Urinary Gonadotrophins in Girls with Turner Syndrome

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Background

Girls with Turner Syndrome (TS) are at an increased risk of primary ovarian insufficiency (POI) with biochemical evidence of hypergonadotropic hypogonadism (HH).

Several studies have shown good correlation between serum and urinary luteinising hormone (LH) and follicle-stimulating hormone (FSH) among children with disorders of puberty.

Objectives

- To determine whether an association between serum and urinary gonadotrophins (UG) remains in hypergonadotropic states.
- To determine whether uFSH could similarly predict POI in TS as Anti-Mullerian Hormone (AMH).

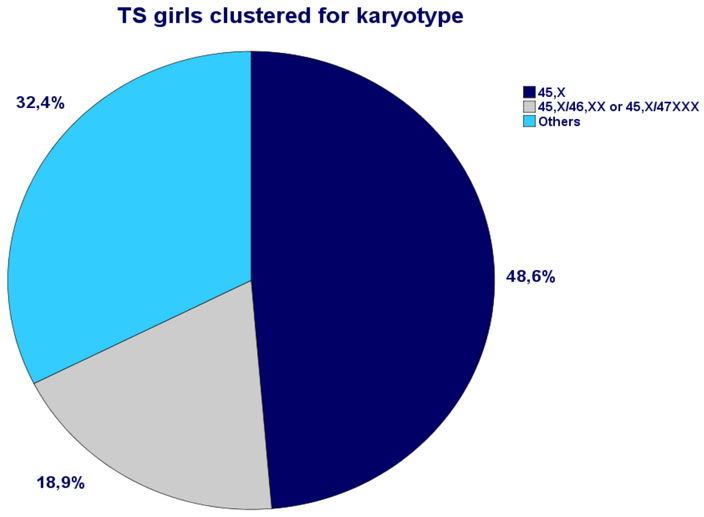
Methods

This is a retrospective analysis on TS girls attending a designated paediatric TS clinic at the Royal Hospital for Children in Glasgow between February 2015 and January 2019.

- A non-timed spot urine sample was collected during the clinic attendance (for some TS girls more than one sample with no standardized interval between collecting).
- Urine samples were analysed to assess urinary LH (uLH) and urinary FSH (uFSH) levels by a chemiluminescent microparticle immunoassay; these values were also corrected for creatinine excretion (uLHCr and uFSHCr).
- If a blood sample was performed, simultaneous serum gonadotrophins (SG) and AMH were recorded.
- POI was defined by the need for hormonal replacement therapy (HRT). An AMH level<4 pmol/L was indicative of POI.

Results

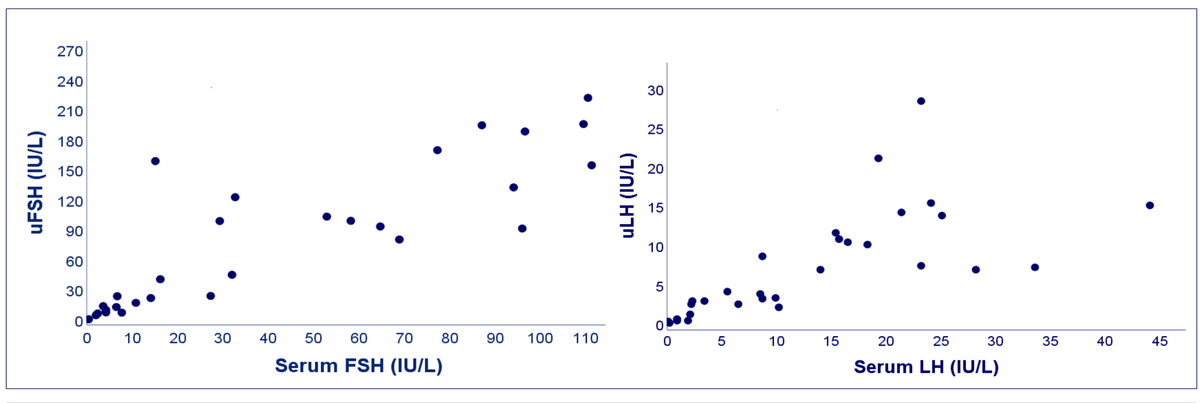
- 96 non-timed spot urine samples were collected from 37 TS girls.
- SG and AMH were available in 30 and 26 girls, respectively.
- Median age at time of sample was 12.89 years (range 3.07-20.2 years).
- 22/26 TS girls at the age of puberty (84.6%) started HRT with a median age of 13.2 years (range 11.8-16.4 years).



- Spontaneous puberty was more frequent in TS patients with 45,X/46,XX or 45,X/47,XXX mosaicism (75%) in comparison with TS patients with monosomy or other karyotypes (25%) with a p-value of 0.006.

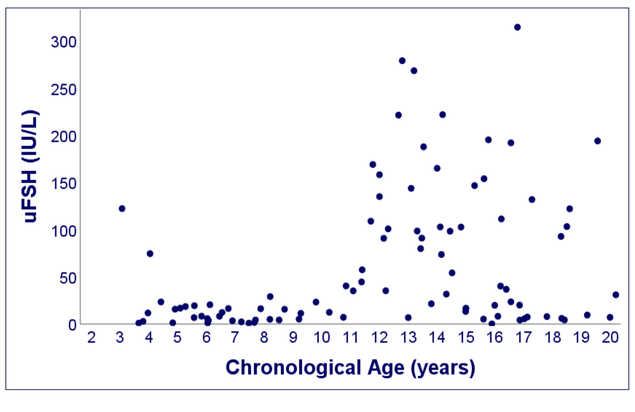
Results

Association between SG and UG (uFSH and uLH)



A strong correlation was found between serum FSH and uFSH (r 0.905, P<0.001) and serum LH and uLH (r 0.860, P<0.001).

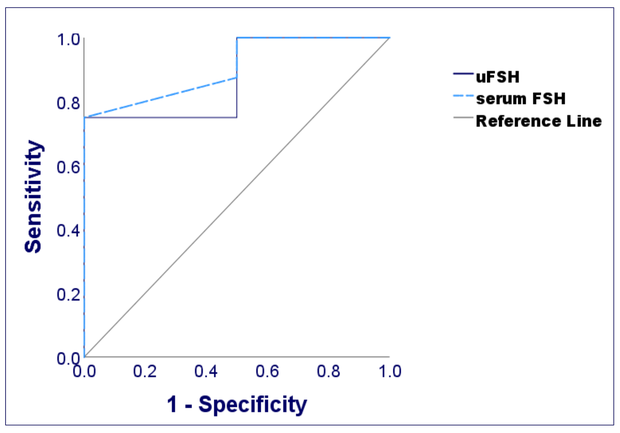
Trend of uFSH according to age in TS girls



Significant increase of uFSH starting around 10-11 years is consistent with HH in TS girls.

ROC curve for analysis: uFSH predictive of an AMH<4pmol/L

Simultaneous urine and plasma samples were available in 10 TS girls ≥ 10 years not on HRT.
→ uFSH>10.85 IU/L can predict an AMH<4pmol/L with 75% sensitivity and 100 % specificity (AUC 0.875), as serum FSH (AUC 0.906).



Discussion

- The correlation between SG and UG holds even in hypergonadotropic states, like TS girls.
- Results on TS girls exhibited that levels of AMH <-2SD predicted failure to enter puberty in prepubertal girls.
- Using ROC curve, we identified uFSH as a comparable predictor of POI among prepubertal TS girls not on HRT.

Conclusion

- uLH and uFSH are non-invasive, useful and reliable markers of ovarian insufficiency even in hypergonadotropic states as TS.
- uFSH could provide an alternative to AMH (in centres which are limited by availability or cost) in predicting POI and the requirement for HRT in pubertal induction.

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