Biochemical Spectrum and Outcome of Acute Hepatic Porphyrias- a single center experience

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Introduction: Porphyrias are a group of disorders caused by error in haem metabolism. There are 4 types of Acute porphyrias: Doss Porphyria (DP), Acute Intermittent Porphyria (AIP), Hereditary Coproporphyria (HCP) and Porphyria Variegate (VP). AIP is the most common porphyria subtype with a prevalence of 1 case per 1,700 individuals. It is a hepatic porphyria caused by low levels of Porphobilinogen Deaminase enzyme (PBGD)[1]. Its inheritance is autosomal dominant and penetrance is very low. Although most individuals with AIP never develop symptoms, symptomatic individuals typically present with intense abdominal pain, nausea, vomiting, anxiety, psychosis, paranoia, constipation, tachycardia and hypertension. In addition to these symptoms seen in AIP, patients with HCP and VP may also manifest with skin symptoms

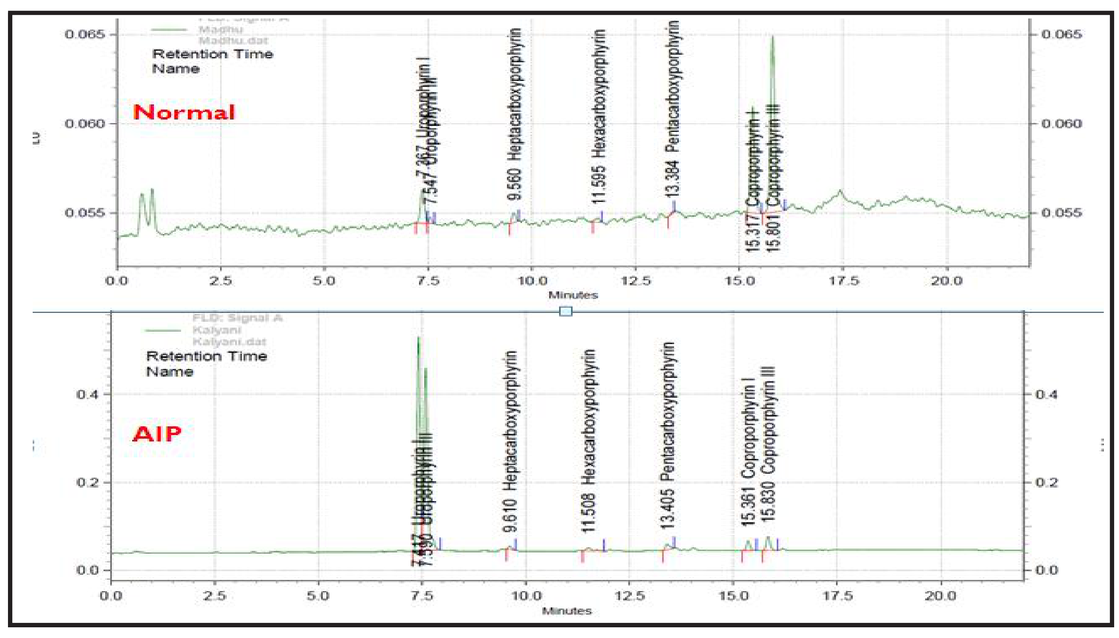
Objective: To review clinical and biochemical spectrum of AIP, VP and HCP at the time of diagnosis and outcome in these 3 conditions

Material & Method: This is a retrospective analysis of Porphyria patients diagnosed at our center during a period between 2016 to 2023. We diagnosed a total of 16 patients with acute porphyrias. Data is included in table 1.

Type	n=	M:F	Age at diagnosis
AIP	14	4 males, 10 females	17±7 yrs (Range: 6 yrs- 29 yrs)
HCP	1	1 female	46 yrs
VP/ HCP	1	1 female	12 yrs

Table 1: Demographic data

Biochemical workup done to ascertain the diagnosis included: serum electrolytes, liver function tests, serum ferritin, urinary δ-aminolaevulinic acid (ALA), Porphobilinogen (PBG), Urine porphyrin isomers and Porphobilinogen Deaminase (PBGD) enzyme analysis in blood.



Porphyrin isomers in urine: Normal v/s AIP patients

Results: We diagnosed 14 patients with AIP and on each with HCP and VP/HCP. **Clinical manifestations are described below**

AIP (n=14)	VP (n=1)	HCP/VP (n-1)
Severe abdominal pain (14/14)	Severe abdominal pain	Severe abdominal pain
Vomiting (8/14)	Vomiting	Vomiting
Constipation (11/14),	Constipation	Reduced appetite
Weakness (12/14)	Weight loss	Cholecystectomy-operated
Psychosis and paranoia (1/14),	Genetically confirmed	Genetic report pending
Convulsions (8/14)		
Tachycardia and hypertension (3/14).		
Anemia (1/14)		
Hyponatremia (11/14)		
Deranged LFT (10/14)		

Severe abdominal pain was the common feature seen in all 3 types of acute porphyrias in our cohort.

Biochemical features: All patients showed significantly elevated levels of urinary precursors- ALA and PBG as well as increased levels of porphyrin isomers in urine. Biochemical parameters are summarized in table below.

Parameter	Ref range	AIP (n=14)	HCP (n=1)	VP/HCP (n=1)
ALA*	< 56	430.30±390.82 (161.52-1670.66)	49.04	207.51
PBG*	<12.3	400.71±277.84 (31.02-891.37)	131.04	210.00
URO**	< 33	3810.26±1806.71 (1238.27-7679.09)	456.60	270.99
COPRO**	< 120	836.05±605.77 (129.95-1681.96)	2241.29	1599.10
URO/COPR	0.07-0.65	8.06±6.85 (1.49-22.62)	0.20	0.17
TPOR**	< 175	3973.91±2895.21 (720.95-10334.68)	2792.93	2035.65

*Values in uM/g creat., **values in ug/g creat

The patients with AIP were managed on high dose IV and oral glucose along with supportive anti-convulsants therapy and managed for hyponatremia. Symptoms of abdominal pain, vomiting, weakness and pain in limbs resolved gradually. None of the patients received Hematin or Hemearginate for therapy as this is not available in India and is not affordable to the patients if imported. However with high dose glucose, acute symptoms resolved. Patients with VP and HCP were also managed symptomatically and they showed improvement in clinical and biochemical features. Although patients improved, follow up has been very poor.

Discussion: Porphyrias are metabolic disorders of the heme biosynthesis. General treatment strategies include admitting the patient to intensive care unit, analgesic therapy, glucose infusion, correction of electrolyte abnormalities & stopping porphyrinogenic medication. IV glucose down regulates metabolic dysregulation. It is recommended to use hematin or hemearginate to reverse or avoid neurologic symptoms[2]. Recently, RNA interference (RNAi) therapy, givosiran, was FDA-approved for reducing the severity and frequency of porphyria attacks in AIP[3]. However, these treatments are not easily available in India and are an expensive treatment which is not affordable to our patients. All our patients were managed on glucose and supportive therapies.

Conclusion: Acute hepatic porphyrias present with life threatening episodes and need urgent treatment with hemearginate to avoid recurrent episodes. However, due to unavailability of hemearginate in India, we are managing our patients symptomatically and with glucose therapy with good results. There are no deaths in our cohort so far. Need for therapy can be decided by considering the level of excretion of porphyrins and clinical symptoms.

Conflict of Interest: None

References:

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