

Burden of Illness in Acute Hepatic Porphyria (AHP): Insights from Patient and Caregiver Members of the British Porphyria Association

Liz Gill¹, Sue Burrell¹, John Chamberlayne¹, Stephen Lombardelli², Jordanna Mora², Nicola Mason³, Marieke Schurer³, Madeline Merkel², Stephen Menger², Bettina Baumann², Laure Weijers³, Angelica Lopez Angarita³, John Ko²

¹British Porphyria Association, Durham City, United Kingdom; ²Anylam Pharmaceuticals, Cambridge, MA; ³BresMed Health Solutions Ltd, Manchester, United Kingdom

Background and Rationale

Acute Hepatic Porphyria (AHP)¹⁻⁵

- AHP, a subset of porphyria, refers to a family of rare, genetic diseases characterized by potentially life-threatening acute attacks and, for some patients, chronic manifestations that negatively impact daily functioning and quality of life
- The four types of AHP are acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), variegate porphyria (VP), and 5'-aminolevulinic acid dehydratase deficiency porphyria (ADP)

Attacks, Chronic Manifestations, and Quality of Life^{4,6}

- Patients can experience acute neurovisceral attacks which can be life-threatening, that commonly manifest as severe, diffuse abdominal pain
- Patients may also experience nausea and fatigue, along with mental and autonomic symptoms
- Patients with AHP experiencing recurrent attacks report diminished QoL compared with population norms. There is also a significant economic burden in this patient group, with increased healthcare utilization and substantial numbers of lost work days, along with many patients not in full-time employment and receiving disability payments

Objective

- To understand the burden of illness (BOI) of AHP in the United Kingdom from the perspective of patients and caregivers

Methods

Methodology

- Data collected in two phases; 1) web-based survey sent to members of the British Porphyria Association (BPA) to collect top-line information on the burden of illness associated with AHP 2) survey participants invited to telephone interviews to discuss their day-to-day experience of AHP
- The web-based survey was open from January 7 - 29, 2019, and interviews followed shortly after
- All patients aged 18 and over with a confirmed diagnosis of AHP and caregivers aged 18 or over of patients with a confirmed diagnosis of AHP were considered eligible to participate in the survey

Figure 1: 2018 Survey Design



*Response rate was calculated based on the BPA database which consists of 270 individuals with or affected by AHP. It was not possible to separate patients and caregivers
 †Not all participants answered every question. Therefore, the number of participants varies for each question

Survey Results (Patients)

Patient Demographics & Diagnosis

- Responses were collected from 38 patients
- Majority of patients were female (74%) and diagnosed with AHP (Table 1)
- Average age of diagnosis was 23.7 (Standard Deviation (SD): 9.9) (Table 2)
- Average time to diagnosis excluding patients with diagnoses prior to being symptomatic was 4.2 years (Table 2)

Table 1: Patient Demographics

	Patients (N=38)
Female, n (%)	36 (95%)
AHP Type	
AIP, n (%)	28 (74%)
VP, n (%)	9 (23%)
HCP, n (%)	1 (3%)

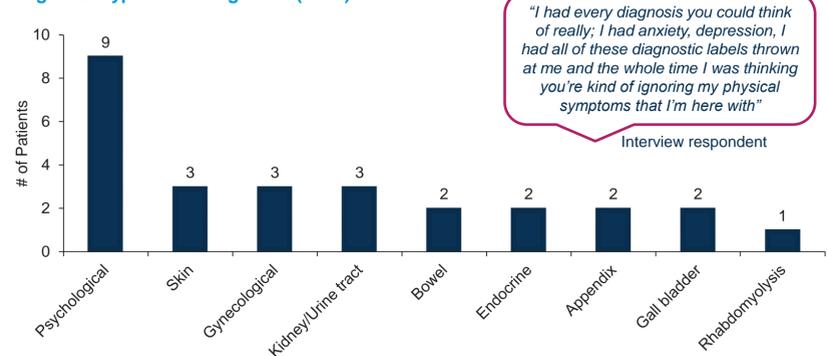
Table 2: Time to Diagnosis

	Mean (SD)	Min	Max
Age diagnosed (AD)	23.7 (9.9)	1	48
Age first experienced symptoms (AS)	22.4 (7.8)	10	45
AD-AS difference (years) full sample	1.1 (8.7)	-26	23
AD-AS difference (years) excl. those with negative difference	4.2 (5.9)	0	23

Misdiagnosis

- A total of 17 (45%) noted being initially misdiagnosed before being diagnosed with AHP
- The majority of misdiagnosed patients were wrongly diagnosed with psychological conditions or told they were making it up (n=9), followed by skin conditions (n=3), gynecological problems (n=3), or conditions and infections of the kidneys/urine tract (n=3) (Figure 2)

Figure 2: Type of Misdiagnoses (n=17)



Acute Attacks

- A total of 32 (84%) patients reported having experienced an acute attack in their lifetime. Only 2 (5%) patients had never experienced an attack [1 AIP and 1 VP], and 4 (11%) were unsure if they had ever experienced an attack
- Of the 32 patients whom reported having experienced an attack in their lifetime, 26 patients provided the number of attacks experienced in the last year and 6 years; 12 (46%) and 4 (15%) reported having no attacks in the last year and 6 years respectively (Figure 3 and Figure 4)

Figure 3: Number of Attacks in Last Year (n=26)

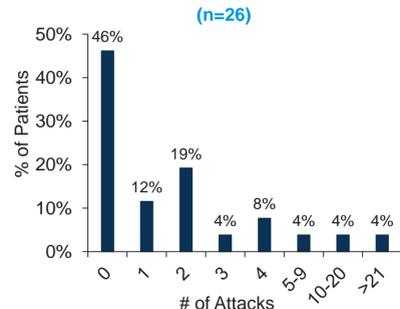
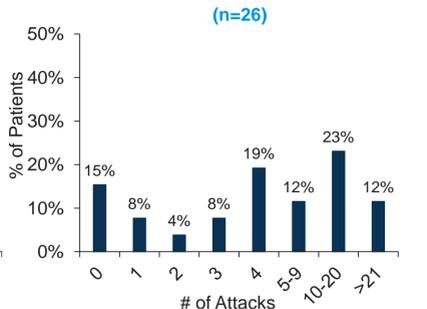


Figure 4: Number of Attacks in Last 6 Years (n=26)



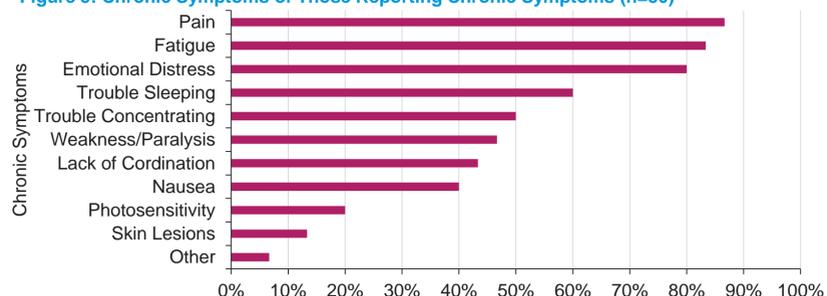
Management of Acute Attacks

- A total of 23 patients reported how many attacks were managed in what setting, in the last 2 years. In total, all patients together experienced 146 attacks in the last 2 years
- A total of 27 patients reported if they received treatments for the management of acute attacks. Hemin alone (30%) and hemin with glucose (33%) were the most commonly used treatments

Chronic Symptoms & Management

- Of the 32 patients who responded, 30 (94%) report chronic symptoms in between attacks
- A majority indicated pain (87%), fatigue/tiredness (83%), emotional distress (80%), and trouble sleeping (60%) (Figure 5)
- Of the 31 patients who responded, 7 (26%) reported receiving routine hemin; 1 received hemin every 3 weeks, 3 received hemin every 2 weeks, and one received hemin weekly

Figure 5: Chronic Symptoms of Those Reporting Chronic Symptoms (n=30)



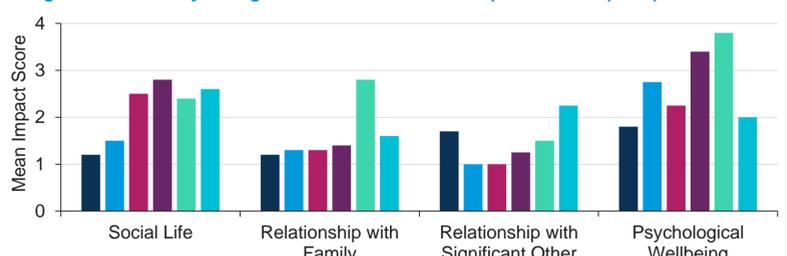
Survey Results (Patients) (continued)

Impact on Quality of Life (QoL)

- A total of 30 patients estimated the impact of AHP on different areas of their lives
- Impact scores were calculated for each domain by assigning each individual answer a number, i.e. 'no impact at all' = 0; 'slightly' = 1; 'moderately' = 2; 'severely' = 3; and 'extremely' = 4
- Mean scores were stratified by the number of attacks experienced in the last 6 years seen below:



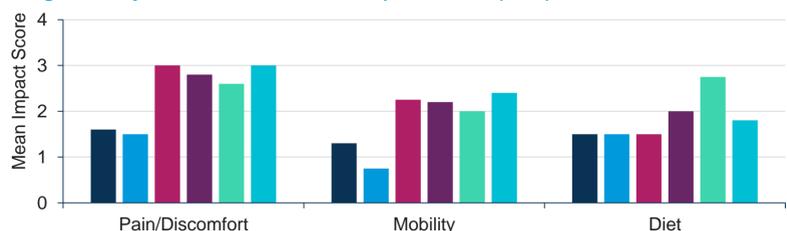
Figure 6: Social/Psychological Domain: AHP Mean Impact on QOL (n=30)



- Regardless of number of attacks experienced, all groups reported at least a mean score of AHP moderately impacting their psychological wellbeing. This score increased to severely and extremely impacting for patients with 4 attacks and 6-15 attacks in the last 6 years, respectively (Figure 6)



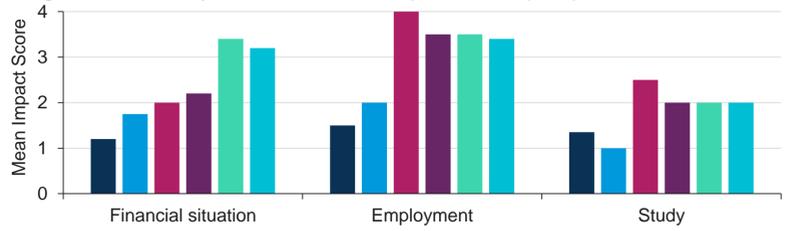
Figure 7: Physical Domain: AHP Mean Impact on QOL (n=30)



- Pain/discomfort and mobility was reported as moderately to severely impacted by AHP for all groups experiencing at least 1 attack in the last 6 years (Figure 7)



Figure 8: Work/Study Domain: AHP Mean Impact on QOL (n=30)



- Financial situation was reported as moderately to extremely impacted by AHP for all groups experiencing at least 1 attack in the last 6 years (Figure 8)
- Regardless of number of attacks experienced, all groups experiencing attacks reported at least a mean score of AHP moderately impacting their employment. This impact increased to severely and extremely impacting for patients with greater than 1 attack in the past 6 years (Figure 8)



Survey Results (Caregivers)

Baseline Characteristics

- Responses were collected from 10 caregivers. Responders were predominately female (70%), and reported care for 9 AIP patients and 1 VP patient
- Majority of caregivers were the parents of the person they cared for (n=6; 60%), followed by the partner/spouse (n=3; 30%) and one person indicated that they were a close friend of someone with AHP (n=1; 10%)
- On average, the caregivers had been caring for someone with AHP for 13.3 years (SD= 7.8)

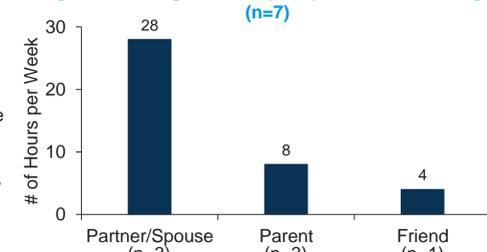
Acute Attacks

- All caregivers (n=10) reported that their loved one had experienced an acute attack and nine caregivers specified how many acute attacks the person they cared for had experienced in the last 6, 2 and 1 year(s)
- The mean number of attacks reported in the past 6, 2 and 1 year(s) was 19.9, 11.7 and 6.9, respectively. However, the variation was large, with a range of 0 to >50 attacks experienced in the last 2 years

Caregiver Time

- Caregivers spent an average of 16 hours per week caring for their loved one
- The partners of patients with acute porphyria reported that they spent the most time caring, with an average of 27.7 hours per week, followed by the parents, who spent an average of 8.3 hours per week on caring activities. The close friend spent about 4 hours a week as a caregiver (Figure 9)

Figure 9: Average Hours Spent per Week on Caring (n=7)



Limitations

- Respondents were members of the BPA and may not be representative of the AHP population
- The sample size was small and there were variable response rates for each question as respondents had the option to not respond to every question

Summary

- 54% of patient respondents report experiencing at least 1 attack in the last year. Of those experiencing attacks, 63% report treatment with hemin or hemin plus glucose
- 95% of patients report chronic symptoms. Of those experiencing chronic symptoms, pain (87%), fatigue/tiredness (83%), and emotional distress (80%) are most commonly experienced
- On average, patient's report AHP at least 'slightly' impacting all domains of quality of life, even amongst patients never experiencing an attack
- AHP has a significant impact on patient's quality of life for patient's experiencing at least 1 attack in the past 6 years. This impact includes relationships, psychological wellbeing, pain/discomfort, mobility, work/study, and patient's financial situations
- AHP caregivers report a significant time burden for caring activities

Acknowledgments & References

A special thank you to all patients and caregivers for their contribution to this study

1. Puy H et al. *Lancet* 2010;375:924-37; 2. Balwani M, Desnick R.J. *Hematology Am Soc Hematol Educ Program* 2012;2012:19-27; 3. Bonkovsky HL et al. *Am J Med* 2014;127:1233-41; 4. Wang B et al. *Hepatology* 2018;3:193-206; 5. Balwani M et al. *Hepatology* 2017;66:1314-1322; 6. Pisichik E, Kauppinen R. *Appl Clin Genet* 2015;8:201-14; 7. Stewart MF *J Clin Pathol* 2012;65:976-80; 8. Gouya et al. Presented at the International Liver Congress, April 2018.