The aetiology of extreme tall stature in a screened Finnish paediatric population

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INTRODUCTION

- Guidelines suggest that extremely tall children (defined as height ≥ +3 SDS) should be referred to specialized health care for a comprehensive diagnostic work-up (1).
- The aetiology of tall stature is poorly characterized.
- No comprehensive studies describing aetiology and clinical features of extremely tall children currently exist.

AIM

To Report:
- diagnoses underlying extreme tall stature
- features associated with syndromic tall stature
  - neurological and psychiatric diagnoses
  - dysmorphic features
- auxological clues indicative of an underlying pathology

in a large cohort of extremely tall children that represent the general Finnish population.

METHOD

- We identified all children with height ≥+3 SDS after the age of three years from the Helsinki University Hospital (HUH) district growth database.
- The district covers a population of 1.2 million and corresponds to 23% of the Finnish population with an annual birthrate of approximately 13500 live births.
- The medical records were comprehensively reviewed and underlying diagnoses, auxological data, and clinical features gathered.

RESULTS

- We identified 424 subjects (214 girls and 210 boys) who fulfilled the inclusion criteria (Fig 1).
- A pathological cause for tall stature (i.e. a primary or a secondary growth disorder) was diagnosed in 61 patients (Fig 2).
  - 17% of the girls and 12% of the boys (P=NS).

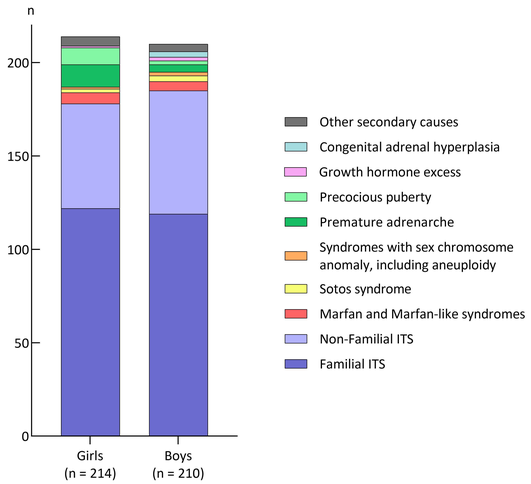

Figure 2. The aetiology of extremely tall stature, defined as height SDS of more than +3 after the age of three years, in children born 1990 or later with a place of residence in the HUH catchment area.

- Secondary causes were diagnosed in 42 (10%) patients.
  - premature adrenarche (n=16) and central precocious puberty (n=11) were more frequent in girls.
- Primary causes for tall stature were diagnosed in 19 (4%) patients.
  - Marfan syndrome (n=10) was the most common primary cause.
  - Sex chromosome aneuploidy (n=3) was rare.
- Genetic studies were employed in 120 subjects.
  - Chromosomal microarray (n=8) or gene panels (n=4) were seldom used.
- Idiopathic tall stature (ITS) diagnosed in 363 (86%) subjects.
  - 141 had a tall parent (parental height above 2 SDS).
- Features associated with syndromic tall stature were noted in almost all patients with a primary cause (95%) and were common among subjects with ITS (29%).
- The risk of underlying growth disorder was influenced by auxological features (Fig 3) (Table 1).

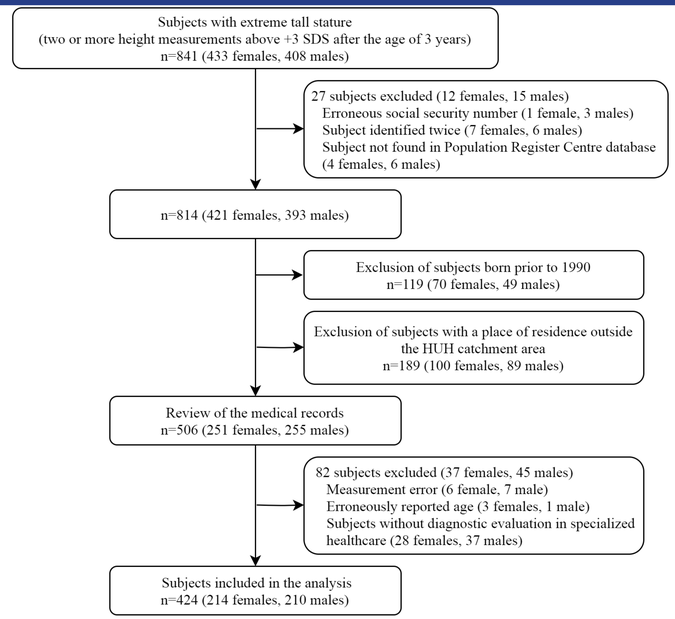

Figure 1. A flowchart depicting the formation of the study cohort of extremely tall statured children.

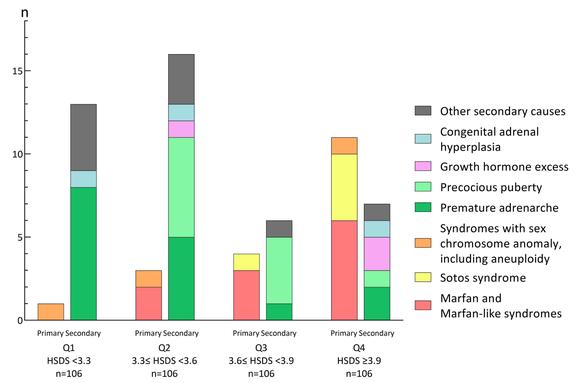

Figure 3. Distribution of the primary and secondary diagnoses according to the degree of tall stature.

	Cut-off	Sensitivity% ; Specificity%	+LR ; -LR	AUC and 95% CI
HSDS	3.7	81% ; 63%	2.2 ; 0.3	0.78 (0.68 – 0.88)
HSDS-THSDS	2.7	83% ;51%	1.7 ; 0.3	0.76 (0.62-0.91)

Table 1. ROC analysis comparing patients with monogenic syndromes and subjects with ITS.

CONCLUSIONS

- A considerable proportion of extremely tall children independent of sex has an underlying growth disorder.
- Clinical features related to syndromic tall stature were frequent in subjects with ITS, supporting the view that syndromic growth disorders with mild phenotypes may be underdiagnosed in extremely tall children.
- Analysis of auxological data may be beneficial in estimating the risk of growth disorders.
- Our results lend support to a comprehensive diagnostic work-up of extremely tall children.

REFERENCES

1. Lauffer P, Kamp GA, Menke LA, Wit JM, Oostdijk W; Towards a Rational and Efficient Diagnostic Approach in Children Referred for Tall Stature and/or Accelerated Growth to the General Paediatrician. Horm Res Paediatr. 2019;91(5):293-310

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