Real-World Healthcare Utilization and Clinical Markers Preceding Dialysis in Patients with Primary Hyperoxaluria (PH) in the United States

Elnara Fazio-Eynullayeva[1], John Karafilidis[2], Lisa Mucha[2], Pamela Blumberg[1], Seth Kuranz[1]

[1]TriNetX, LLC, Cambridge, MA, USA; [2]Dicerna Pharmaceuticals Inc, Lexington, MA, USA

BACKGROUND

- Primary hyperoxaluria (PH) is a group of rare genetic disorders marked by the accumulation of oxalate resulting in urolithiasis, nephrocalcinosis, chronic kidney disease (CKD), and for a subset of patients eventually end-stage renal disease (ESRD).[1,2]
- ESRD in patients with PH is commonly treated with dialysis, kidney transplant, and dual kidney/liver transplant.[3]

OBJECTIVE

- The objective of this study was to examine demographics, clinical characteristics, and healthcare utilization among dialysis-treated PH patients during the time leading up to dialysis start and healthcare utilization, clinical outcomes, and costs following dialysis start.

METHODS

Study Design

- This was a real-world retrospective observational study using deidentified PH patient electronic medical record (EMR) data.
- The EMR data came from the TriNetX Dataworks USA Network, a federated network of 44 Healthcare Organizations (HCOs) across the U.S. treating 65+ million de-identified patients at the time of study conduct.

Study Population

- The EMR data of patients with a record of PH diagnosis (ICD-10 code E72.53) on or after October 1, 2018 and at least one encounter for hemodialysis or peritoneal dialysis (Figure 1) was extracted for analysis.

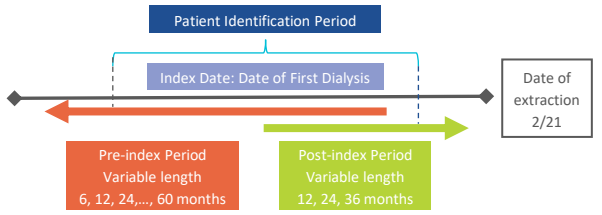
Figure 1. Deidentified Sample Construction

5,011	≥1 encounter with a diagnosis code for primary hyperoxaluria (PH) at any time
730	PH diagnosis on or after October 1, 2018
652	Treated at a Dataworks' HCO contributing both inpatient and outpatient EMR data
58	≥1 encounter(s) specific to hemodialysis or peritoneal dialysis
47	≥1 encounter(s) ≥6 months prior to first dialysis date of service
47	Not enrolled in a clinical trial any time during the study period

Study Period

- The deidentified patient record was entered into the study sample on the date of the first recorded encounter for dialysis during Jan. 2010 – Jan.2021. This date is referred to as the index date (Figure 2).
- The pre-index study period was up to 5 years prior to that date, not including the index date.
- The post-index study period was up to 3 years after and included the index date .

Figure 2. Study Time Period



METHODS CONTINUED

Study Measures

- Measures reported in the pre-index period are:
  - Demographic characteristics (age, sex, and race)
    - Captured on the index date
  - Comorbidities were assessed using the Liu Comorbidity Index (Liu CI) developed specifically for use in studies of dialysis patients[4]
    - We used the version of the score which does not incorporate the cause of ESRD; therefore, the possible range of scores was 0-21
  - Kidney stone events (KSE) and healthcare resource utilization (HCRU) were assessed at multiple timepoints in the pre-index period
    - The entire pre-index period, and at 6 months, 1 year, 2 years, 3 years, 4 years and 5 years pre-index
- Measures reported in the post-index period are:
  - Healthcare utilization costs assessed at multiple timepoints during the post-index period
    - 1 year, 2 years, and 3 years post-index
  - Transplant failure among those with a transplant.

Statistical Analyses

- Counts and percentages are reported for categorical measures
- Mean and standard deviations (SD) are reported for continuous measures
- Transplant failure is captured using Kaplan-Meier curves by type of transplant (kidney only vs. dual kidney and liver)

RESULTS

Patient Characteristics

- Of the 47 patients who met the study criteria, the mean (SD) age was 58.7 (14.8) years, 53% were female, and 85% were white (Table 1).
  - Among these patients, 42 (89.4%) had their EMR going back 1 year, 35 (74.5%) going back 2 years, 32 (68.1%) going back 3 years, 31 (66.0%) going back 4 years, and 27 (57.4%) going back 5 years
- Only 22 patients (46.8%) had a recorded diagnosis of PH prior to the start of dialysis.

Pre-Index Healthcare Resource Utilization

- During the 6 months immediately preceding dialysis, 91% of patients had ≥1 outpatient office visit, 17% ≥1 emergency department visit, and 53% ≥1 inpatient stay (Figure 3).
- During the entire 5-year pre-index period, 98% of patients had ≥1 physician office visit, 51% ≥1 emergency department visit, and 70% ≥1 inpatient stay.

Kidney Stone Events

- 19 (40.4%) patients had ≥1 KSE during the variable pre-index period (Table 2).
- The mean number of KSEs was 4.2 (15.0) among those with ≥1 KSE.
- The frequency of KSEs (number of events per year) doubled from 1 to 2 per person per year as patients neared dialysis.

Post-Index Healthcare costs

- For all patients, mean health care costs were $217,784 ($515,809), $291,236 ($596,074), and $353,852 ($699,749) in the 1, 2, and 3-year post-index periods.
- High costs were driven by inpatient admissions.

Transplant Failure

- Transplant failure was observed in 15 (65.2%) of the 23 patients with a transplant including 1 of 5 (20.0%) patients with a dual kidney/liver transplant and 14 of 18 (77.8%) of patients with a kidney transplant (Figure 4).

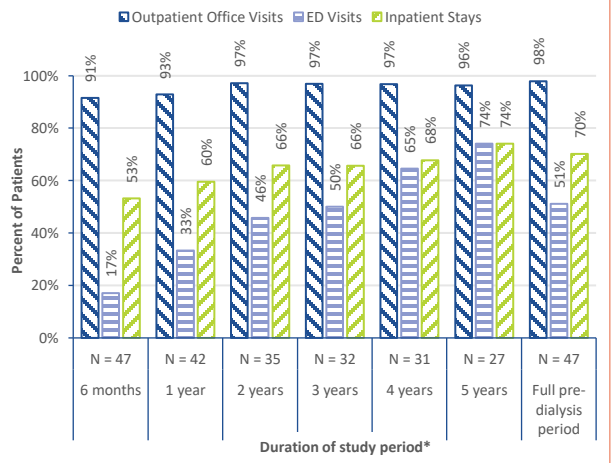
LIMITATIONS

- The main study limitation is that the dataset does not capture dialysis treatments received at dialysis centers not owned by the HCO contributing the EMR data, so our study results may be underestimated.
- Patients may have received additional healthcare services outside of their index HCO which would not be captured in this analysis

Table 1: Patient Characteristics

	PH Patients N = 47
Age at index, mean (SD)	58.7 (14.8)
Female sex, mean (SD)	25 (53.2)
Race, n (%)	
White	40 (85.1)
Black or African American	4 (8.5)
Other	0 (0.0)
Unknown	3 (6.4)
Pre-index PH diagnosis, n (%)	22 (46.8)
Liu CI Score, mean (SD)	4.9 (5.0)
Min-Max	0-19
Top 5 Liu Comorbidities, n (%)	
Diabetes	23 (48.9)
Dysrhythmia	16 (34.0)
Other cardiac disease	15 (31.9)
Congestive heart failure	12 (25.5)
Peripheral vascular disease	11 (23.4)
Transplant (any)	23 (48.9)
Kidney only	18 (38.3)
Dual kidney and liver	5 (10.6)

Figure 3. Healthcare Resource Utilization in the Pre-index Period



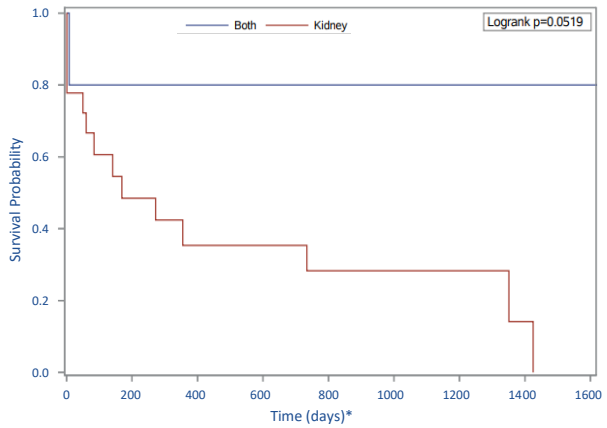
*Study period cohorts are not mutually exclusive and patients are included in each cohort for which they have sufficient pre-index data.

Table 2: Prevalence and Number of Kidney Stone Events (KSEs) in the pre-index period*

	Full pre-dialysis period N = 47	6 months N = 47	1 year N = 42	2 years N = 35	3 years N = 32	4 years N = 31	5 years N = 27
≥1 KSE, n (%)	19 (40.4)	10 (21.3)	11 (26.2)	10 (28.6)	9 (28.1)	11 (35.5)	10 (37.0)
Number of KSEs, mean (SD)	4.2 (15.0)	1.0 (3.5)	1.9 (6.4)	2.5 (8.0)	3.4 (10.2)	4.9 (14.5)	5.5 (15.4)
KSEs per year, mean	n/a	2.0	1.9	1.3	1.1	1.2	1.1

*Study period cohorts are not mutually exclusive and patients are included in each cohort for which they have sufficient pre-index data.

Figure 4: Kaplan-Meier curve of transplant failure



*Time to transplant failure was calculated from index date (first dialysis date of service).

CONCLUSIONS

- In this real-world study, delayed diagnosis was observed with more than one-half of patients with no recorded PH diagnosis until after initiating dialysis
- In addition, high rates of costly HCU, including ED visits and inpatient stays, were observed during the same timeframe
- Healthcare costs were substantial, exceeding $200,000 in the first year following the start of dialysis.
- The number of KSEs increased over the study period, which may be indicative of worsening renal function due to PH prior to dialysis

REFERENCE

1. Zhao F, Bergstralh EJ, Mehta RA, et al. Predictors of Incident ESRD among Patients with Primary Hyperoxaluria Presenting Prior to Kidney Failure. Clin J Am Soc Nephrol. 2016;11(1):119-126. doi:10.2215/CJN.02810315
2. Shah RJ, Vaughan LE, Enders FT, Milliner DS, Lieske JC. Plasma Oxalate as a Predictor of Kidney Function Decline in a Primary Hyperoxaluria Cohort. International Journal of Molecular Sciences. 2020;21(10):3608. doi:10.3390/ijms21036084
3. Hoppe B, Beck BB, Milliner DS. The primary hyperoxalurias. Kidney Int. 2009;75(12):1264-1271. doi:10.1038/ki.2009.322.
4. Liu J, Huang Z, Gilbertson DT, Foley RN, Collins AJ. An improved comorbidity index for outcome analyses among dialysis patients. Kidney Int. 2010;77(2):141-151. doi:10.1038/ki.2009.4133.

Presented at ASN Kidney Week 2021, November 2-7, 2021.

Disclosure: Medical writing support was provided by Jessamine Winer-Jones of TriNetX, LLC and was funded by Dicerna Pharmaceuticals.
Study Funding: Study funded by Dicerna Pharmaceuticals, Inc. Lexington, MA, USA