Mass spectrometry-based assessment of childhood androgen excess in 487 consecutive patients over 5 years

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Background

- Childhood androgen excess is a common presentation.
- Clinical, biochemical and radiological investigations are required to establish the diagnosis from a range of underlying pathologies (**Fig. 1**).
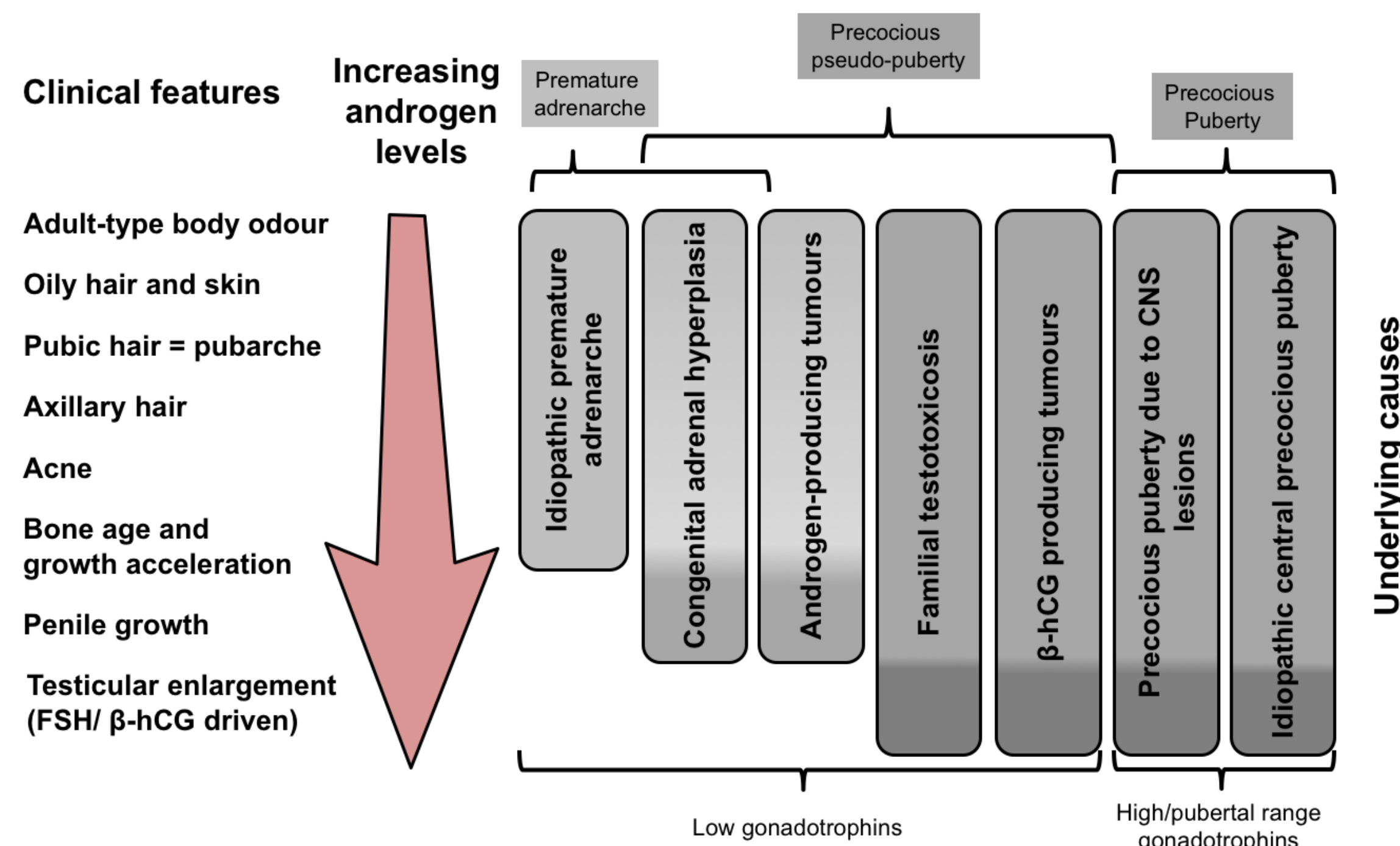

Fig.1 (modified after Idkowiak et al., EJE 2011)

- LC-MS/MS can measure all androgens simultaneously, but the interpretation can be challenging.
- There is paucity of data reporting serum androgens in a mixed sample of children with androgen excess conditions.

Objectives

- To investigate the diagnostic utility of simultaneous measurement of serum dehydroepiandrosterone sulphate (DHEAS), androstenedione (A4) and testosterone (T) in children with suspected androgen excess.
- To delineate the biochemical signature of underlying diagnoses.
- To define serum cut-off levels that may be predictive for sinister pathology.

Methods and Design

- Retrospective analysis of 487 children with simultaneous measurement of DHEAS, A4 and T from 2013-2017 in a single centre.
- Children with ≥ 1 androgen elevated above the Tanner-specific upper reference range (n=199) were clinically phenotyped (**Table 1, Fig. 2**).

Table 1: Characterisation of the study subjects

		Total	Pre-pubertal	pubertal
Subjects with ≥ 1 androgens increased		199	140 (70.3%)	59 (29.7%)
Age (years)*		8.26 (6.7; 13.3)	7.37 (4.6; 8.5)	14.9 (13.4; 15.5)
Gender	Girls	141 (70.8%)	89 (63.6%)	52 (88.1%)
	Boys	58 (29.2%)	51 (36.4%)	7 (11.9%)
BMI SDS*		1.35 (0.17; 2.6)	1.26 (-0.1; 2.5)	1.88 (0.6; 2.66)
Ethnicity	Caucasian	91 (44.2%)	64 (44.2%)	27 (44.2%)
	South-Asian	76 (38.7%)	50 (36.9%)	26 (44.1%)
	Afro-Caribbean	16 (8.0%)	13 (9.4%)	3 (4.9%)
	Mixed background	3 (1.5%)	2 (1.5%)	1 (1.6%)
	unknown	13 (6.5%)	11 (7.2%)	3 (4.9%)

* Values given as median and interquartile ranges

References

1) Idkowiak, J., Lavery, G. G., et al. (2011). Premature adrenarche: novel lessons from early onset androgen excess. European Journal of Endocrinology / European Federation of Endocrine Societies, 165(2), 189–207.

2) Elhassan, Y. S., Idkowiak, et al. (2018). Causes, Patterns, and Severity of Androgen Excess in 1205 Consecutively Recruited Women. The Journal of Clinical Endocrinology and Metabolism, 103(3), 1214–1223

Results

Fig.2: **Distribution of diagnoses** in 487 children with simultaneous measurement of DHEAS, A4 and T.
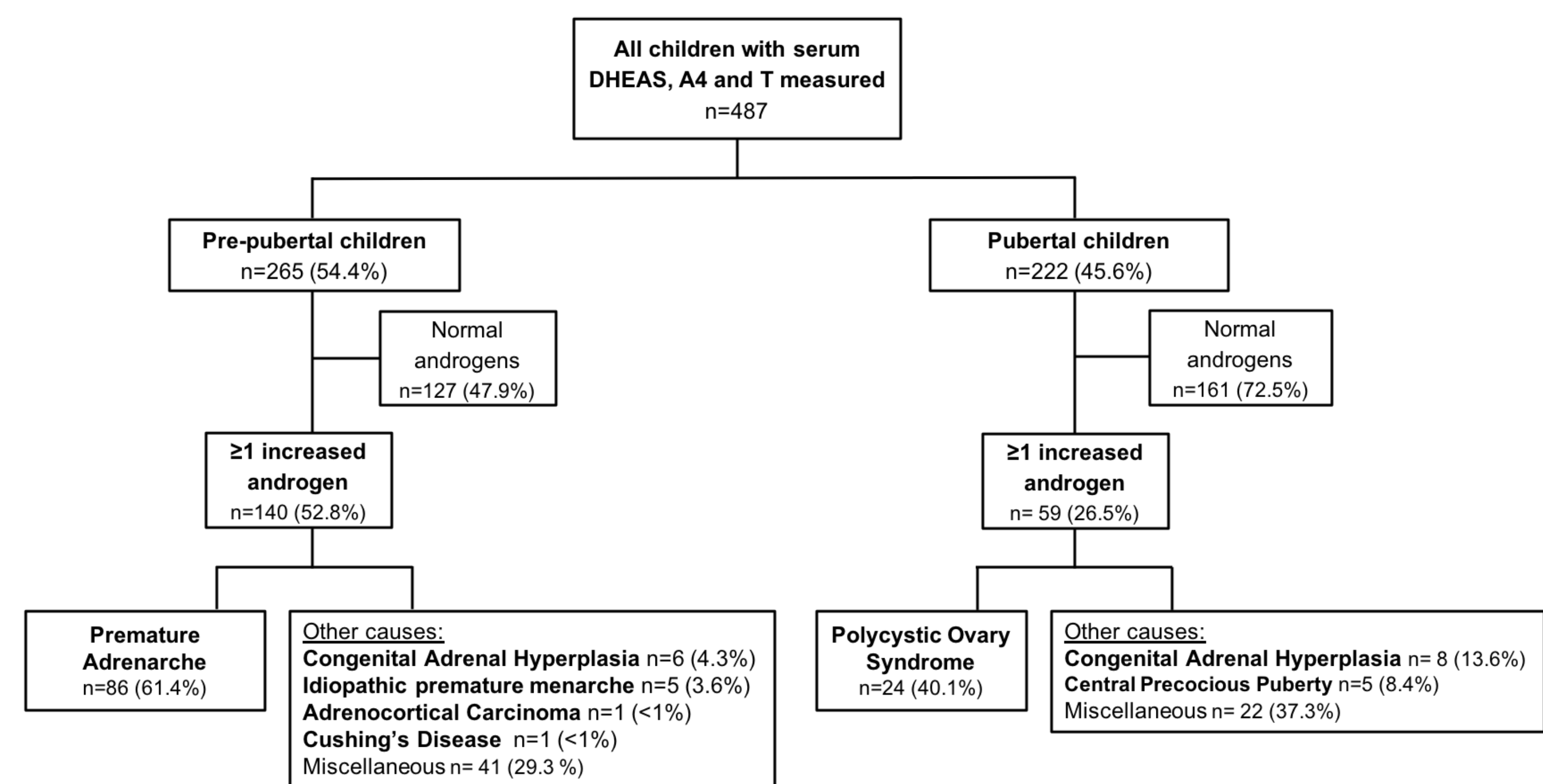

Fig.3: Patterns of androgen excess according to underlying diagnoses
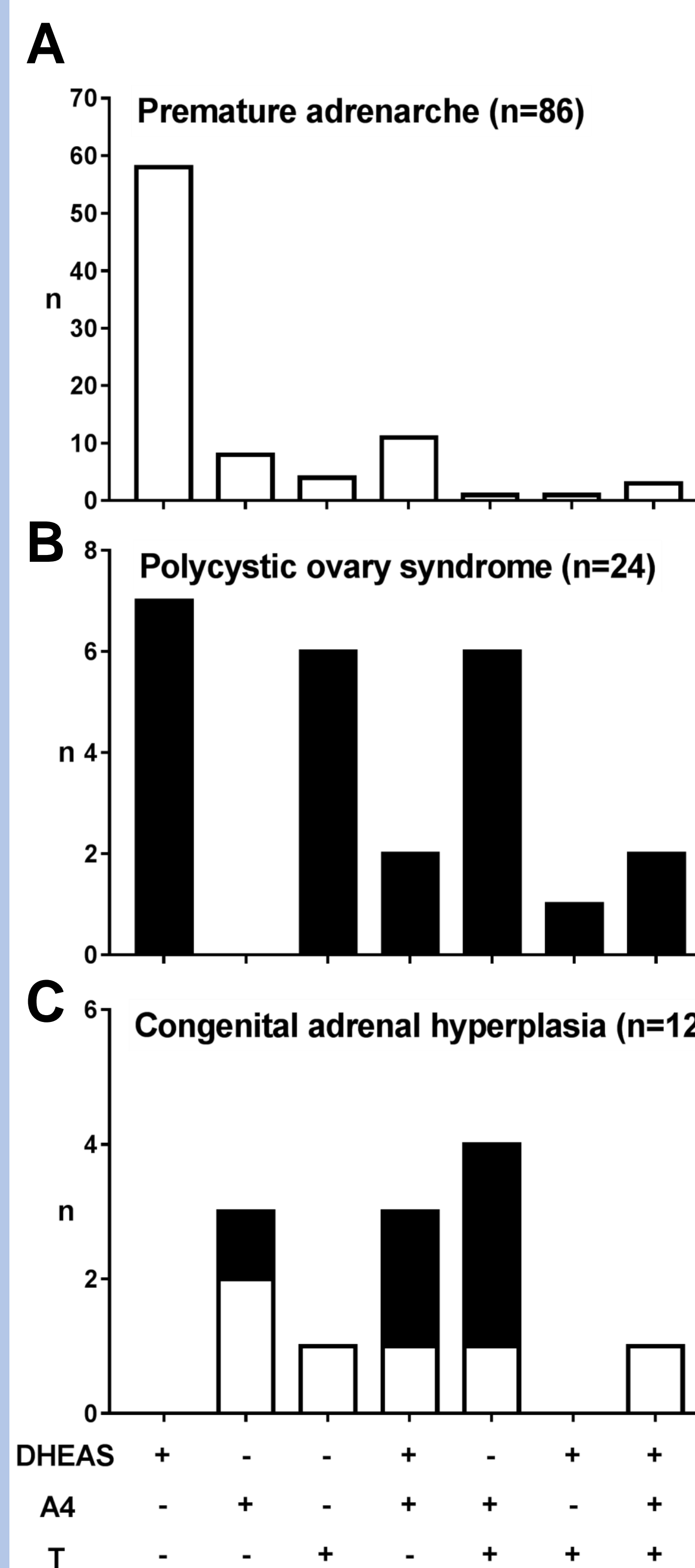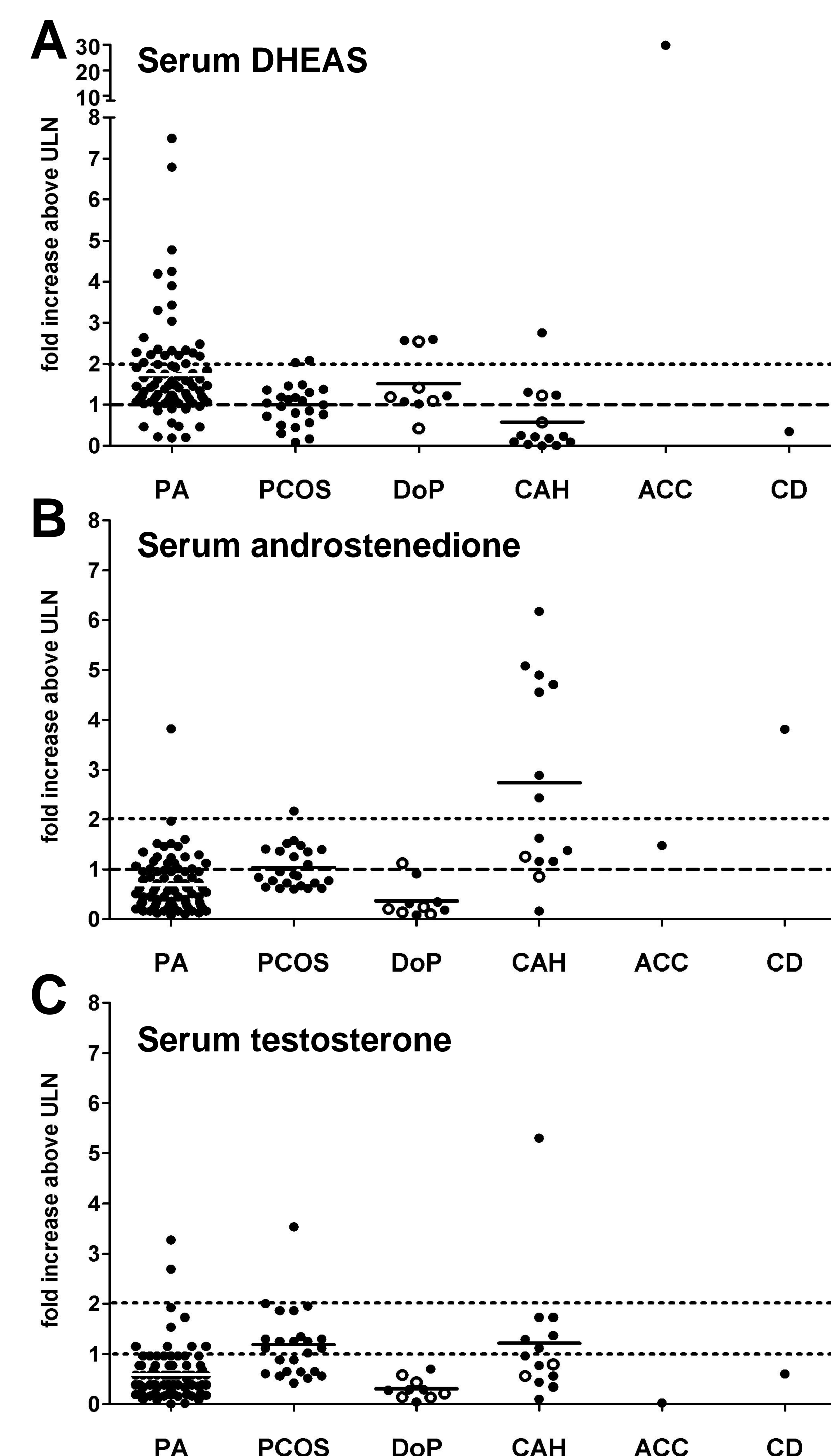

Fig.4: Severity of androgen excess according to underlying diagnoses

Summary and Conclusions

- PA is characterised by isolated DHEAS excess (**Fig. 3 A & 4**).
- CAH commonly presents with A4 excess but normal DHEAS (**Fig. 3.& 4**).
- The androgen excess signature in adolescent PCOS is similar to that of pre-menopausal women (2) and characterised by mild DHEAS, A4 and T excess (**Fig. 2C & 3**).
- Severe DHEAS excess (2- to 8-fold increase) is usually seen in PA, but remarkably elevated DHEAS (25-fold) was observed in our ACC case.

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