

The yield of genetic testing in management of nephrolithiasis

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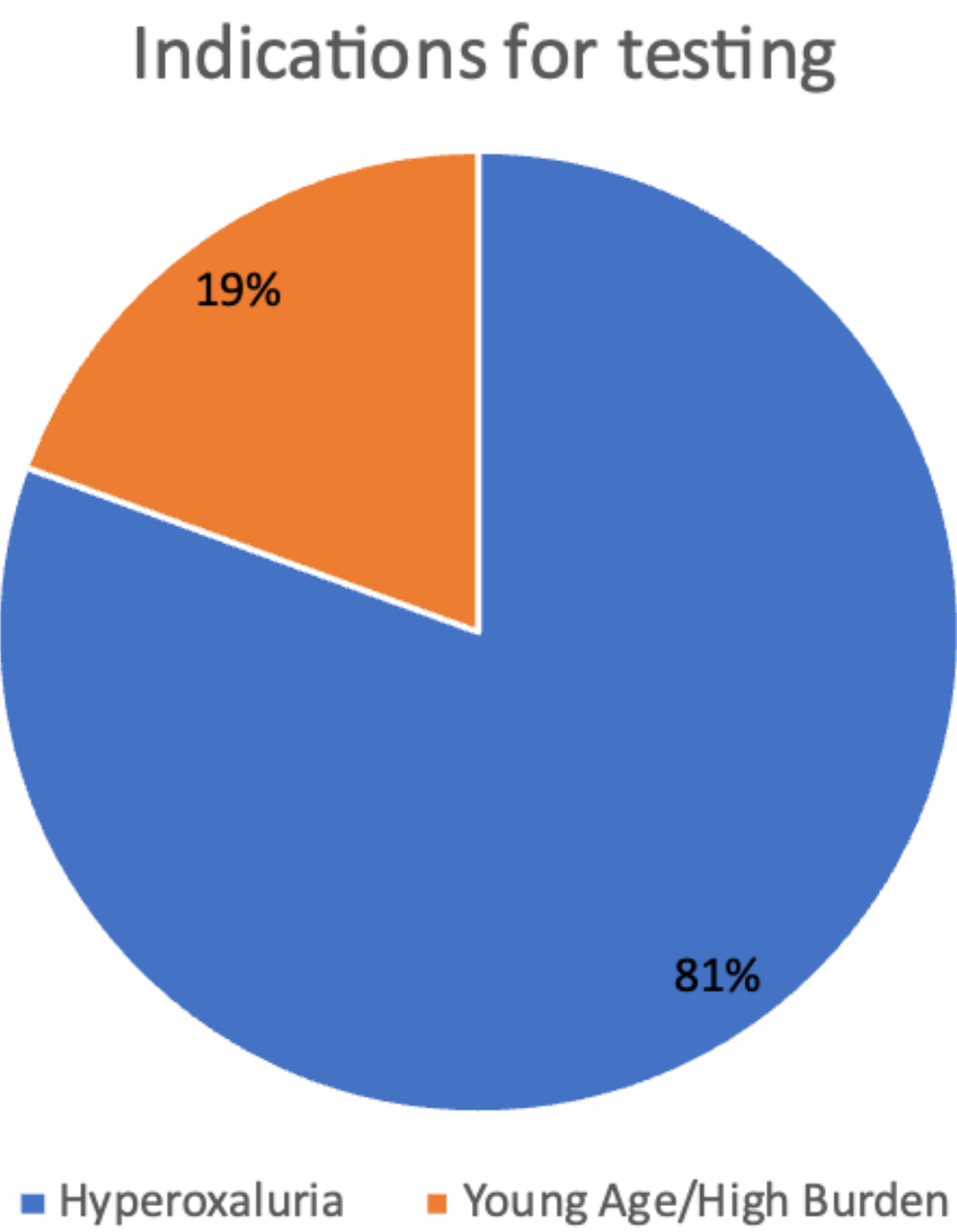
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BACKGROUND

- Kidney stones are common with lifetime prevalence of 5-10%
- Stones have estimated heritability of 50%; monogenic mutations are thought to account for ~15% of cases
- New treatments are becoming available to target these monogenic mutations
- Commercial gene panels are becoming more accessible, but yield of testing remains unknown

METHODS

1. Collected gene panels (PerkinElmer™) and 24-hour urine studies from UCSF patients with stone disease
2. Compared patient characteristics for those with and without mutations
3. Used receiver operator characteristic analysis to identify candidate thresholds for genetic testing.



14% of kidney stone patients have a potentially targetable mutations which can be identified on a commercial gene panel.

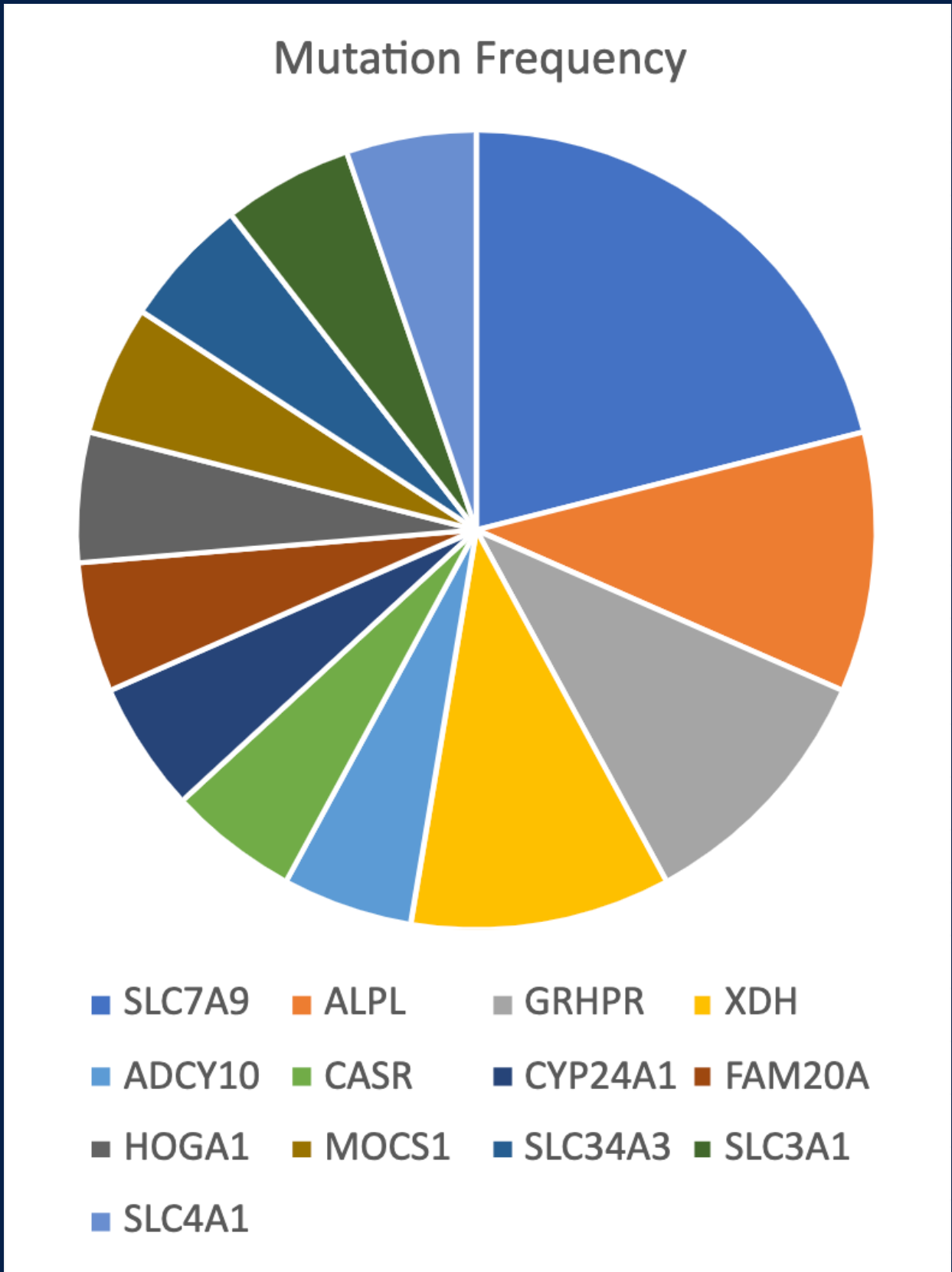


Figure 1: Observed Mutations

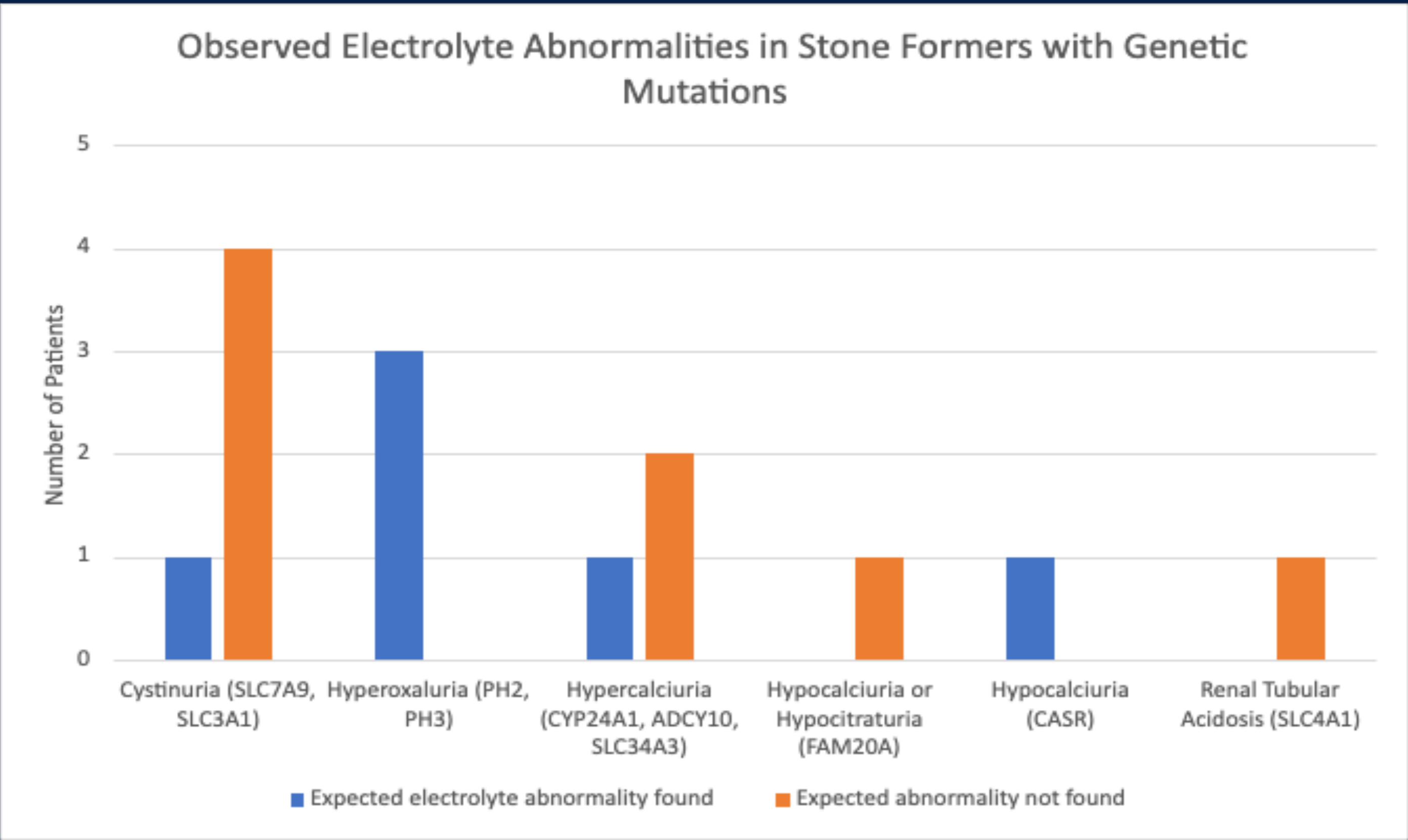


Figure 2: Observed electrolyte abnormalities in patients with genetic findings suggestive of abnormalities.

	Genetic findings (n=22); % (n)	No genetic findings (n=14); % (n)	p
Age (mean +/- SD)	56.1±16.4	48.8±19.6	0.26
Age at first stone event	44.3±20.7	35.3±23.0	0.24
Family History of Stones	41 (9)	29 (4)	0.45
Male Sex	68 (15)	71 (10)	0.84
Hypertension	32 (7)	7 (1)	0.08
Diabetes	27 (6)	0	0.03
Body Mass Index	31.4±8.1	26.7±7.5	0.09

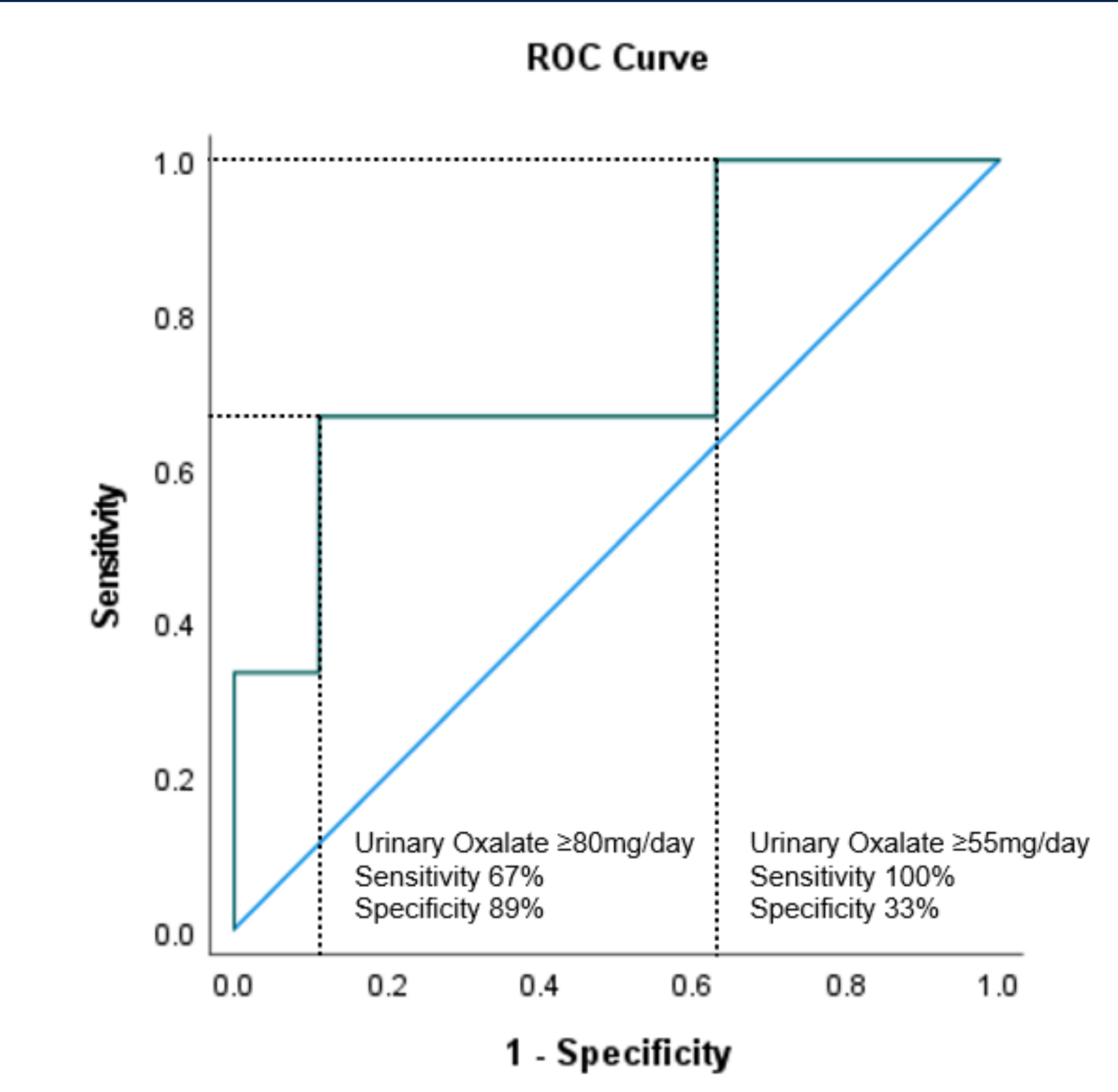


Figure 3: Diagnosis of primary hyperoxaluria in two different urinary oxalate cut-off values (55mg/day and 80mg/day)



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RESULTS

- 14/36 patients were found to have genetic mutations
- Five mutations were pathogenic, the rest were variants of uncertain significance (VUS)
- Oxalate ≥80mg/day may have favorable test characteristics for primary hyperoxaluria
- Patients with genetic findings trended younger and were less likely to have diabetes

DISCUSSION

- Genetic testing revealed a higher yield than previously reported
- Testing may have a increased yield in patients who are younger and have fewer signs of metabolic syndrome
- 24-hour urine may be helpful to establish cutoffs for testing

ACKNOWLEDGEMENTS

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