End-Stage Kidney Disease (ESKD), Chronic Kidney Disease (CKD) Progression among Hispanic/Latino Population with Primary Immunoglobulin A Nephropathy (IgAN)

Kaiser Permanente Research

John J. Sim[1,2], Nancy Cannizzaro[2], Qiaoling Chen[2], Sasikiran Nunna[3], Ancilla W. Fernandes[3], Cibele Pinto[3], Mohit Mathur[4]
1. Division of Nephrology and Hypertension, Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA USA 2. Department of Research and Evaluation, Kaiser Permanente Southern California, Pasadena, CA USA 3. Otsuka Pharmaceutical Development & Commercialization, Inc., Rockville, MD USA 4. Visterra, Inc., Waltham, MA USA

ABSTRACT

Background: IgAN is the most common primary glomerulonephritis worldwide with up to 40% of IgAN patients progressing to kidney failure within 20 years following diagnosis.1 Almost all patients with IgAN are expected to progress to kidney failure during their lifetime, regardless of age or estimated glomerular filtration rate (eGFR) at diagnosis.2 IgAN is characterized by race/ethnic predilection, heterogeneity in disease progression , and potential race/ethnic variations in treatment response. Previous studies have assessed disease progression in Asian and non-Hispanic white patients; however, there remains a lack of understanding of IgAN disease progression in Hispanic/Latino patients.

Methods: In a longitudinal cohort study (1/1/2000-12/31/2021) performed within Kaiser Permanente Southern California members (age≥18 years), a subset of Hispanic/Latino patients with biopsy-proven primary IgAN were identified. Secondary IgAN was excluded. The outcome of interest was the annualized eGFR change with aggressive decline as eGFR decline >5 mL/min/1.73 m2/year. The annualized rate of change of eGFR was calculated using an ordinary least squares (OLS) regression method fitted to all eGFR readings for each patient. The slope of the regression line describes the rate of change in kidney function (eGFR) over time. Only outpatient eGFR values starting at baseline were evaluated. The composite kidney outcome was evaluated as 50% eGFR decline and end stage kidney disease (ESKD) (treatment with dialysis or transplant or reaching a sustained eGFR<15 with a confirmation using any second eGFR <15 at 30 days or more from that initial eGFR<15).

Results: A total of 262 adult Hispanic/Latino patients were identified to have biopsy-proven primary IgAN with mean (SD) age 44.8 (14) years and 51.1% males. The median (IQR) eGFR was 56.1 mL/min/1.73 m2 (36.6, 82.6) and the median (IQR) protein creatine ratio (uPCR) was 1.8 g/g (1.0, 3.2) with 74% having a uPCR >1 g/g. A total of 108 (41%) received. immunosuppressive medications. Among 262 patients with serial eGFR data, 31.3% patients had rapid decline in kidney function with eGFR decline of >5mL/min/1.73 m2/year. The mean annual eGFR (SD) decline was -4.6 (10.5). The median eGFR change among Hispanic/Latino patients was -3.1 (-6.8,-0.6) mL/min/1.73m2/year which is higher than among Asians -2.4 (-6.6, -0.4); Whites -2.2 (-7.9, 0.0); Blacks -1.5 (-4.6, 3.3). The composite kidney outcome occurred at a rate (95%CI) of 75.6 per 1000 persons-years (61.2, 93.4) with a median (IQR) time to composite outcome event of 2.8 years (0.8, 5.3). For Hispanics/Latino the median time to ESKD was 3.5 years (1.4, 7.2) and median age at ESKD was 46.1 yrs (40.2, 55.0). This was similar to KPSC Asian/Pacific Islander patients who had a median time to ESKD of 3.7 years (1.8, 7.1) and mean age at ESKD onset of 47.1 years (41.8, 60.9).

Conclusion: Our findings within a real-world setting, demonstrate that Hispanic/Latino patients with IgAN have a high rate of CKD progression and ESKD. This suggests that disease progression and severity among Hispanic/Latino patients is higher than expected. Although Asian/Pacific Islanders have been reported to have one of the fastest disease progression and burden, our study suggests that more research is needed to understand the unmet needs of Hispanic/Latino patients. This can also elucidate an understanding of whether Hispanic/Latino ethnicity is a risk factor for disease severity, ESKD and CKD progression.

REFERENCES:
1. Wyatt R.J., Julian B.A. IgA nephropathy. N. Engl. J. Med. 2013;368:2402–2414. doi: 10.1056/NEJMra1206793.
2. Pitcher D, Braddon R, Hendry B, et al. Long-term outcomes in IgA Nephropathy. Clin J Am Soc Nephrol. 2023 Jun 1;18(6):727-738.

BACKGROUND

- IgAN is the most common primary glomerulonephritis worldwide.

- It has been previously estimated that approximately 40% of IgAN patients progress to kidney failure within 20 years following diagnosis, though more recent studies suggest a more aggressive disease course.[1,2]

- Most IgAN patients progress to kidney failure, regardless of age or estimated glomerular filtration rate (eGFR) at diagnosis.[2]

- The natural history of IgAN among Hispanic/Latino patients has not been well documented in comparison to other racial/ethnic groups such as White and Asian patients.

METHODS

- A longitudinal cohort study (1/1/2000-12/31/2021) was conducted using data from Kaiser Permanente Southern California, an integrated health system in the United States.

- Hispanic/Latino patients (age≥18) with biopsy proven primary IgAN were included.

- Individuals with eGFR<15 mL/min/1.73 m2/year, on dialysis, or who had renal transplant at baseline were excluded.

We evaluated:

- The annualized eGFR change with rapid decline as eGFR decline >5mL/min/1.73 m2/year. Annualized rate of change of eGFR was calculated using an ordinary least squares regression method fitted to all eGFR readings for each patient.

- The composite of 50% eGFR decline and end stage kidney disease (ESKD) (treatment with dialysis or transplant or reaching a sustained eGFR<15 with a confirmation using any second eGFR <15 at 30 days or more from that initial eGFR<15).

Figure 1. Consort Diagram

Onset of ESKD was defined as dialysis, renal transplant, or eGFR<15

Secondary IgAN was defined as with concurrent lupus nephritis/ANCA vasculitis/IgA Vasculitis/Henoch-Schonlein purpura diagnosis included in pathology report, with IgA Vasculitis/Henoch-Schonlein purpura ICD diagnosis codes within 1-year prior to or after biopsy, or with Hepatitis B/Hepatitis C/Liver Cirrhosis/Liver transplant/Coeliac (Celiac) disease/Ulcerative colitis/Crohn's disease/Ankylosing spondylitis/Dermatitis her petiformis ICD diagnosis codes within 1-year prior to biopsy

RESULTS

Table 1. Baseline Characteristics Hispanic/Latino Adults with Primary IgAN

	N=262
Age	
Mean (SD)	44.8 (14.0)
18 to 24 years, n (%)	43 (16.4%)
25 to 44 years, n (%)	95 (36.3%)
45 to 64 years, n (%)	97 (37.0%)
65 years and over, n (%)	27 (10.3%)
Sex, n (%)	
Female	128 (48.9%)
Male	134 (51.1%)
Systolic blood pressure*, Mean (SD)	129.2 (13.1)
Diastolic blood pressure*, Mean (SD)	76.7 (8.9)
Hypertension§, n (%)	166 (63.4%)
Diabetes§, n (%)	39 (14.9%)
Coronary Artery Disease§, n (%)	4 (1.5%)
Heart failure§, n (%)	5 (1.9%)
Stroke§, n (%)	1 (0.4%)
History of Myocardial infarction§, n (%)	4 (1.5%)
Atrial Fibrillation§, n (%)	5 (1.9%)
Peptic ulcer§, n (%)	1 (0.4%)
Hematuria§, n (%)	124 (47.3%)
Baseline eGFR*‡	
Mean (SD)	62.3 (31.5)
Median (IQR)	56.1 (36.6, 82.6)
90+, n (%)	56 (21.4%)
60-89, n (%)	63 (24.0%)
45-59, n (%)	42 (16.0%)
30-44, n (%)	66 (25.2%)
15-29, n (%)	35 (13.4%)
Treatment with immunosuppressive agents†, n (%)	108 (41.2%)
ACEI§, n (%)	127 (48.5%)
ARB§, n (%)	53 (20.2%)
GLP-1§, n (%)	0 (0.0%)
SGLT-2i§, n (%)	1 (0.4%)
Baseline urine protein creatinine ratio (UPCR)#	
Mean (SD)	2.6 (2.5)
Median (IQR)	1.8 (1.0, 3.2)
<0.5, n (%)	32 (12.2%)
0.5-<1, n (%)	27 (10.3%)
1-2, n (%)	74 (28.2%)
>2, n (%)	114 (43.5%)
Unknown, n (%)	15 (5.7%)

*Based on the most recent record within 1-year prior to or as of renal biopsy.

§Comorbidity and medication were based on data within 1-year prior to or as of renal biopsy.

†With immunosuppressive agents during 4-week prior to and 1-year post renal biopsy.

‡Measurements at inpatient setting were excluded. #Record measured closest to renal biopsy during 1-year before and 30-day after biopsy was retained. Urine albumin-creatinine ratio and total urine protein within 24hour were converted to UPCR by divided by 700 and 1000, respectively.

Table 2. Annual eGFR Decline among Hispanic/Latino IGAN patients

	N=262
Annual eGFR change	
Mean (SD)	-4.6 (10.5)
Median (IQR)	-3.1 (-6.8, -0.6)
Unknown	23
Annual eGFR decline >5mL	
No	157 (59.9%)
Yes	82 (31.3%)
Unknown	23 (8.8%)

The slope of the regression line describes the rate of change in kidney function (eGFR) over time. Only outpatient eGFR values starting at baseline were evaluated.

Table 3. Composite Kidney Outcome (50% eGFR decline or ESKD)

	Total f/u time (years)	Median f/u time (years) median (IQR)	No. of events	Incidence rate /1000 py median (IQR)	Time to event (years) median (IQR)	Age at event median (IQR)
Composite kidney outcome	1217	3.3 (1.4, 6.7)	92	75.6 (61.2, 93.4)	2.8 (0.8, 5.3)	46.3 (39.8, 54.9)

f/u: follow-up; py: person-year; IQR: interquartile
50% eGFR decline was defined as first eGFR decline>=50% with a confirmation using any second eGFR decline >= 50% at 30days or more from that initial 50% decline

Table 4. ESKD Only as Outcome: Hispanic/Latino

	Total f/u time (years)	Median f/u time (years) median(IQR)	No. of events	Incidence rate /1000 py median(IQR)	Time to event (years) median(IQR)	Age at event median (IQR)
ESKD	1256	3.5 (1.4, 7.2)	79	62.9 (50.1, 78.9)	2.8 (0.8, 5.6)	46.1 (40.2, 55.0)

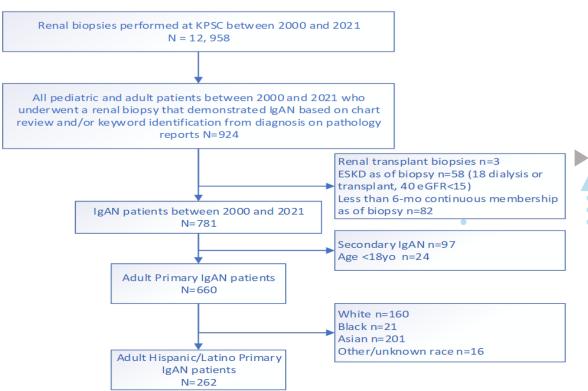f/u: follow-up; py: person-year; IQR: interquartile

- 262 adult Hispanic/Latino patients were identified to have biopsy-proven primary IgAN with mean (SD) age 44.8 (14) years and 51.1% males.
- The median (IQR) eGFR was 56.1 mL/min/1.73 m2 (36.6, 82.6) and the median (IQR) protein creatine ratio (uPCR) was 1.8 g/g (1.0, 3.2) with 74% having a uPCR ≥1 g/g. A total of 108 (41%) received. immunosuppressive medications.
- Among 262 patients with serial eGFR data, 31.3% patients had rapid decline in kidney function with eGFR decline of >5mL/min/1.73 m2/year.
- The mean annual eGFR (SD) decline was -4.6 (10.5).
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- The composite kidney outcome occurred at a rate (95%CI) of 75.6 per 1000 persons-years (61.2, 93.4) with a median (IQR) time to composite outcome event of 2.8 years (0.8, 5.3).
- For Hispanics/Latino the median time to ESKD was 3.5 years (1.4, 7.2) and median age at ESKD was 46.1 yrs (40.2, 55.0).
- This was similar to KPSC Asian/Pacific Islander patients who had a median time to ESKD of 3.7 years (1.8, 7.1) and mean age at ESKD onset of 47.1 years (41.8, 60.9).

CONCLUSIONS

- In a real-world clinical environment based in the United States, we observed that Hispanic/Latino patients with primary IgAN are biopsy diagnosed at relatively advanced stages of CKD in terms of eGFR and proteinuria.
- Our findings demonstrate a high rate of CKD progression along with ESKD among this population.
- Compared to Hispanics, Asian/Pacific Islander had similar sex/gender ratio and a median time to ESKD of 3.0 years and mean age at ESKD onset of 47 years.
- Asian/Pacific Islanders have been associated with higher risk disease progression and burden,[2] and our study suggests that Hispanic/Latino patients with IgAN may have a similar clinical course.

References:
1. Wyatt R.J., Julian B.A. IgA nephropathy. N. Engl. J. Med. 2013;368:2402–2414. doi: 10.1056/NEJMra1206793.
2. Pitcher D, Braddon R, Hendry B, et al. Long-term outcomes in IgA Nephropathy. Clin J Am Soc Nephrol. 2023 Jun 1;18(6):727-738.

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