

Clinical Utility of Urinary Steroid Metabolite Ratios in Children Undergoing Investigations for Suspected Disorders of Steroid Synthesis

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Background

- Calculation of a urinary steroid profile metabolite ratio (uSMR) may be a useful method of improving diagnostic yield when investigating disorders of steroid hormone synthesis
- We aimed to determine the range of uSMR and the relationship between the uSMR and the diagnostic outcome in cases investigated for disorders of steroid hormone synthesis

Methods

- Ten ratios¹ (Table 1) were calculated on steroid metabolite data previously analysed by GC-MS in urine samples collected between 2008 and 2010 from 94 children undergoing investigations
- To obtain reference data, urine samples were also analysed in 252 children with no background of endocrine concerns

Enzyme Defect	Diagnostic Ratio
21-Hydroxylase deficiency	17HP/(THE+THF+5αTHF)
21-Hydroxylase deficiency	PT/(THE+THF+5αTHF)
21-Hydroxylase deficiency	PTONE/(THE+THF+5αTHF)
11β-Hydroxylase deficiency	THS/(THE+THF+5αTHF)
3β-Hydroxysteroid dehydrogenase deficiency	DHEA/(THE+THF+5αTHF)
P450 oxidoreductase deficiency	(17HP+PT)/(An+Et)
Apparent mineralocorticoid excess	(THF+5αTHF)/THE
Apparent cortisone reductase deficiency	THE/(THF+5αTHF)
5α-reductase deficiency	Et/An
17β-Hydroxysteroid dehydrogenase deficiency	(An+Et)/(THE+THF+5αTHF)

Table 1: Urinary steroid profile diagnostic ratios for specific enzyme effects¹

Results

- Of the 94 cases, 38 (40%) were male and the median age at the time of the test was 6.5 years (range 1 day - 18 years)
- The most common indication for urinary steroid analysis was to investigate early puberty (22%)
- Of the 252 controls, 115 (46%) were male and the median age at the time of the test was 10 years (range 1 month- 18 years)
- 40 cases (43%) had at least one ratio >2SDS above the mean for the reference range and the number of ratios per case which were >2SDS ranged from 1 to 6 (median 0)
- A high THS/(THE+THF+5αTHF) was the most commonly abnormal ratio and found to be >2SDS in 18 cases
- A total of 9/94 (10%) cases were diagnosed with a steroid hormone disorder (true positives); 4(44%) with 21-hydroxylase deficiency, 2(22%) with 11β-hydroxylase CAH, 2 (22%) with 5α-reductase deficiency and 1 (11%) with Cushing's disease. All except one of these patients had at least 1 ratio >2SDS and the case with the normal steroid hormone ratios was later diagnosed with 5α-reductase deficiency

Results

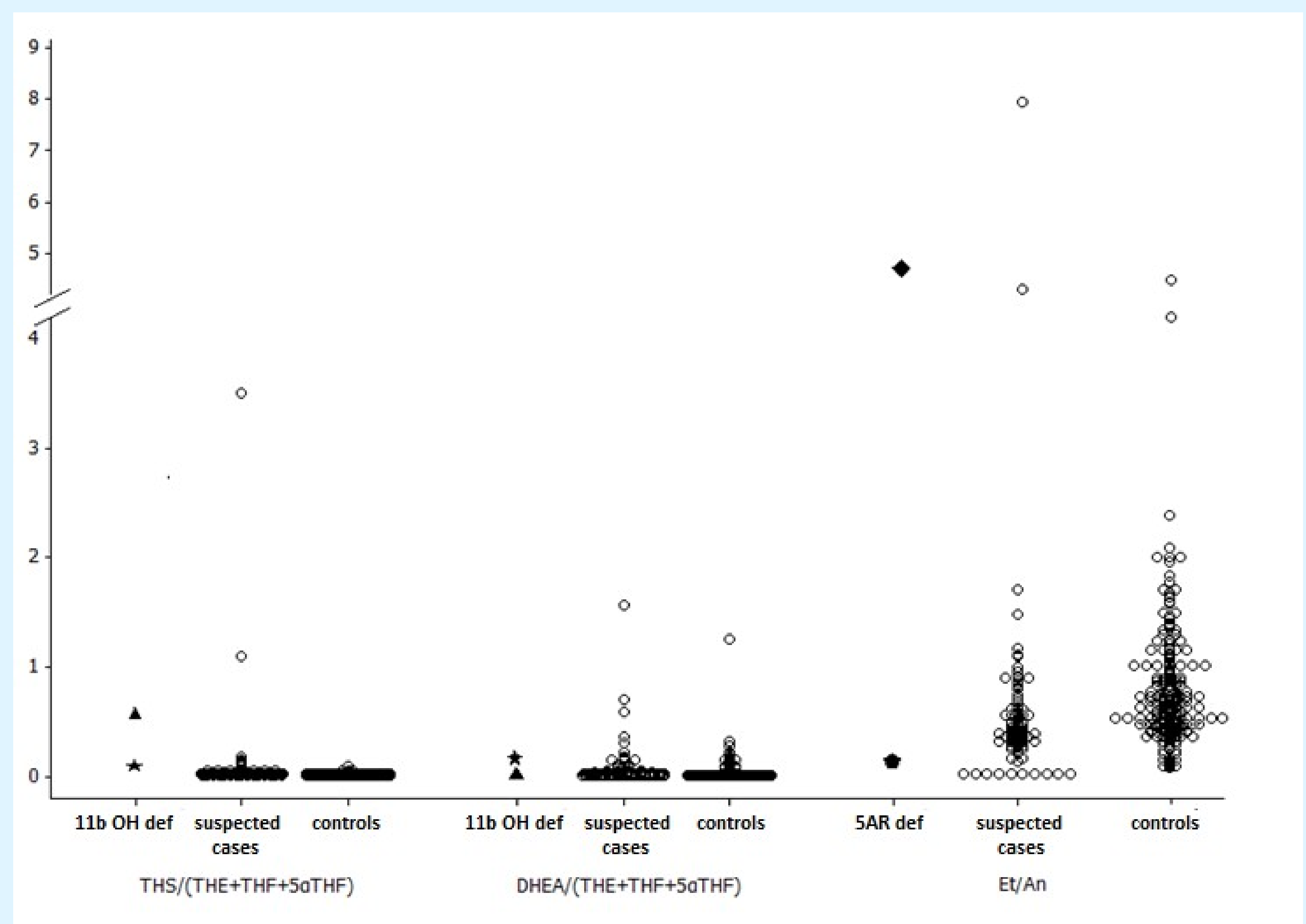
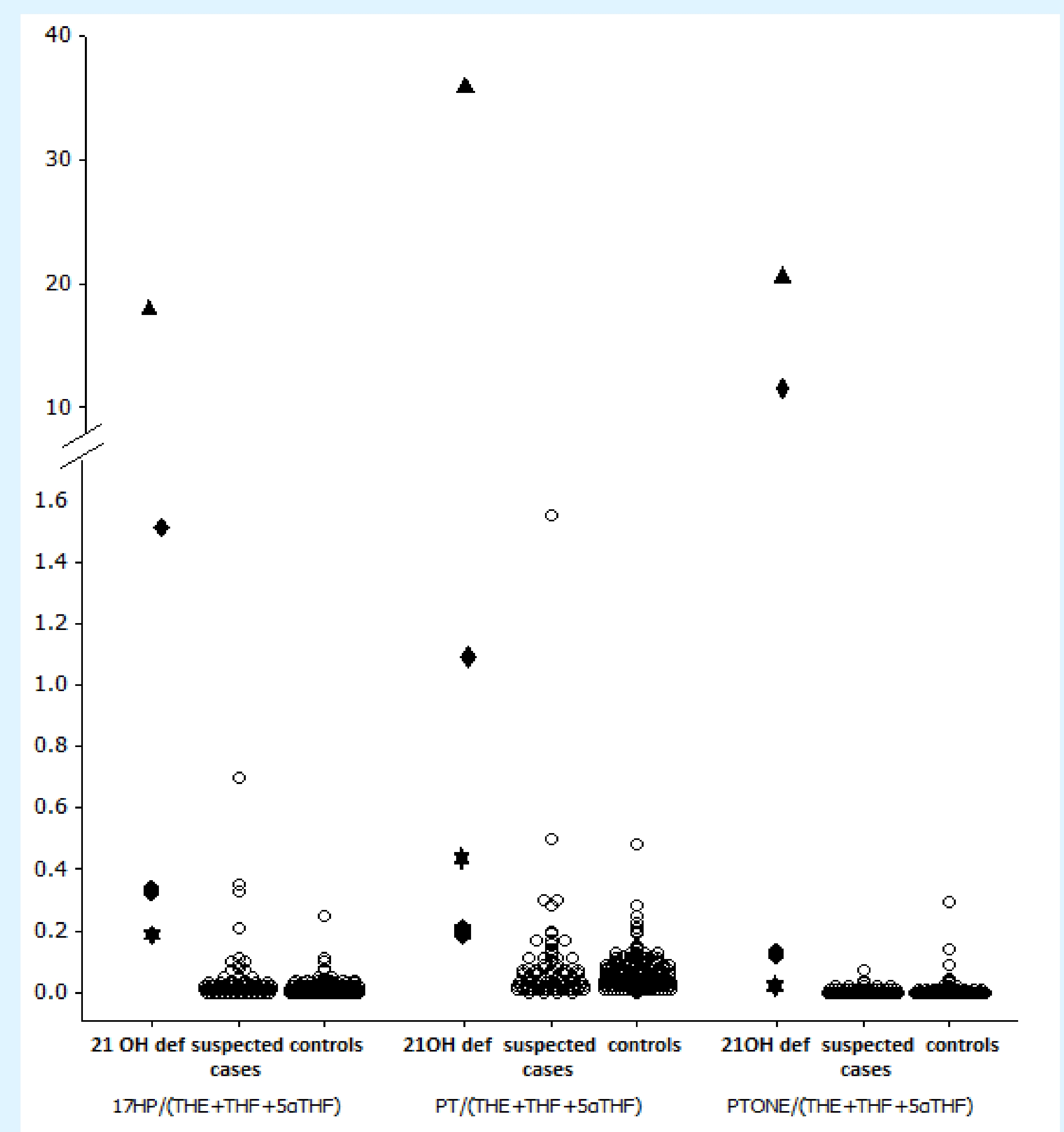


Figure 1: Individual value plots demonstrating uSMR for controls, suspected cases and confirmed cases of 21-hydroxylase def, 11β-hydroxylase def & 5α-reductase def

Conclusions

- Abnormal urinary steroid metabolite ratios are commonly encountered in children undergoing investigations for disorders of steroid synthesis
- The use of ratios may not identify all disorders of steroid synthesis, especially 5α-reductase deficiency

¹ Krone N, Hughes BA, Lavery GG et al. Gas chromatography/mass spectrometry (GC/MS) remains a pre-eminent discovery tool in clinical steroid investigations even in the era of fast liquid chromatography tandem mass spectrometry (LC/MS/MS). J Steroid Biochem Mol Biol. 2010 Aug;121(3-5):496-504