Chronic symptoms reported by patients with acute hepatic porphyria in the POWER study in a subgroup analysis of nonrecurrent patients

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Conclusions

- **Patients with recurrent AHP experience a higher level of chronic symptom severity and a greater impact on their social life and cognitive health than patients with nonrecurrent AHP**
- **Patients with nonrecurrent AHP have a similar overall symptom and HRQoL profile to patients with recurrent AHP, including pain, muscle weakness, constipation, anxiety, and depression**
- **The results demonstrate a substantial chronic disease burden in patients with AHP, even among those who experience <4 attacks per year**

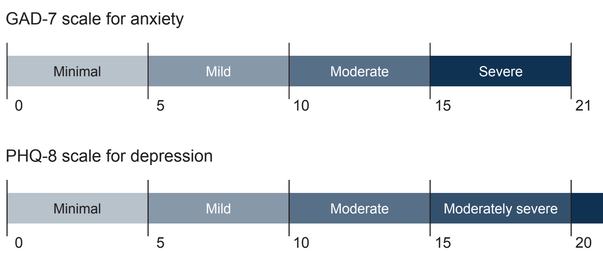
Introduction

- Acute hepatic porphyria (AHP) refers to a group of 4 rare, chronic, multisystem disorders caused by deficient hepatic heme biosynthesis:[1]
  - acute intermittent porphyria (AIP)
  - hereditary coproporphyria (HCP)
  - variegate porphyria (VP)
  - δ-aminolevulinic acid dehydratase deficiency porphyria (ADP)
- Patients with AHP may experience acute neurovisceral attacks and potential long-term complications[1,2]
  - ≥4 attacks per year is defined as recurrent AHP by the International Porphyria Network[3]
- Between attacks, patients may experience chronic symptoms that negatively impact health-related quality of life (HRQoL)[4,5]
- POrphyria Worldwide Patient Experience Research (POWER) was a global online survey of patients with AHP[6]
  - Designed by patients, physicians, patient advocacy groups, and researchers
  - Demonstrated substantial chronic disease burden across social, emotional, and physical health domains
- This *post hoc* analysis investigated chronic disease burden in subgroups of patients with recurrent and nonrecurrent AHP

Methods

- Eligibility criteria:
  - ≥18 years of age
  - ≥1 AHP attack in the past 2 years or prophylactic treatment with hemin or gonadotropin-releasing hormone
  - not receiving givosiran
- Survey included standardized patient-reported outcome scales
  - Likert scales measured chronic symptom severity and current health perceptions
  - Generalized Anxiety Disorder-7 questionnaire (GAD-7) and Patient Health Questionnaire-8 (PHQ-8) measured anxiety and depression, respectively (**Figure 1**)
  - West Haven-Yale Multidimensional Pain Inventory (WHYMPI) measured the impact of chronic pain
- Survey also included *de novo* questions regarding:
  - the impact of living with AHP
  - disease treatment and management
  - support systems
  - employment
  - pain
- *Post hoc* analysis categorized patients into groups based on attack status (recurrent or nonrecurrent) and prophylactic treatment status
  - Group A: ≥4 attacks/year (recurrent AHP) or receiving prophylaxis
  - Group B: <4 attacks/year (nonrecurrent AHP) and not receiving prophylaxis
- Results are descriptive; *p* values are nominal

Figure 1. GAD-7 and PHQ-8 scoring scales



GAD-7, Generalized Anxiety Disorder-7 questionnaire; PHQ-8, Patient Health Questionnaire-8.

Results

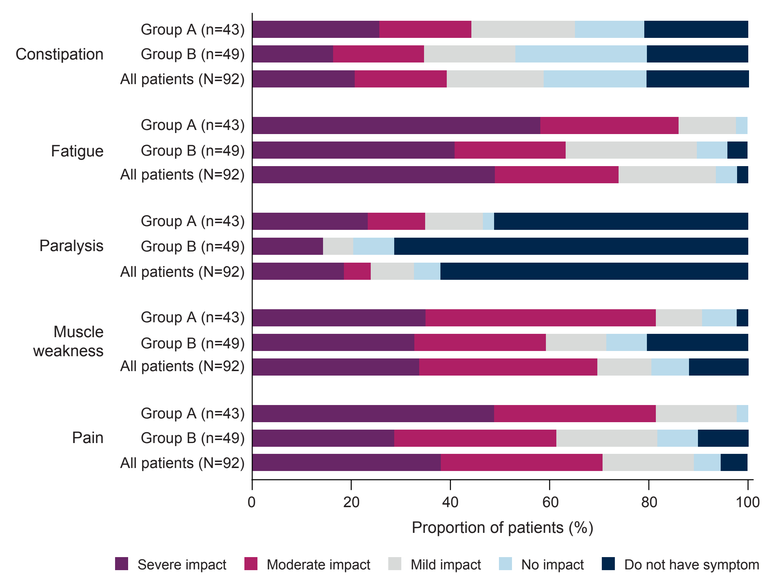
- 92 patients (Group A: 43/92 [46.7%]; Group B: 49/92 [53.3%]) completed the survey (**Table 1**)
  - Most were female (83/92 [90.2%]) and most were diagnosed with AIP (68/92 [73.9%])
  - Median (standard deviation) age: 41.1 (12.4) years
  - Median (range) number of attacks in the past 2 years: 4.5 (0-304)
- All patients reported chronic symptoms, with no notable differences between groups
- Severity of chronic symptoms varied; Group A generally reported a higher level of severity (**Figure 2**)
- Patients' perceptions of their current health were generally similar between groups
  - However, more patients in Group A than Group B reported their cognitive health as "poor" (20.9% vs 10.2%; **Figure 3**)
- No notable between-group differences in GAD-7 or PHQ-8 scores
  - 51.2% of patients in Group A vs 46.9% of patients in Group B reported moderate to severe anxiety (**Figure 4**)
  - 60.5% of patients in Group A vs 57.1% of patients in Group B reported moderate to severe depression (**Figure 4**)
- Both groups reported a similar impact of pain across all WHYMPI domains (**Table 2**)
- Both groups strongly agreed that AHP impacted various domains of their social life (**Figure 5**)
  - Two most impacted domains:
    - feeling frustrated that people close to them did not understand the challenges related to AHP (39.1% overall [Group A, 41.9%; Group B, 36.7%])
    - feeling guilty and upset about how symptoms and disabilities affect others around them (34.8% overall [Group A, 41.9%; Group B, 28.6%])
  - More patients in Group A than Group B strongly agreed that they felt lonely or isolated because of their AHP (39.5% vs 18.4%)

Table 1. Demographics and baseline disease characteristics

Characteristic/demographic	Group A (n=43)	Group B (n=49)	All patients (N=92)
Age at screening, years, mean (SD)	40.8 (11.2)	41.3 (13.4)	41.1 (12.4)
Female, n (%)	37 (86.0)	46 (93.9)	83 (90.2)
AHP diagnosis, n (%)			
AIP	27 (62.8)	41 (83.7)	68 (73.9)
HCP	8 (18.6)	4 (8.2)	12 (13.0)
VP	6 (14.0)	3 (6.1)	9 (9.8)
ADP	1 (2.3)	0	1 (1.1)
Unknown	1 (2.3)	1 (2.0)	2 (2.2)
Time to diagnosis, years, mean (SD)[a]	6.4 (8.4)	6.4 (11.5)	6.4 (10.1)
Duration of active disease, years, mean (SD)	15.8 (10.8)	17.9 (14.9)	16.9 (13.0)
Number of AHP attacks in the past 2 years, median (range)	12.0 (0-304)	2.0 (0-6)	4.5 (0-304)

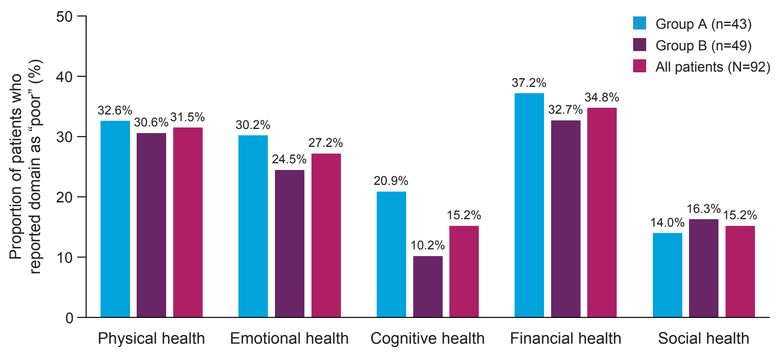
Group A had ≥4 attacks/year (recurrent AHP) or were receiving prophylaxis. Group B had <4 attacks/year (nonrecurrent AHP) and were not receiving prophylaxis.
[a]Calculated based on age of first experiencing signs or symptoms of AHP and age at diagnosis.
ADP, δ-aminolevulinic acid dehydratase deficiency porphyria; AHP, acute hepatic porphyria; AIP, acute intermittent porphyria; HCP, hereditary coproporphyria; N, total number of patients included; n, patients included per subgroup; SD, standard deviation; VP, variegate porphyria.

Figure 2. Impact of chronic symptoms



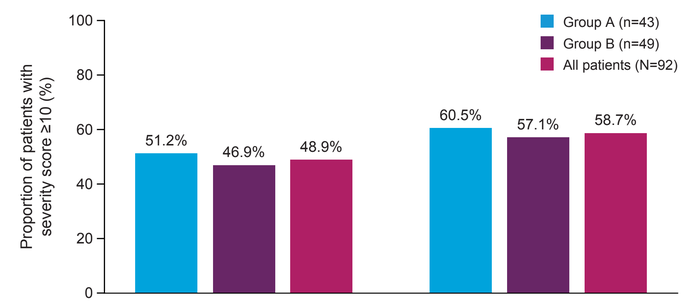
Chronic symptoms are those that are experienced often but not necessarily during an attack. Group A had ≥4 attacks/year (recurrent AHP) or were receiving prophylaxis. Group B had <4 attacks/year (nonrecurrent AHP) and were not receiving prophylaxis.
AHP, acute hepatic porphyria; N, total number of patients included; n, patients included per subgroup.

Figure 3. Proportion of patients who reported poor perception of their current health in each domain



Patient perceptions of their current health were reported across five levels: poor, fair, good, very good, and excellent. The proportions who reported a poor perception of their current health are shown. Group A had ≥4 attacks/year (recurrent AHP) or were receiving prophylaxis. Group B had <4 attacks/year (nonrecurrent AHP) and were not receiving prophylaxis.
AHP, acute hepatic porphyria; N, total number of patients included; n, patients included per subgroup.

Figure 4. Proportion of patients with moderate to severe anxiety and depression



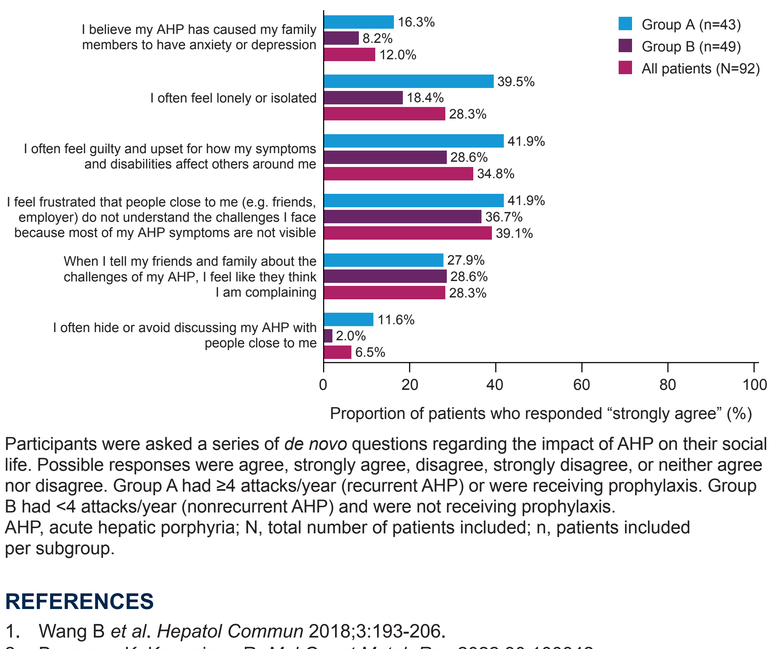
Anxiety was assessed with the GAD-7 questionnaire. Depression was assessed with the PHQ-8. Scores ≥10 on either scale indicate moderate to severe anxiety or depression. Group A had ≥4 attacks/year (recurrent AHP) or were receiving prophylaxis. Group B had <4 attacks/year (nonrecurrent AHP) and were not receiving prophylaxis.
AHP, acute hepatic porphyria; GAD-7, General Anxiety Disorder-7 questionnaire; N, total number of patients included; n, patients included per subgroup; PHQ-8, Patient Health Questionnaire-8.

Table 2. Impact of pain according to the WHYMPI scale

Subscale score[a]	Group A (n=43)	Group B (n=49)	All patients (N=92)	*p* value (Group A vs Group B)
Interference, mean (SD)	4.2 (1.8)	3.6 (2.0)	3.9 (1.9)	0.1648
Support, mean (SD)	4.7 (1.7)	4.6 (1.6)	4.6 (1.7)	0.5852
Pain severity, mean (SD)	3.7 (1.7)	3.0 (2.1)	3.4 (1.9)	0.0786
Life control, mean (SD)	2.9 (1.9)	3.4 (1.9)	3.2 (1.9)	0.1712

Group A had ≥4 attacks/year (recurrent AHP) or were receiving prophylaxis. Group B had <4 attacks/year (nonrecurrent AHP) and were not receiving prophylaxis. *p* values were calculated from a two-sample t-test.
[a]Each individual subscale of the WHYMPI has a maximum score of 6; higher scores indicate a higher intensity in that subscale.
AHP, acute hepatic porphyria; N, total number of patients included; n, patients included per subgroup; SD, standard deviation; WHYMPI, West Haven-Yale Multidimensional Pain Inventory.

Figure 5. Proportion of patients who responded "strongly agree" to statements regarding the impact of AHP on their social life



Participants were asked a series of *de novo* questions regarding the impact of AHP on their social life. Possible responses were agree, strongly agree, disagree, strongly disagree, or neither agree nor disagree. Group A had ≥4 attacks/year (recurrent AHP) or were receiving prophylaxis. Group B had <4 attacks/year (nonrecurrent AHP) and were not receiving prophylaxis.
AHP, acute hepatic porphyria; N, total number of patients included; n, patients included per subgroup.

REFERENCES

1. Wang B *et al*. *Hepatol Commun* 2018;3:193-206.
2. Baumann K, Kauppinen R. *Mol Genet Metab Rep* 2022;30:100842.
3. Stein PE *et al*. *J Inherit Metab Dis* 2023;46:662-74.
4. Wheeden K *et al*. *Adv Ther* 2022;39:4330-45.
5. Simon A *et al*. *Patient* 2018;11:527-37.
6. Dickey A *et al*. *JIMD Rep* 2022;64:104-13.

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DISCLOSURES

SB is the Co-CEO of the British Porphyria Association (BPA) and President of the Global Porphyria Advocacy Coalition (GPAC). In her role as Expert Patient and Patient Advocacy Group Leader, she has received speaker fees, consultancy fees, and advisory board compensation from Alnylam Pharmaceuticals. The BPA and GPAC have also received sponsorship and grants from Alnylam Pharmaceuticals, Clinuvel Ltd, Disc Medicine, Mitsubishi Tanabe Pharma America, Portal Therapeutics, and Recordati Rare Diseases for events, market research, and disease awareness initiatives, including sponsored collaborations on social media. **NC** has served as a consultant for Alnylam Pharmaceuticals. **KW** has served as a consultant for Alnylam Pharmaceuticals and CRISPR Therapeutics. **RKL** has consulted for Alnylam Pharmaceuticals and Recordati Rare Diseases. She has received research funding from Disc Medicine. **WD**, **TLK**, **SM**, **SL**, and **DM** are employees of and own stock and stock options in Alnylam Pharmaceuticals. **AD** has received payment for consultancy and speaker fees from Alnylam Pharmaceuticals, including fees for consulting on this study. She has also received consultancy fees from Recordati Rare Diseases.

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