

BACKGROUND

- Primary hyperoxaluria (PH) is a family of rare genetic disorders.¹
- PH causes hepatic oxalate overproduction that may lead to frequent kidney stone events, progression to chronic kidney disease (CKD) and end-stage kidney disease (ESKD), and then other systemic morbidities.^{2,3}
- While the extent of the morbidity of PH is being further established, even less is known about the real-world experience of patients with each type of PH and their caregivers experience.

OBJECTIVE

- To assess the burden of PH among patients and caregivers with respect to healthcare resource utilization (HRU), health-related quality of life (HRQOL), and activity level (e.g., work productivity and school attendance).

METHODS

Study Design

- A cross-sectional, web-based survey was conducted among adults (≥18 years) with PH and caregivers of up to 2 children (≤17 years) with PH in the United States (US).
- The study received ethics-board approval from the New England Independent Review Board and the survey was administered from June 1 to September 4, 2020.

Recruitment

- Individuals who indicated their interest in participating in research about the burden of PH were invited to participate; these individuals were recruited through a patient panel, social media, and hyperoxaluria advocacy group newsletters.
- Participants received an honorarium for their time.

Outcomes

- Participants were asked about their and/or their child's demographics, medical care, HRU, HRQOL, and work productivity or school attendance through a series of survey questions and the following two patient-reported outcome instruments:

- The Kidney Disease Quality of Life (KDQOL-36™),⁴ a HRQOL measure that has been used in individuals with chronic kidney disease and those undergoing dialysis, was administered to adult patients.
 - The KDQOL-36™ is a 36-item validated questionnaire that contains the following domains: SF-12[®] Physical Component Summary (PCS), SF-12[®] Mental Component Summary (MCS), burden of kidney disease, symptoms/problems of kidney disease, and effects of kidney disease.
 - Five scores were generated, all ranging from 0 to 100 with higher scores indicating better HRQOL; PCS and MCS scores are normed to the US population (mean=50, Standard Deviation [SD]=10).

- The Work Productivity and Activity Impairment (WPAI)⁵ was administered to both adult patients and caregivers to assess impact on work productivity and activity due to PH over the previous 7 days.
 - The WPAI is a validated questionnaire that yields 4 types of scores expressed as impairment percentages:
 - Absenteeism (work time missed)
 - Presenteeism (impairment while at work)
 - Work productivity loss (overall work impairment)
 - Activity Impairment (impairment in regular daily activities)
 - All WPAI scores range from 0 to 100% with higher scores indicating more impairment and less productivity.

Data Analysis

- Outcomes were summarized using descriptive statistics; means and SD for continuous variables, and frequency counts and percentages for categorical variables.

RESULTS

Patient Characteristics (Table 1)

- The patient sample was comprised of 21 patients.
- All PH types were represented including patients who had PH2 (14%) and PH3 (14%).
 - PH type was not known for two patients (10%).

Caregiver Characteristics (Table 2)

- Responses for the 14 children came from 13 caregivers who had a median age of 38 years (range 27-50).
- The majority of caregivers were employed (69%).

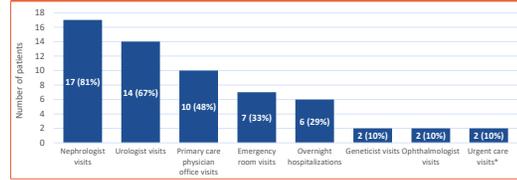
Healthcare Resource Utilization

- Over the prior 6 months, PH patients visited numerous types of health care specialists including nephrologists (81%), urologists (67%), and ophthalmologists (10%), and over a quarter (29%) were hospitalized (Figure 1).
- PH patients visited the emergency room most frequently for pain (43%), fever (29%), infection (29%), dehydration (14%), kidney stones (14%), hyperemesis (14%), and swelling (14%).
- Management of PH required a substantial time investment for patients and caregivers as the median distance and time spent traveling to reach the patients' farthest PH-related medical provider was 50 miles and 90 minutes, respectively.

Dialysis Use

- Approximately one quarter (24%) of the patient sample (4 children and 1 adult) were either on hemodialysis (n=3) or peritoneal dialysis (n=2), which required a substantial investment of time for treatment with a median of 24 hours per week (range 18-36).

Figure 1. Types of Health Care Services Utilized by PH Patients for PH-Related Medical Care in Past Six Months (n=21)



*Free-standing centers

Table 1. Characteristics of PH Patients (n=21)

Characteristics	Number (%)
Female	15 (71)
Age, years	
0-17	14 (67)
18-46	7 (33)
PH type	
Type 1	13 (62)
Type 2	3 (14)
Type 3	3 (14)
Unknown*	2 (10)
Employed among adult patients (n=7)	4 (57)
Age at diagnosis, years (median, range)	5.0 (0.2-62.0)
Health insurance	
Private insurance	12 (57)
Medicaid/CHIP	4 (19)
Medicare	1 (5)
VA or DOD or Tricare	1 (5)
No health insurance	2 (10)
Prefer not to answer/I do not know	1 (5)

Abbreviations: CHIP=Children's Health Insurance Program; DOD=Department of Defense; PH=Primary Hyperoxaluria; VA=Veterans Affairs. *PH type not known at the time of survey administration

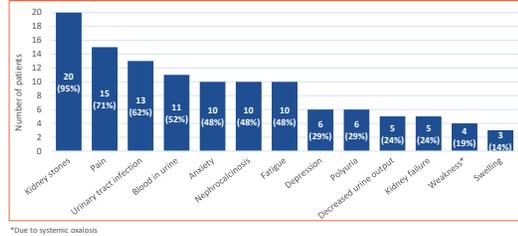
Table 2. Characteristics of Caregivers (n=13)

Characteristics	Number (%)
Female	12 (92)
Age, years (median, range)	38 (27-50)
Main caregiver	
Yes	6 (46)
Share caregiving responsibilities equally with another caregiver	7 (54)
Employed	9 (69)

PH-related Complications

- Patients had experienced many PH-related complications in their lives including kidney stone events (95%), pain (71%), and urinary tract infections (62%); many also experienced anxiety about their PH (48%) (Figure 2).
- 35% of patients experienced kidney stone events more than once a year, and the majority (80%) had moderate or severe pain from their last kidney stone event.
- Approximately half of the kidney stone events experienced by patients over the previous 5 years required stone removal procedures, such as lithotripsy, percutaneous nephrolithotomy, and ureteroscopy.

Figure 2. Symptoms and Complications Ever Experienced by PH Patients (n=21)



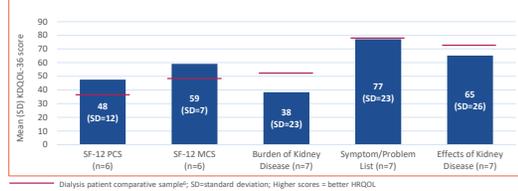
*Due to systemic oxalosis

Health-Related Quality of Life

Patient Reported Quality of Life

- The mean scores by domain for the KDQOL-36™ are found in Figure 3.
- Comparative samples from the existing KDQOL-36™ literature were sought to provide context to these scores. Adults with PH (n=6) reported better SF-12[®] PCS and MCS scores, but worse kidney-related domain scores relative to a sample of US dialysis⁶ patients identified from the literature.

Figure 3. Mean (SD) KDQOL-36™ Scores for Adult PH Patients



Dialysis patient comparative sample; SD=standard deviation; Higher scores = better HRQOL

REFERENCES

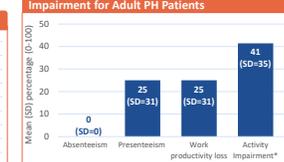
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Caregiver Reported Quality of Life

- Over half of caregivers reported experiencing moderate to severe anxiety about the possibility of future PH-related outcomes for their child: kidney stones (54%), kidney disease progression (62%), and ESKD (62%).
- Caregivers reported that PH impacted both their sleep (median=3.0 nights/week; range 0-7) and their children's sleep (median=3.5 nights/week; range 0-7).

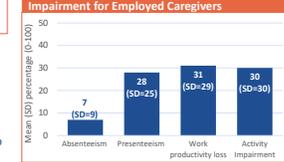
Work Productivity

Figure 4. Work Productivity and Activity Impairment for Adult PH Patients



*Activity impairment assessed in all PH patients (n=7)
SD=standard deviation; Higher scores = more impairment/less productivity

Figure 5. Work Productivity and Activity Impairment for Employed Caregivers



SD=standard deviation; Higher scores = more impairment/less productivity

Patients

- Employed adults with PH (n=4), reported a mean presenteeism and overall work productivity loss of 25%; no absenteeism was reported (Figure 4).
- Adults with PH reported activity impairment at 41%.

Caregivers

- Employed caregivers (n=9), reported experiencing an impairment in work and activity due to their children's PH, ranging from 7% to 31% (Figure 5).

Impact on School

- Of the children who attended school (n=11), a median of 15 hours (range 0-40) of class was missed in a typical month due to their PH.

CONCLUSIONS

- This research quantifies the burden of PH experienced by patients and caregivers.
- Numerous clinician visits, ER visits, hospitalizations, and time spent receiving dialysis reflected the burden associated with managing PH.
- The burden of PH extends beyond the patient, as evidenced by the burden experienced by caregivers, including anxiety, sleep loss, work productivity loss, and impact on activities.
- In addition to patients reporting multiple clinical sequelae associated with PH, such as kidney stone events and pain, the results of this research demonstrate that both patients and caregivers can experience substantial burden related to HRU, HRQOL, and productivity.

Limitations

- Since this research was conducted during the COVID-19 pandemic, HRU and work productivity findings are likely underestimated.
- As anticipated, the sample size was small due to PH being a rare disease; as such, statistical testing was not performed.

Disclosures: DSG has provided research services to Dicerna Pharmaceuticals, Inc., consulting services to Alnylam Pharmaceuticals and Synlogic, and is an owner and patent holder of Dr. Amies, Inc.; FM has provided research services to Dicerna Pharmaceuticals, Inc., and consulting services to Transer Therapeutics; SRL was a paid employee of Dicerna Pharmaceuticals, Inc. at the time this study was conducted; LM is a paid employee of Dicerna Pharmaceuticals, Inc.; CF is a paid employee of Stratevi who received funding from Dicerna Pharmaceuticals, Inc. for conducting this study.
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