Baseline Characterization and Treatment Pathways of Patients With Alport Syndrome Across Geographies: Exploring a Rare Disease in a Multi-Database Retrospective Cohort Study

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Background

Alport Syndrome (AS) is a rare and often undiagnosed genetic kidney disease which usually manifests in early childhood and is characterized by mutations in the type IV collagen resulting in defective collagen production. Consequently, patients may present with hematuria or progressive loss of kidney function leading to kidney failure in addition to ocular abnormalities and hearing loss. While there is no current cure for AS, standard of care includes the use of angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB) and sodium-glucose cotransporter-2 inhibitors (SGLT2i) to delay the onset of kidney failure. [1–3] Contemporary real-world evidence on the characteristics and treatment patterns among patients with AS is lacking. This study aimed to generate a robust body of evidence to provide insights into the burden of disease for patients with AS across multiple countries. The primary objective was to describe baseline patient characteristics including demographics at index and comorbidities any time in the medical history in patients identified with AS. Secondary objectives included the description of treatment use at baseline [-90,0 days] and treatment patterns over time after index diagnosis.

Methods

We conducted a longitudinal, retrospective cohort study of patients with AS in six databases from three different countries mapped to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM). Specifically, we included two claims databases from the US (MarketScan and OPTUM Claims), one Electronic Health Records (EHR) database from the US (OPTUM EHR), two EHR databases from the United Kingdom (CPRD GOLD and CPRD Aurum) and one EHR database from Japan (RWD Co). The index date was the date of first AS diagnosis. The study period was between January 2012 and the latest data cut. The study population included all patients with a diagnosis code for AS aged between 1 and 40 years at index and with at least 12 months of continuous enrolment in the database prior to index date. Patients with prior kidney failure any time before or on the index date were excluded. We described demographics (age, gender, race) and comorbidities of clinical interest including hematuria, proteinuria, hearing impairment, vision impairment, arterial hypertension and kidney disease using appropriate descriptive statistics. In addition, we described ACEi, ARB and SGLT2i use at baseline and over time. Observational Health Data Sciences and Informatics (OHDSI) tools were used for the analysis.

Results

Overall, 1819 patients met the inclusion criteria in all 6 multi-national databases (Table 1).

Attrition table	CPRD Aurum EHR	CPRD GOLD EHR	MarketScan Claims	OPTUM Claims	OPTUM EHR	RWD Co EHR Claims
Total # of patients in database (in million)	39.9M	17.4M	176.9M	77.2M	41.4M	4.3M
Step 1: Inclusion criteria: At least 1 diagnosis code of Alport syndrome	542	283	2116	1613	2424	100
Step 2: Inclusion criteria: Age between 1 and 40 years	398	212	1303	784	1302	65
Step 3: Inclusion criteria: 1 year of continuous enrolment before index date ([-365,0] days)	310	153	696	370	948	35
Step 4: Study start date 01-Jan-2012	162	59	696	370	904	19
Step 5: Exclusion criteria: Exclude patients with kidney failure prior to or at index date **Final Cohort**	**158**	**58**	**585**	**314**	**688**	**16**

Table 1. Attrition table

There was a higher proportion of females with AS in all data sources except UK CPRD GOLD. In the US, patients were diagnosed with AS around the age of 20. Male patients were 7-10 years younger than females when diagnosed with AS. In the UK, patients were diagnosed with AS in their early teens. Age at diagnosis was similar in CPRD GOLD but younger for males in CPRD Aurum. Across all data sources hematuria (12-56%), proteinuria (6-44%) and kidney disease (22-69%) were common. Arterial hypertension ranged from 5 to 44%. Hearing impairment was more prevalent in males compared to females in all databases. Hematuria and kidney disease were more prevalent in females compared to males in the US. Vision impairment was prevalent in up to a quarter of patients (3-25%). Baseline treatment for AS and its cardiovascular and kidney complications was low. ACEi was the most frequently used treatment in the 90 days prior to diagnosis (16-26%) in the US and the UK. SGLT2i use in the 90 days prior to diagnosis was negligible to zero.

Conclusion

This contemporary multi-country study, one of the largest to date, provides new insights into the demographics, clinical characteristics, and treatment utilization of patients with AS. These data may be useful to gain knowledge about the disease, provide better support to clinicians and healthcare providers and most importantly, improve patient's quality of life. Additionally, this study demonstrates and emphasizes that the use of data sources standardized to the OMOP CDM and using OHDSI tools provides an excellent opportunity to gain insights into rare diseases across multiple geographies and healthcare settings in a standardized approach where contemporary real-world evidence is scarce.

References

1. Chavez E, Rodriguez J, Drexler Y, Fornoni A. Novel Therapies for Alport Syndrome. Front Med. 2022;9:1–12.
2. De Gregorio, V, Caparali, EB, Shojaei, A, Ricardo, S, Barua, M. Alport Syndrome: Clinical Spectrum and Therapeutic Advances. Kidney Med. 2023;5:100631.
3. Weinstock BA, Feldman DL, Fornoni A, Gross O, Kashtan CE, Lagas S, Lennon R, Miner JH, Rheault MN, Simon JF; Workshop Participants. Clinical trial recommendations for potential Alport syndrome therapies. Kidney Int. 2020;97:1109-1116.