidence interval; **CKD**, chronic kidney disease; **eGFR**, estimated glomerular filtration rate; **ESKD**, end-stage kidney disease; **IQR**, interquartile range; **PCR**, urine protein to creatinine ratio. *Paediatric vs. adult comparison; **Chi-square; Albumin to creatinine ratio values converted to PCR by applying a factor of 1.43;[3] ‡Mann-Whitney; #See Figure 1; ¥No upper CI available.

DISCLOSURES & FUNDING

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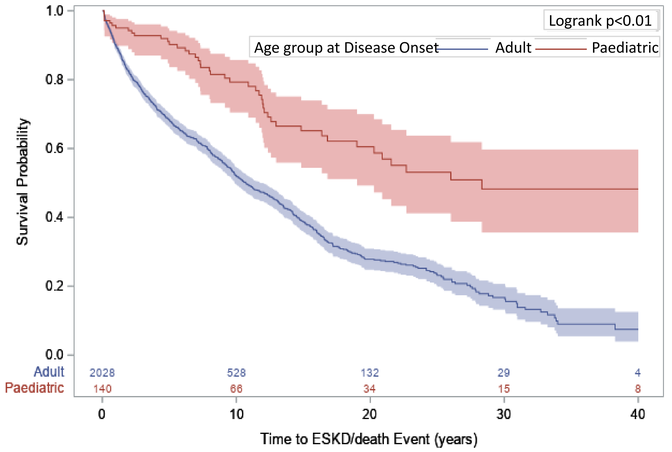
Figure 1. Kaplan-Meier survival curves (95% CI) for time to first ESKD/death event among paediatric and adult patients with IgAN



Conclusion

Summary and Discussion

- Adults represent >90% of the cohort with a median baseline age of 39 years reflecting a disease with onset predominantly in the early stages of adulthood
- Median PCR at onset was 1.52 g/g with ~27% of patients having nephrotic range proteinuria
- Median follow-up was 9.5 years with ESKD or death occurring in 50% of patients (<1% death)
- Paediatric and adult patients showed 50% renal survival probability of 28 & 11 years, respectively
- The shorter 50% survival probability and time-to-ESKD for adults may reflect diagnosis of adults at a later CKD stage, as median rate of eGFR loss (2.4 mL/min/1.73m^2/year) was comparable between children and adults
- These data confirm a poor outcome of IgAN in this cohort and detail the renal survival probabilities in children and adults

Strengths and Limitations

- Large cohort with lengthy follow-up and high level of completeness for renal events derived from a nationwide database involving a large proportion of UK kidney units
- The inclusion criteria for RaDaR-IgAN leads to enrolment of patients with progressive disease who represent a high risk IgAN population
- Reporting of proteinuria and eGFR data at disease onset is incomplete and may not be representative of the full cohort, however data are likely to be missing at random with limited bias

Conclusions

- In a large IgAN cohort, analyses indicate disease progression and poor outcomes in children and adults, highlighting a need for early diagnosis and effective treatments for IgAN patients with renal impairment and/or overt proteinuria ≥1 g/24h