Changes in Acute Hepatic Porphyria Health Impacts Since Initial Diagnosis: Results from the Porphyria Worldwide Patient Experience Research (POWER) Study

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Conclusions

- **Patients with AHP experience negative impacts across multiple health domains and worsening in some disease characteristics since initial diagnosis**
- **Results from this cohort of patients with AHP suggest patients with a longer duration of disease activity (≥6 years) had poorer perceived health status than patients with shorter disease activity (0–5 years)**

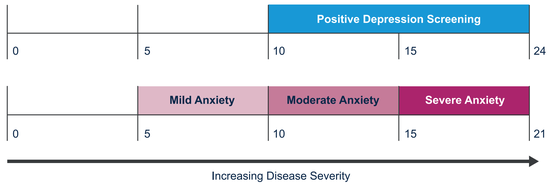
Introduction

- Acute hepatic porphyria (AHP) is a rare and potentially life-threatening inherited disease caused by genetic mutations in the heme biosynthetic enzymes affecting the liver[1]
- Patients can experience acute neurovisceral attacks, chronic symptoms, long-term complications, and negative impacts on many quality-of-life domains
- Despite the long-term nature of some consequences of AHP, limited evidence is available on disease changes and impacts on patient health over time
- This study evaluated AHP patients' perceptions of changes in their disease characteristics and impacts on quality-of-life domains since AHP diagnosis among the overall study population and in subgroups based on time since first symptoms/diagnosis

Methods

- Adults with >1 AHP attack within the past 2 years or receiving intravenous hemin and/or glucose for attack prevention were recruited via patient advocacy groups and physician referral from the United States, Italy, Spain, Australia, Mexico, and Brazil
  - Patients taking givosiran were excluded
- Patients were administered an online survey from January 19 to April 26, 2021 to evaluate perceptions of changes in overall health and disease characteristics since diagnosis/disease onset
  - Data analysis was conducted only for patients who completed the entire survey
- Subgroup analyses were conducted to evaluate differences in patients experiencing active disease for 0–5 years versus those experiencing active disease for ≥6 years
- Demographic and disease characteristics were evaluated descriptively among the overall and subgroup patient populations
- Patient-reported outcomes (PROs) to evaluate anxiety and depression were assessed among subgroups using the 7-item Generalized Anxiety Disorder (GAD-7) scale (0–21) and the 8-item Patient Health Questionnaire (PHQ-8) depression scale (0–24), respectively (**Figure 1**)

Figure 1. PHQ-8 and GAD-7 Scales



Results

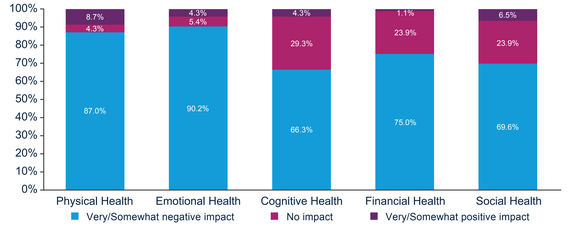
- A total of 92 patients with AHP completed the survey. Their mean age was 41.1 years, and 90% of the patients were women (**Table 1**)
- In the overall population, the mean time to diagnosis was 6.4 years, and the mean duration of disease was 16.9 years (**Table 1**)

Table 1. Patient Demographics and Health Characteristics

Characteristic	Total Sample (N=92)
Age, years, mean (SD)	41.1 (12.4)
Female, n (%)	83 (90.2)
Diagnosis, n (%)	
Acute intermittent porphyria	68 (73.9)
Hereditary coproporphyria	12 (13.0)
Variegate porphyria	9 (9.8)
5-Aminolevulinic acid dehydratase deficiency porphyria	1 (1.1)
Age at diagnosis, mean (SD), years	30.8 (10.8)
Age at first symptoms, mean (SD), years	24.3 (10.7)
Time to diagnosis, mean (SD), years	6.4 (10.1)
Duration of disease, mean (SD), years	16.9 (13.0)
AHP attacks within past 2 years, median (IQR)	4.5 (2, 12)
AHP attacks leading to hospitalization, median (IQR)	2.0 (0, 3)

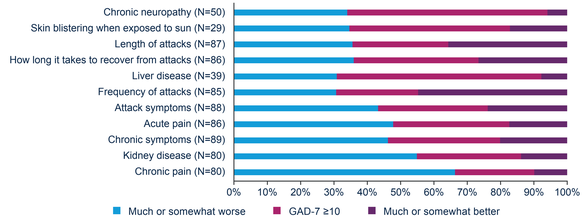
- Most patients experienced negative (very or somewhat negative) impacts on emotional health (90%), physical health (87%), financial health (75%), social health (70%), and cognitive health (66%) since their diagnosis (**Figure 2**)

Figure 2. Impact of AHP on Health Domains over Time



- Patients described disease characteristics as worsening (much worse or somewhat worse) since their diagnosis, including chronic pain (66%), kidney disease (55%), and acute pain (48%) (**Figure 3**)

Figure 3. Patient Perceptions of Changes in Disease Characteristics Since Disease Onset



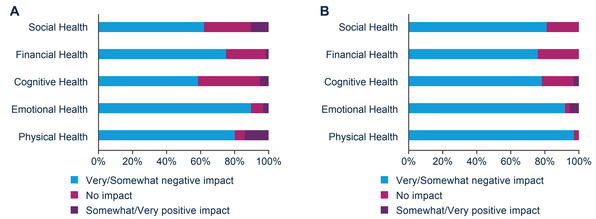
- In subgroup analyses, 22% (N=20) of patients were found to have had active disease for 0–5 years, and 73% (N=67) had active disease for ≥6 years (**Table 2**)
- Patients with active disease for 0–5 years were younger on average than patients with active disease for ≥6 years (33.9 vs 43.4 years, respectively) (p=0.002; **Table 2**)
- Patients with active disease for 0–5 years experienced a median of 2.5 attacks within the past 2 years, whereas patients with active disease for ≥6 years experienced a median of 5 attacks within the past 2 years (**Table 2**)

Table 2. Subgroup Demographics and Health Characteristics

Characteristic	Duration of Active Disease	
	0–5 Years (N=20), n (%)	≥6 Years (N=67), n (%)
Age, years, mean (SD)	33.9 (10.6)	43.4 (12.3)
Female, n (%)	17 (85)	61 (91)
Diagnosis, n (%)		
Acute intermittent porphyria	16 (80)	49 (73.1)
Variegate porphyria	0	8 (11.9)
5-Aminolevulinic acid dehydratase deficiency porphyria	1 (5)	0
AHP attacks within past 2 years, median (IQR)	2.5 (1, 7.5)	5 (2, 15.0)
AHP treatment, n (%)		
Hemin, routine or scheduled	4 (20.0)	17 (25.4)
Hemin, on-demand, as needed for an attack	9 (45.0)	26 (38.8)
IV glucose, routine or scheduled	3 (15.0)	14 (20.9)
IV glucose, on-demand, as needed for an attack	13 (65.0)	37 (55.2)

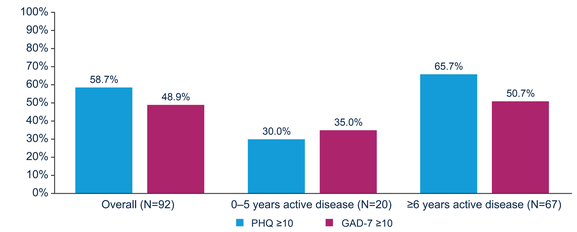
- Patients with longer active disease more often reported a very or somewhat negative impact over time on most measured health domains compared with patients with shorter duration of active disease (p>0.05 for all domains; **Figure 4**)

Figure 4. Patient Perceptions of Changes in Disease Characteristics Since Disease Onset among Patients with Active Disease for (A) 0–5 Years and (B) 6+ Years



- 35% of patients experiencing AHP for 0–5 years reported a GAD-7 score ≥10, compared with 51% of patients experiencing AHP for ≥6 years (p=0.216; **Figure 5**)
  - Severe anxiety (GAD-7 score ≥15) was reported in 20% and 28% of these patients, respectively
- On the PHQ-8 scale, 30% of patients experiencing AHP for 0–5 years reported a score ≥10, indicating moderate-to-severe depression, compared with 66% of patients experiencing AHP for ≥6 years (p=0.005; **Figure 5**)

Figure 5. PHQ-8 and GAD-7 Scores



Limitations

- PROs evaluated in this study are limited by incomplete data and the subjective nature of reporting
- This study presents survey data and thus may be subject to response bias

Disclosures: Stephen Meninger is employed by and owned stock and stock options in Alnylam Pharmaceuticals. **Danielle Nance** served on advisory boards for Aptevo, BPL, Goval, HemaBiologics, Medexus, and Spark; served on the speaker bureau for Alnylam Pharmaceuticals; and received grant/research funding and consulting honoraria for participation in this research from Alnylam Pharmaceuticals. **Desiree Lyon** received grant and sponsorship funding to the American Porphyria Foundation from Alnylam Pharmaceuticals. **Sean Hegarty, Rocco Falchetto, Jasmin Barman-Aksözen,** and **Tarek Mnif** reported having nothing to disclose. **Stephen Lombardelli** is employed by and owned stock and stock options in Alnylam Pharmaceuticals. **Amy Dickey** served on the advisory board for and received funding for conference travel and consulting honoraria from Alnylam Pharmaceuticals.
Abbreviations: AHP, acute hepatic porphyria; GAD-7, Generalized Anxiety Disorder-7; IQR, interquartile range; IV, intravenous; PHQ-8, Patient Health Questionnaire-8; PRO, patient-reported outcome; SD, standard deviation.
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Reference: 1. Wang B. *Transl Gastroenterol Hepatol.* 2021;6:24.
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