The symptom and quality-of-life burden of Acute Hepatic Porphyria (AHP): Evidence from a systematic literature review

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Conclusions

- **Individuals with AHP experience a wide range of symptoms and impacts on their quality of life**
- **They also struggle to obtain accurate diagnosis and appropriate treatment**
- **There is a need for awareness and understanding of AHP in the broader scientific community**
- **The results of this review will be used to construct a draft PRO questionnaire for use in real-world settings to foster dialogue between patients and providers**
  - **Further research will engage clinical experts and individuals with AHP to obtain their input on the draft questionnaire**

Background and aims

- AHP is a rare group of genetic disorders of liver heme synthesis[1]
- Acute neurovisceral attacks can be incapacitating and sometimes life-threatening[1]
- Symptoms of AHP may also be chronic, being experienced between attacks[2]
- AHP symptoms can negatively affect physical, mental, and social function
- To date, no AHP-specific tool is available to collect patient-reported outcomes (PRO) in real-world settings
- As a first step in developing such a tool, a review of published literature identified relevant and important symptoms and health-related quality of life (HRQoL) impacts of AHP

Methodology

Literature search

- Conducted on 01 August 2024 in MEDLINE®, Embase, and PsycINFO®
- Search terms included AHP or its subtypes, and terms for symptoms and HRQoL impacts
- Supplemental search was later conducted using online resources (e.g., PubMed) and reference lists of reviewed publications

Selection and analysis

- Abstracts identified in the search were screened for relevance
- Peer-reviewed publications between 2009 – 2024 were selected for review if they discussed AHP symptoms and HRQoL impacts experienced by adults
- 467 citations were identified via databases; 16 publications were selected and reviewed in full (**Table 1**)

Table 1. Description of publications selected for review (N=16)

Study type	Study objective	Population
Observational study (Germany)[6]	Obtain clinical and HRQoL data	62 with AIP or VP
Observational study (Spain)[7]	Assess AIP health impacts between attacks	55 with AIP
Observational study (US)[4]	Describe clinical features of AHP	108 with AHP
Observational study (US)[10]	Describe natural history and clinical management of AHP	112 with AHP
Focus groups (US)[14]	Describe AHP pain experience	16 with AHP
Interviews (international)[12]	Describe AHP patient experience	21 with AHP
Interviews (Sweden)[18]	Describe AIP attacks in women	5 women with AIP
Interviews (US)[16]	Describe AIP disease experience	19 with AIP
Interviews (US)[17]	Describe AHP sporadic attacks	14 with AHP
Online survey/interviews (UK)[9]	Describe AHP patient and caregiver burden	38 with AHP; 10 caregivers
Online survey (China)[19]	Describe clinical features and HRQoL of AIP	27 with AIP
Online survey (international)[8]	Describe HRQoL impacts of AHP	92 with AHP
Online survey (Israel)[11]	Describe clinical features of HCP and VP	61 with VP or HCP
Online survey (Norway)[13]	Describe porphyria symptoms and HRQoL	134 with AHP, 379 with PCT
Retrospective (Netherlands)[15]	Describe AIP disease burden	88 with AIP
Public FDA meeting (US)[5]	Obtain patient and caregiver experiences and perspectives	120 with AHP

AHP=acute hepatic porphyria; AIP=acute intermittent porphyria; HCP=hereditary coproporphyria; PCT=porphyria cutanea tarda; VP=variegate porphyria

Verbatim patient descriptions of AHP as reported in the literature

"…there is no pain like porphyria pain. … This pain is not of this world"[18]

Abdominal pain feels like…[5]
"Broken glass churning on fire"
"Burning steel spikes"
"A thousand flaming swords"

"Well, it causes chronic fatigue, so I'm always tired."[17]

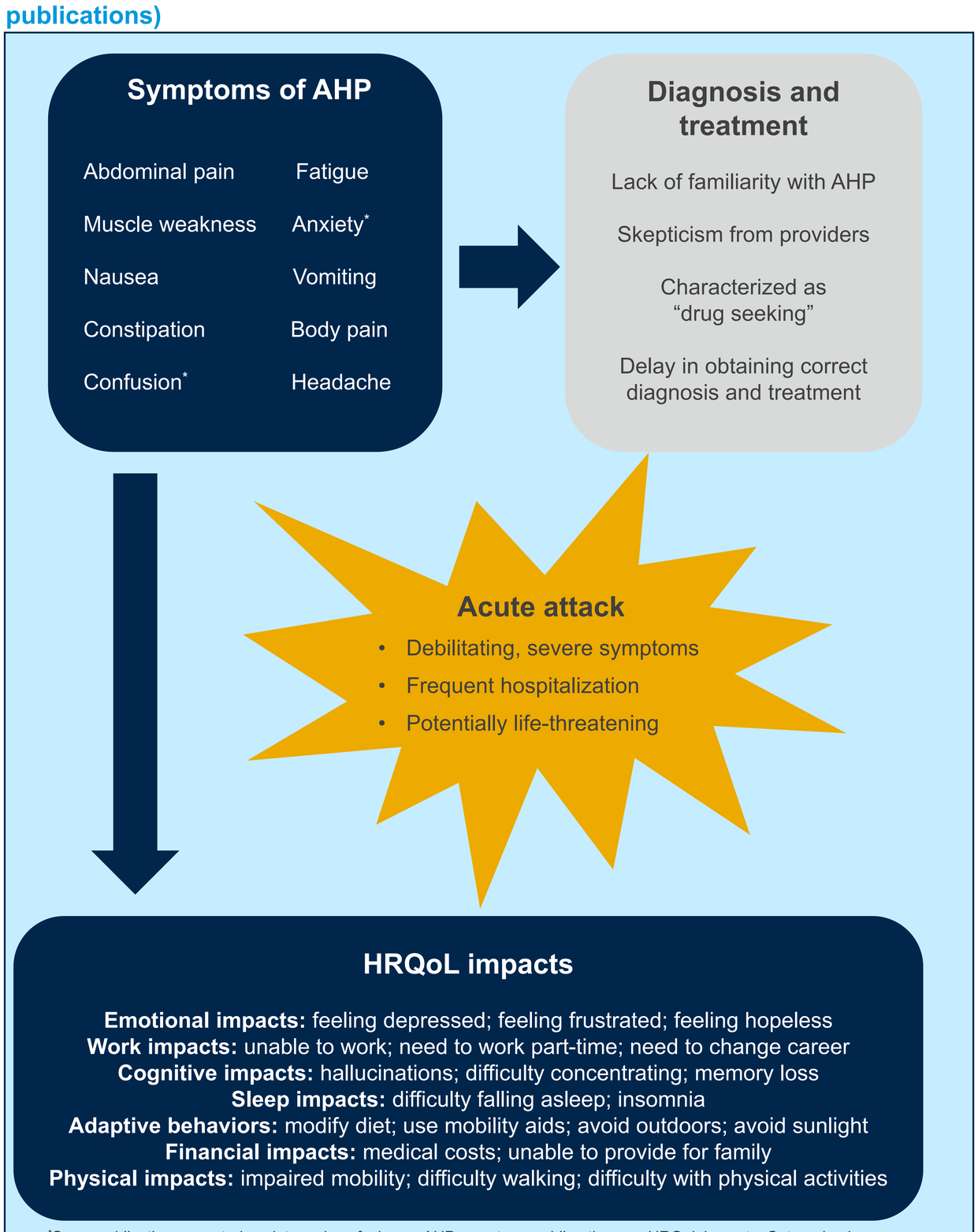
"My nausea is uncontrollable."[16]

"It feels like you're wearing a lead suit..."[12]

Results

- 61 symptoms and 82 HRQoL impacts of AHP were mentioned at least once in reviewed publications
- Publications also provided information on health care challenges faced by individuals with AHP
- The most frequently identified (in ≥50% of publications) symptoms and HRQoL impacts are presented in the AHP conceptual model[3] (**Figure 1**)

Figure 1. Literature-based AHP conceptual model (concepts identified in ≥50% of publications)



*Some publications reported anxiety and confusion as AHP symptoms, while others as HRQoL impacts. Categorized as symptoms here upon clinical advice

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Abbreviations: AHP-acute hepatic porphyria; AIP=acute intermittent porphyria; HCP-hereditary coproporphyria; HRQoL=health-related quality of life; PCT=porphyria cutanea tarda; PRO=patient reported outcomes; VP=variegate porphyria

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References

[1]Wang B, Rudnick S, Cengia B, Bonkovsky HL. Acute Hepatic Porphyrias: Review and Recent Progress. Hepatol Commun. Feb 2019;3(2):193-206. doi:10.1002/hep4.1297
[2]Wheeden K, Lyon Howe D, Burrell S, et al. Patient Perspective on Acute Hepatic Porphyria with Sporadic Attacks: A Chronic Disease with Substantial Health-Related Quality of Life Impacts. Adv Ther. Sep 2022;39(9):4330-4345. doi:10.1007/s12325-022-02172-8
[3]Wilson IB, Cleary PD. Linking clinical variables with health-related quality of life. A conceptual model of patient outcomes. Jama. 1995;273(1):59-65.
[4]Bonkovsky, H. L., Maddukuri, V. C., Yazici, C., Anderson, K. E., Bissell, D. M., Bloomer, J. R., ... & Desnick, R. J. (2014). Acute Porphyrias in the USA: Features of 108 Subjects from Porphyrias Consortium. The American journal of medicine, 127(12), 1233-1241
[5]Bonkovsky et al. The Voice of the Patient: Report of an Externally-Led Patient-Focused Drug Development Meeting – Acute Porphyrias. American Porphyria Foundation. Apr 2017.
[6]Bronisch, O., Stauch, T., Haverkamp, T., Beykirch, M. K., & Petrides, P. E. (2019). Acute porphyrias: a German monocentric study of the biochemical, molecular genetic, and clinical data of 62 families. Annals of hematology, 98(12), 2683-2691.
[7]Buendía-Martínez, J., Barreda-Sánchez, M., Rodríguez-Peña, L., Ballesta-Martínez, M. J., López-González, V., Sánchez-Soler, M. J., ... & Guillén-Navarro, E. (2021). Health impact of acute intermittent porphyria in latent and non-recurrent attacks patients. Orphanet Journal of Rare Diseases, 16(1), 106.
[8]Dickey, A., Wheeden, K., Lyon, D., Burrell, S., Hegarty, S., Falchetto, R., ... & Nance, D. (2023). Quantifying the impact of symptomatic acute hepatic porphyria on well-being via patient-reported outcomes: Results from the Porphyria Worldwide Patient Experience Research (POWER) study. JIMD reports, 64(1), 104-113.
[9]Gill, L., Burrell, S., Chamberlayne, J., Lombardelli, S., Mora, J., Mason, N., ... & Ko, J. J. (2021). Patient and caregiver experiences of living with acute hepatic porphyria in the UK: a mixed-methods study. Orphanet Journal of Rare Diseases, 16(1), 187.
[10]Gouya, L., Ventura, P., Balwani, M., Bissell, D. M., Rees, D. C., Stölzel, U., ... & Anderson, K. E. (2020). EXPLORE: a prospective, multinational, natural history study of patients with acute hepatic porphyria with recurrent attacks. Hepatology, 71(5), 1546-1558.
[11]Kaftory, R., Edel, Y., Snast, I., Lapidoth, M., Mamet, R., Elis, A., ... & Levi, A. (2021). Greater disease burden of variegate porphyria than hereditary coproporphyria: An Israeli nationwide study of neurocutaneous porphyrias. Molecular Genetics and Metabolism Reports, 26, 100707.
[12]Lombardelli, S., Brown, M., Meninger, S., & Naik, H. (2023). Patient experience with acute hepatic porphyria before and after long-term givosiran treatment: a qualitative interview study. Journal of Hepatology, 78, S993-S994.
[13]Mykletun, M., Aarsand, A. K., Støle, E., Villanger, J. H., Tollånes, M. C., Baravelli, C., & Sandberg, S. (2014). Porphyrias in Norway. Tidsskrift for Den norske legeforening.
[14]Naik, H., Stoecker, M., Sanderson, S. C., Balwani, M., & Desnick, R. J. (2016). Experiences and concerns of patients with recurrent attacks of acute hepatic porphyria: a qualitative study. Molecular genetics and metabolism, 119(3), 278-283.
[15]Neeleman, R. A., Wagenmakers, M. A., Koole-Lesuis, R. H., Mijnhout, G. S., Wilson, J. P., Friesema, E. C., & Langendonk, J. G. (2018). Medical and financial burden of acute intermittent porphyria. Journal of Inherited Metabolic Disease: Official Journal of the Society for the Study of Inborn Errors of Metabolism, 41(5), 809-817.
[16]Simon, A., Pompilus, F., Querbes, W., Wei, A., Strzok, S., Penz, C., ... & Marquis, P. (2018). Patient perspective on acute intermittent porphyria with frequent attacks: a disease with intermittent and chronic manifestations. The Patient-Patient-Centered Outcomes Research, 11(5), 527-537.
[17]Wheeden K, Lyon Howe D, Burrell S, et al. Patient Perspective on Acute Hepatic Porphyria with Sporadic Attacks: A Chronic Disease with Substantial Health-Related Quality of Life Impacts. Adv Ther. Sep 2022;39(9):4330-4345. doi:10.1007/s12325-022-02172-8
[18]Wikberg, A., Jansson, L., & Lithner, F. (2000). Women's experience of suffering repeated severe attacks of acute intermittent porphyria. Journal of advanced nursing, 32(6), 1348-1355.
[19]Yang, J., Zhu, T., Zhao, Y., Yu, X., Zhu, H., Jiang, Y., & Li, X. (2018). Acute intermittent Porphyria in the north of China: the acute attack effect on quality of life and psychological condition. BioMed research international, 2018(1), 3216802.