

# POWER Study (Porphyria Worldwide Patient Experience Research): Patient Impact of Acute Hepatic Porphyria

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## Conclusions

- Most acute hepatic porphyria (AHP) patients from this global patient survey reported significant impact in multiple domains of emotional, mental, and physical health including, chronic pain, employment and work productivity, depression, and anxiety
- Results from standardized patient reported outcomes instruments suggest the AHP patient population has comparable pain and work productivity impairment to that of other severe chronic conditions
- A majority of AHP patients suffer significant mental health burden based on standardized patient reported outcome instruments intended to screen for anxiety and depression

## Background and Rationale

### Acute Hepatic Porphyria (AHP)

- AHP refers to a family of rare, genetic diseases due to a deficiency in one of the enzymes involved in heme biosynthesis in the liver<sup>1,2</sup>
  - Acute intermittent porphyria (AIP) is the most common type, with mutation in the hydroxymethylbilane synthase (HMBS) gene<sup>3,4</sup>
- AHP is associated with life-threatening attacks and, for some patients, chronic debilitating symptoms that negatively impact daily functioning and quality of life<sup>5</sup>
- AHP disproportionately impacts women of working and childbearing age, and diagnosis is often delayed<sup>5,6</sup>
- Prior to the US approval of givosiran for the treatment of AHP in adults in 2019, treatment of AHP primarily relied on symptomatic management of attacks, including hemin and glucose<sup>6-8</sup>
- Previous research suggests AHP limits patients' ability to function normally in daily living, negatively impacts their personal relationships with others, and leads to poor quality of life outcomes<sup>2,5,9-12</sup>

### Objective

- To bring to light the emotional, mental, and physical burden of AHP on the individual and their social circle

## Methods

### Global Patient Survey

- Adult patients from the US, Italy, Spain, Australia, Mexico, and Brazil diagnosed with AHP were recruited and took part in an online, self-assessed survey between January 19, 2021 and April 26, 2021
- Patients who experienced at least one AHP attack in the past two years or were receiving hemin and/or glucose for attack prevention were included. Patients receiving givosiran were excluded
- The survey included standardized patient reported outcome scales and de novo items regarding impact of living with AHP, disease treatment and management, employment and support system, family planning, and pain
- Descriptive analyses were conducted with the overall sample of patients who completed all questions (e.g., demographics, health characteristics, disease history, standardized patient reported outcomes scales, etc.)

### Standardized Patient Reported Outcomes

- The Patient Health Questionnaire-8 (PHQ-8) and the Generalized Anxiety Disorder-7 (GAD-7) scales are validated measures for assessing depressive and general anxiety symptom severity, respectively<sup>13,14</sup>
- Scores on the PHQ-8 can range from 0-24, with higher scores indicating greater depressive symptom severity, and scores  $\geq 10$  indicate a positive screen for major depressive disorder (Figure 1)
- Scores on the GAD-7 range from 0-21, with higher scores indicating greater anxiety symptom severity, and scores of 5, 10, and 15 represent cutoff scores for mild, moderate, and severe anxiety, respectively (Figure 1)

Figure 1: PHQ-8 and GAD-7 Scores

PHQ-8	Increasing Disease Severity			
	Minimal Depression	Mild Depression	Moderate Depression	Severe Depression
0	5	10	15	24
GAD-7	Increasing Disease Severity			
	Minimal Anxiety	Mild Anxiety	Moderate Anxiety	Severe Anxiety
0	5	10	15	21

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Disclosures: AD and SM received consulting honorarium from Alynam Pharmaceuticals, Inc. for their participation in this research. AHP has received grant and sponsorship funding from Alynam Pharmaceuticals, Inc. SM, ML, JM, and JK are employees and shareholders of Alynam Pharmaceuticals. SJ is a contractor of Alynam Pharmaceuticals. MD, AB, JM, and TM are employees of Kantar Health. Abbreviations: AHP, acute hepatic porphyria; AIP, acute intermittent porphyria; PHQ-8, patient health questionnaire-8; GAD-7, general anxiety disorder-7; WHYMPI, West Haven-Yale multidimensional pain inventory; WPAI, work productivity and activity impairment; SD, Standard Deviation; IQ, Interquartile; RA, rheumatoid arthritis; IBS, irritable bowel syndrome

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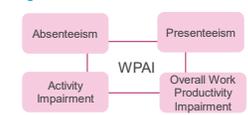
## Methods (cont.)

- The West Haven-Yale Multidimensional Pain Inventory (WHYMPI) (Figure 2) is a measure designed to examine the impact of chronic pain on patients' lives<sup>15</sup>
  - Pain is measured on multiple dimensions with individual subscales (each scored 0-6) that have been validated. Higher scores indicate a higher intensity in that subscale
- The Work Productivity and Activity Impairment (WPAI) scale (Figure 3) is a 6-item validated instrument that measures 4 domains (related to the effect of health problems on the ability to work and perform regular activities) with a 1-week recall period<sup>16</sup>
  - The WPAI yields scores on absenteeism (work time missed), presenteeism (impairment at work), work productivity loss (overall work impairment), and activity impairment
  - Higher values, in the form of percentages (0-100%), indicate greater impairment due to the respondent's health

Figure 2: WHYMPI Subscales



Figure 3: WPAI Domains



## Results

### Demographics and Disease Characteristics

- Ninety-two AHP patients completed the survey, mean (SD) age 41.1 (12.4) years, 90.2% female, and 73.9% AIP (Table 1)
- Patients experienced a median of 4.5 attacks in the past 2 years (Table 1)
- The most common AHP treatments included trigger avoidance (64.1%), on-demand IV glucose (56.5%), on-demand IV hemin (39.1%), and routine or scheduled hemin (23.9%)<sup>9</sup>
- The mean time from first symptom to diagnosis was 6.4 years, while mean duration of active disease was 16.9 years

Table 1: Patient Demographics

Characteristic	Total Sample (N=92), n (%)
Age, years, Mean (SD)	41.1 (12.4)
Sex, female	83 (90.2%)
Diagnosis: <sup>a</sup>	
Acute intermittent porphyria (AIP)	68 (73.9%)
Hereditary coproporphria (HCP)	12 (13.0%)
Variegated porphyria (VP)	9 (9.8%)
Delta-aminolevulinic acid dehydratase deficiency porphyria (ADP)	1 (1.1%)
Time to Diagnosis (years), Mean (SD)	6.4 (10.1)
Duration of Disease (years), Mean (SD)	16.9 (13.0)
AHP Attacks in the past 2 years, Median (IQ)	4.5 (2-12)

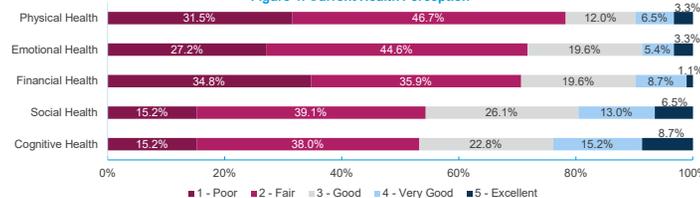
<sup>a</sup> Less common treatments included gabapentin/enkephalin, ketamine, agripent, hololet, hololet, routine or scheduled IV glucose, and others. Treatments are not mutually exclusive, and patients may be on multiple different therapies

<sup>b</sup> The remaining 2.2% of patients did not know their type of AHP

### Current Health Perception

- A majority of patients reported their current physical (78.3%), emotional (71.7%), financial (70.7%), social (54.3%), and cognitive health (53.3%) as poor or fair (Figure 4)

Figure 4: Current Health Perception

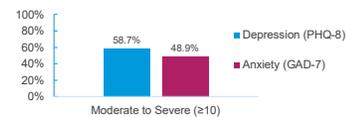


## Results (cont.)

### PHQ-8 and GAD-7

- Overall, the mean scores for PHQ-8 and GAD-7 scales were 12.1 and 10.3, respectively (Figure 5)
- 54 (58.7%) patients scored  $\geq 10$  on the PHQ-8 scale, signifying depression
- 45 (48.9%) patients scored  $\geq 10$  on the GAD-7 scale, signifying anxiety

Figure 5: Patients Reporting Moderate to Severe Depression and Anxiety (N=92)



Moderate to Severe ( $\geq 10$ )

Subscale	Mean Score (SD)	Median
Interference	3.6 (1.7)	3.9
Support	4.5 (1.6)	5.0
Pain Severity	3.4 (1.6)	3.3
Life-Control	3.3 (1.7)	3.5
Affective Distress	3.7 (0.8)	4.0

Table 2: WHYMPI Scores (N=92)

Domain	Valid n	Mean % Impairment (SD)
Absenteeism	43	32.6 (35.9)
Presenteeism	38	36.8 (34.1)
Overall Work Productivity Impairment	43	52.3 (39.1)
Activity Impairment	81	51.6 (35.3)

Table 3: WPAI Scores

### WHYMPI

- AHP patients responding to the WHYMPI survey reported a mean score of 3.6 on interference of pain, 4.5 on support (or concern from spouse or significant other), 3.4 in pain severity, 3.3 in perceived life-control, and 3.7 on affective distress (Table 2)

### WPAI

- Among the 43 patients that were employed, 32.6% of work time missed was reported. Of the 38 patients that were present at work, 36.8% of work productivity was impaired due to AHP (Table 3)
- Overall work productivity impairment in all employed participants regardless of missed work was reported to be 52.3%
- In all respondents, patients reported an activity impairment score of 51.6%

## Discussion

- Participants in the POWER study reported substantial emotional burden associated with AHP with ~60% and ~50% of patients experiencing moderate to severe depression and anxiety, respectively
  - A national US survey in 2019 reported moderate or severe depression in 7% of adults (PHQ-8 score  $\geq 10$ )<sup>17</sup> and mild, moderate, or severe symptoms of anxiety in 9.5%, 3.4%, and 2.7% adults, respectively (GAD-7  $> 5, 10, 15$ )<sup>18</sup>
- Based on findings from the POWER study, reported pain experienced by AHP patients is comparable to that of chronic pain and cancer patients
  - One study of 120 chronic pain patients yielded mean scores of 3.74, 4.31, 3.55, 3.63, and 3.23 in WHYMPI subscales of interference, support, pain severity, life-control, and affective distress, respectively<sup>15</sup>
  - A study of 520 cancer patients reported mean scores of 2.69, 4.83, 1.42, 0.42 and 1.56 in subscales of interference, support & self control, pain severity, pain perception, and negative mood, respectively<sup>19a</sup>
- Based on findings from the POWER study, reported work impairment experienced by AHP patients is comparable to that of rheumatoid arthritis (RA) and irritable bowel syndrome (IBS) patients
  - In a study of 150 RA patients, scores of 8.7, 24.0, 29.1, and 33.3 in WPAI domains of absenteeism, presenteeism, overall work productivity impairment, and activity impairment were reported<sup>20</sup>
  - In a study of 135 IBS patients, scores of 4.4, 32.4, 34.2, and 41.1 were reported in the respective domains above<sup>21</sup>

<sup>a</sup> This study utilized a Turkish version of the WHYMPI scale which includes differences in factor structure relative to the American version used in this study. Based on literature this difference is due to cultural differences in perception of disease. However, the results did capture the underlying impact of pain.

## Limitations

- Patient reported outcomes are limited by incomplete data and subjective nature of reporting
- Recruitment was executed through patient advocacy groups so findings may only highlight patients more active in their disease management
- Diagnosis of AHP was reported by patients and not confirmed by a physician
- Findings presented only include data from complete surveys, thus responder bias may exist
- Additional survey analyses including patient subgroup analyses are planned to more fully understand the burden of AHP on patients and their social circle