

The Patient Odyssey to Confirmed Acute Hepatic Porphyrria Diagnosis: Clinical Characteristics and Healthcare Utilization of Patients Preceding Diagnosis of Acute Hepatic Porphyrria

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Background and Rationale

Acute Hepatic Porphyrrias (AHPs)

- Family of rare, genetic diseases caused by deficient activity in one of the eight enzymes involved in hepatic heme biosynthesis; acute intermittent porphyria (AIP) is the most common subtype
- Accumulation of neurotoxic heme intermediates, aminolevulinic acid (ALA) and/or porphobilinogen (PBG), can cause chronic debilitating symptoms and potentially life-threatening attacks, often requiring immediate medical attention
- Nonspecific symptoms often lead to misdiagnosis, with a mean delay in diagnosis of 15 years, and inappropriate medical interventions have been reported in literature¹

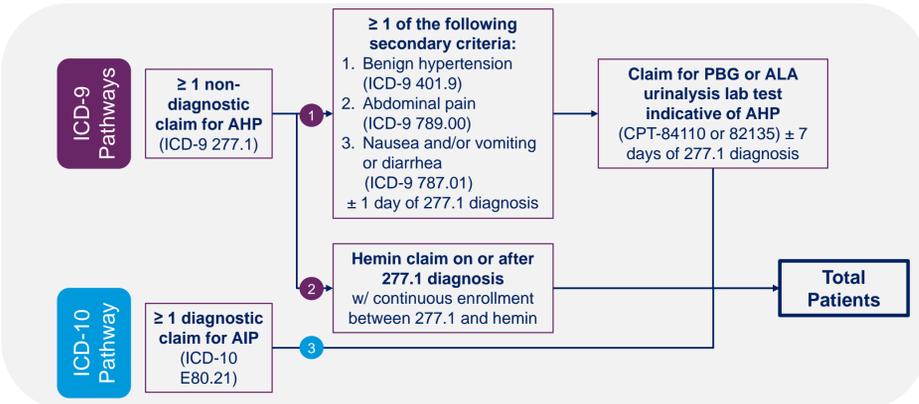
Objective

- To follow patients' healthcare journeys from first suspected symptom to AHP/AIP diagnosis

Methods

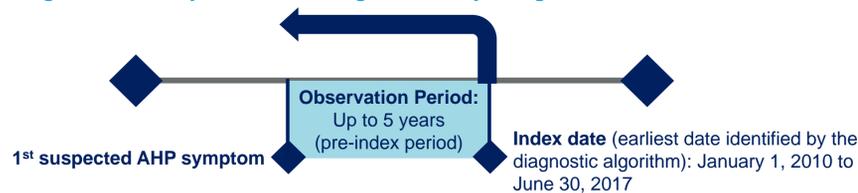
Retrospective Claims Database Study Design

Figure 1: AHP/AIP diagnostic claims algorithm



- IBM MarketScan Commercial Claims and Medicare Supplemental Databases were used to identify patients diagnosed with AHP/AIP between January 1, 2010 to June 30, 2017 using a previously described algorithm² (Figure 1)
- Of the patients identified by the diagnostic algorithm, only those with at least 5 years of continuous enrollment were included in the analysis
- Symptoms, diagnoses, AHP-like attacks, and healthcare resource utilization (HCRU) including medications, outpatient physicians visits, inpatient admissions, and emergency department (ED) visits were summarized descriptively during the observations period (obs. period)
- Obs. period was defined as the period between a patient's first suspected AHP/AIP symptom(s) identified in claims and their index date, defined as the earliest date at which the patient was identified using the diagnostic algorithm (Figure 2)

Figure 2: Journey to AHP/AIP diagnosis study design



Results

Demographics at Index Date

- 609 unique patients were identified using the diagnostic AHP/AIP algorithm; 126 (20.7%) had at least 5 years of continuous enrollment and were included in the analysis
- Mean age at index date was 46.6 years (SD 18.3), 62.7% were female, most patients had commercial health insurance (87.3%), and most had an index year in 2014 or later (Table 1)
- Mean obs. period was 3.9 years (SD 1.3)

Results (cont.)

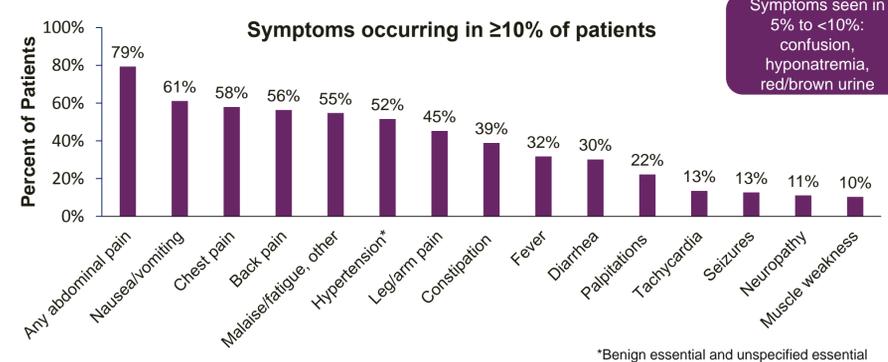
Table 1: Demographic characteristics at index date

Characteristic	AHP/AIP Patients (N = 126)	
	n/Mean (SD)	%
Age	46.6 (18.3)	-
Gender, Female	79	62.7%
Payer:		
Commercial	110	87.3%
Medicare	16	12.7%
Geographic Region		
Northeast	15	11.9%
North Central	25	19.8%
South	51	40.5%
West	19	15.1%
Unknown	16	12.7%
Index Year Group		
2010-2011	13	10.3%
2012-2013	12	9.5%
2014-2015	36	28.6%
2016-2017	65	51.6%

AHP-Related Symptoms Identified

- Most common 1st AHP-like symptoms identified in claims in ≥10% of patients were any abdominal pain (27%), benign essential and unspecified essential hypertension (19%), back pain (15%), nausea/vomiting (14%), chest pain (13%), and leg and arm pain (10%)
- Throughout the obs. period, pain was among the most commonly reported symptom (any abdominal, chest, leg/arm), as well as nausea/vomiting, malaise/fatigue, and hypertension (Figure 3)
- Some more commonly referenced AHP-associated symptoms were reported prior to the index date (e.g., hyponatremia, red/brown urine) (5-10%)

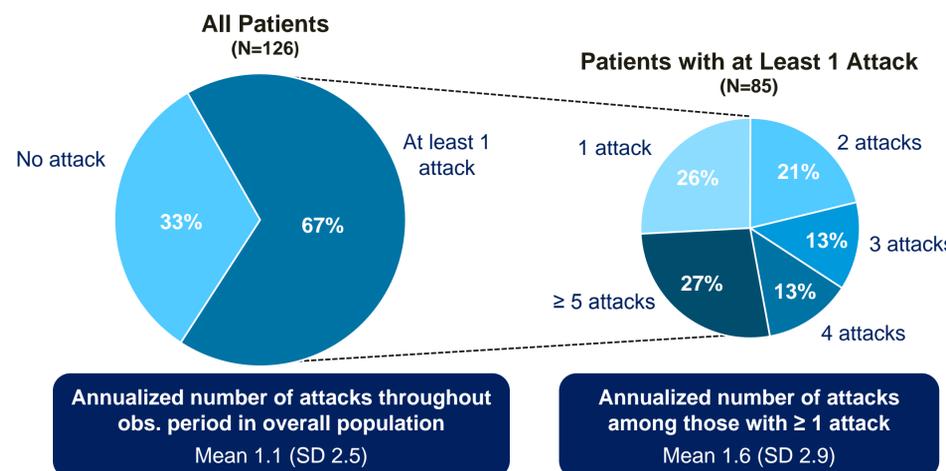
Figure 3: Symptoms reported in claims throughout the obs. period



AHP-like Attacks

- Attacks identified before the index date occurred in two-thirds of patients (67%) (Figure 4)
- Of those with at least 1 attack, the majority (53%) had 3 or more attacks during the obs. period

Figure 4: Attacks observed in claims throughout the obs. period



*Attacks are defined as an outpatient ED visit or inpatient admission with a diagnosis of porphyria, abdominal pain, back pain, chest pain or nausea/vomiting in any position on the claim. Attacks identified within a 7 day period were counted as a single attack.

Results (cont.)

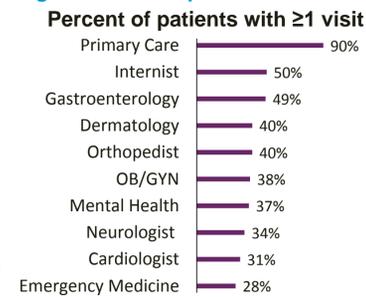
Inpatient Admissions and ED Visits

- 51% of patients had an inpatient admission during the obs. period
 - Of those with ≥ 1 admission:
 - Mean admissions per patient per year: 1.2 (SD 2.9, median 0.4)
 - Mean length of stay (days): 4.0 (SD 2.6, median 3.4)
- 73% of patient had an ED visit during the obs. period
 - Of those with ≥ 1 ED visit:
 - Mean visits patient per year: 1.9 (SD 3.0, median 0.9)

Outpatient Office Visits

- Most commonly seen physicians during the obs. period were primary care physicians and internists (Figure 5)
 - Of those with ≥ 1 primary care visit, mean (SD) visits in obs. period: 18.1 (19.8)
 - Of those with ≥ 1 internist visits, mean (SD) visits in obs. period: 9.2 (11.8)
- Gastroenterology (GI) was the most commonly seen specialist during the obs. period
 - Of those with ≥ 1 GI visit, mean (SD) visits in obs. period: 3.3 (3.4)

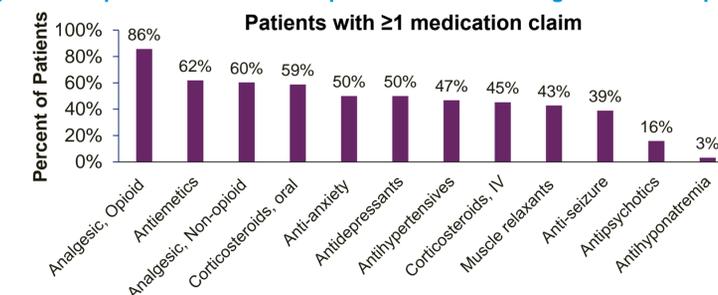
Figure 5: Top 10 outpatient office visits throughout the obs. period



Commonly Used Medications

- Analgesics were among the most highly seen outpatient medications claims prior to patients' index dates (Figure 6)
 - Opioid analgesics were the most frequently reported prescription claim
 - Opioid prescription claims during obs. period, mean (SD): 20.9 (30.2)
 - Claims for antiemetics were the second most frequently reported prescription

Figure 6: Outpatient medications reported in claims throughout the obs. period



Limitations

- Administrative claims do not capture patients' full clinical histories
- Inability to distinguish true diagnoses versus misdiagnoses
- Results may not fully represent the range of all AHP/AIP patients' journeys to diagnosis due to the population included in the analysis (e.g., strict requirement for a standard continuous enrollment) and characteristics of the database (i.e., mostly commercially covered lives)

Summary

- Prior to AHP/AIP diagnosis, the most common symptoms reported were GI-related
- High HCRU, including hospitalizations and ED visits, were observed prior to diagnosis
- GI was the most commonly consulted specialty prior to diagnosis
- The majority of patients had at least one claim for an opioid analgesic and antiemetic prior to diagnosis, which is consistent with the common signs and symptoms indicative of AHP/AIP
- Opportunity exists for earlier recognition of AHP/AIP based on patient history of neurovisceral/gastrointestinal symptoms and HCRU

References: 1. Bonkovsky, H.L., et al. Acute porphyrias in the USA: features of 108 subjects from porphyrias consortium. *Am J Med.* 2014;27(12):1233-41. 2. Agarwal S, et al. Developing an algorithm to identify patient with acute intermittent porphyria in an administrative claims database. *Value Health.* 2018;21(1):S213.