

Primary Hyperoxaluria

Diagnostic Considerations in Pediatric Patients

Clinical Presentation of PH

Median age of symptom onset: 5-6 years

Signs and symptoms

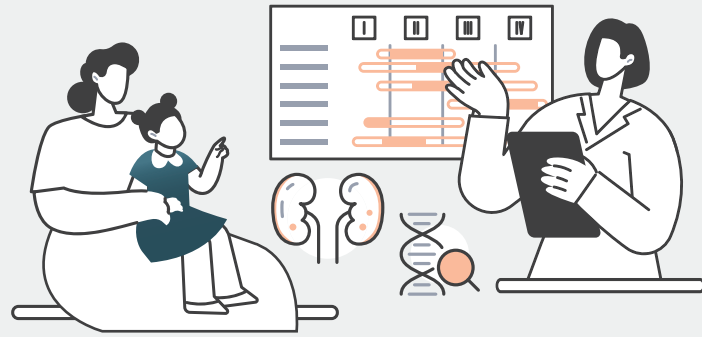
Frequent or large kidney stones

CKD

Nephrocalcinosis

Hematuria

Failure to thrive in infants



Kidney stone and urine characteristics:

- Calcium oxalate monohydrate stones
- Oxalate crystals in urine sediment
- Urine oxalate excretion

Nephrocalcinosis or Kidney Stones With eGFR >30 mL/min/1.73 m²

- ≥2 urine oxalate assessments, preferably from 24-hour collection of urine
- Spot urine oxalate-to-creatinine ratio in young children

Normal urine oxalate

Hyperoxaluria

- Check additional causes of kidney stones or nephrocalcinosis
- If excluded, check urine oxalate for severe disease and determine if genetic assessment is needed

- PH genetic assessment
- Urine hyperoxaluria metabolites
 - Glycolate (PH1)
 - L-glycerate (PH2)
 - HOG (PH3)
- Enteric cause of hyperoxaluria excluded

Metabolic Testing

24-hour urinary oxalate excretion with creatinine:

- Normal range: <0.5 mmol/1.73 m²/day
- Diagnosis requires marked elevation: ≥0.7 mmol/1.73 m²/day
 - PH1 and PH2 may be 1.5-3 mmol/1.73 m²/day

Spot urine oxalate-to-creatinine ratio if 24-hour collection infeasible:

>16 years	<0.04
6-12 years	<0.07-0.08
2-5 years	<0.098-0.1
6 months - 2 years	<0.13-0.17
≤6 months	<0.32-0.36
Age	Normal Spot Urine Oxalate-to-Creatinine Ratio (mmol/mmol)

Genetic Testing to Confirm and Differentiate PH

Associated Urinary Metabolites	Increased glycolate	Increased L-glycerate	Increased HOG
Subtype	PH1	PH2	PH3
Associated Mutations	AGXT	GRHPR	HOGA1

**Nephrocalcinosis or Kidney Stones With
eGFR <30 mL/min/1.73 m²**



Plasma oxalate assessment



Hyperoxalemia, corrected for GFR



- **Urgent PH genetic assessment**
- **Enteric disease excluded**

Genetic Testing to Confirm and Differentiate PH

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Other Assessments



Bone survey



Thyroid function



ECG/ECHO



Hemoglobin



Retinal exam



EMG/NCV

Differential Diagnosis

- Dietary hyperoxaluria: excessive oxalate intake
- Enteric hyperoxaluria: increased intestinal oxalate absorption associated with fat malabsorption
 - Causes:
 - IBD
 - Short bowel
 - Pancreatic insufficiency
 - Malabsorptive bariatric surgery
- Miscellaneous causes of hyperoxaluria:
 - Ethylene glycol poisoning
 - Medication induced (orlistat, vitamin C)



Questions to Ask Patients or Caregivers

- Is there pain from the kidney stones?
- Is there fatigue?
- Is there other pain (eg, stomach, leg, headaches)?
- Is there bed-wetting or frequent or painful urination?
- Are there any skin problems (eg, blisters)?



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CKD, chronic kidney disease; ECG, electrocardiogram; ECHO, echocardiogram; eGFR, estimated glomerular filtration rate; EMG, electromyography; GFR, glomerular filtration rate; IBD, inflammatory bowel disease; NCV, nerve conduction velocity; PH, primary hyperoxaluria; PH1, primary hyperoxaluria type 1; PH2, primary hyperoxaluria type 2; PH3, primary hyperoxaluria type 3; UTI, urinary tract infection.