

# Turners Syndrome - clinical presentation, genetics, investigation and management:

## A 10-year review

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### Background

Turner syndrome (TS) has a highly variable phenotype and genotype.<sup>1</sup> The severity of the phenotype depends on the extent of X chromosome loss,<sup>2</sup> and is explained by haploinsufficiency.<sup>3</sup> The genotype ranges from complete absence of the second sex chromosome to partial alteration or deletion. This may occur alone as a single cell line or a combination (mosaicism). Classical X chromosome monosomy (45,X) is seen in over 50% of cases of TS.<sup>3</sup>

TS is a multi-system disorder with short stature and premature ovarian failure being the most consistent features and seen in over 90% of patients.<sup>3</sup> Mosaic genotypes tend to attenuate the phenotype and hence may affect age of presentation.<sup>4</sup> The majority of patients with TS are diagnosed during childhood when they present with short stature.<sup>5</sup>

Several comorbidities are commonly seen in children with TS due to multi-system involvement and thus it requires a multidisciplinary approach coordinated by the paediatric endocrinologist.<sup>5</sup>

We reviewed our over-12s Turners clinic over a period of 10 years to evaluate the pattern of diagnosis and co-morbidities.

### Results

The age at diagnosis was 10.4 (1.9-15.0) years. The presenting complaints was identified in 18 (64.3%) patients and tended to vary by age of presentation:

- Congenital heart disease (CHD) in 2 of 3 diagnosed at birth;
- Short stature in all 9 diagnosed at 1-13.9years;
- Delayed/arrested puberty in 7 diagnosed at ≥14years.

Karyotype results were available for 27 (96.4%) patients (Fig. 1). All the 3 diagnosed at birth had classic TS compared to 23% of those diagnosed after infancy.

Routine referrals, as recommended by the TS Consensus Study Group, were made in some, but not all, patients (Fig. 2).

Twenty-five (89.2%) patients had documented comorbidities (Table 1). All the girls had elevated gonadotrophin prepuberty, while serum oestrogen was below detection in 17(63%). Raised ALT (≥35iu/l) in the absence of clinical symptoms of liver disease was seen both pre- and post- puberty (2/26 and 5/25 respectively). The 2 girls with pre-pubertal raised ALT remained so after puberty. Raised triglycerides (TGL) noted pre-puberty (2/12) persisted (3/22 post puberty). There was no significant difference in the BMI SDS change of either those with normal and raised ALT or TGL.

Twenty-six (92.9%) had growth hormone therapy (GHT), duration 3.7(2.6-5.6) years with an improvement in height-SDS at the end of GHT of 0.3±1.0. Patients with late diagnosis were relatively shorter at the start of GHT (≥14years: -2.9±0.6; ≤13years; -2.1±0.7; p=0.05) and

### Methods

A retrospective audit of girls with TS who attended the over-12 Turners syndrome clinic at Nottingham Children's Hospital between 2008 and 2017 was undertaken.

The medical records were reviewed to establish the age at diagnosis, presenting complaint, co-morbidities, referrals and karyotype of each patient. The data was analyze using R: A Language and Environment for Statistical Computing. Data was expressed as mean±SD (if normally distributed), median (IQR) or frequency (%) as appropriate. Groups were compared using Student t-test (significance level p< 0.05).

the final height-SDS difference, was significantly different (p<0.01).

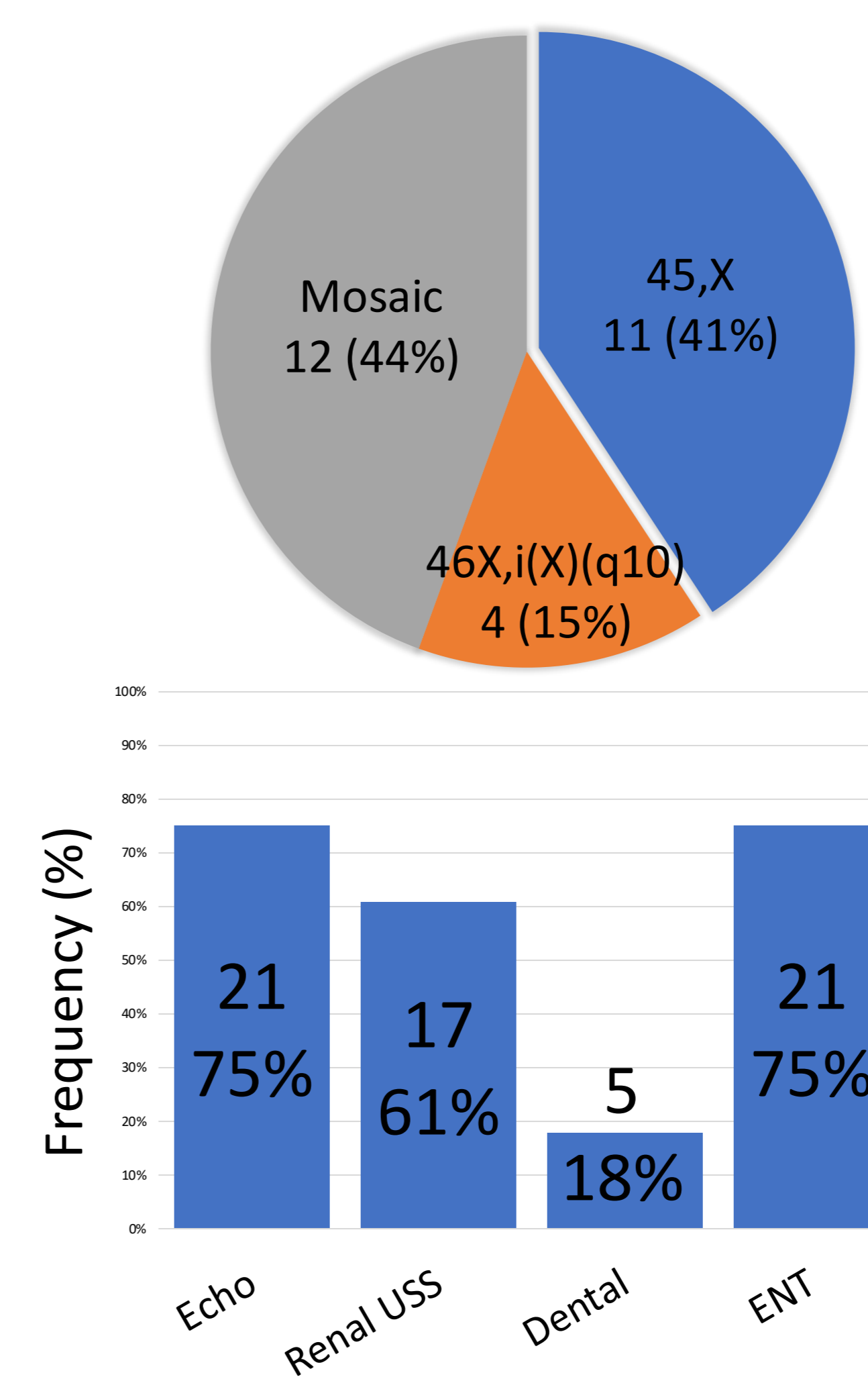


Fig. 1 Karyotype of patients. n (%)

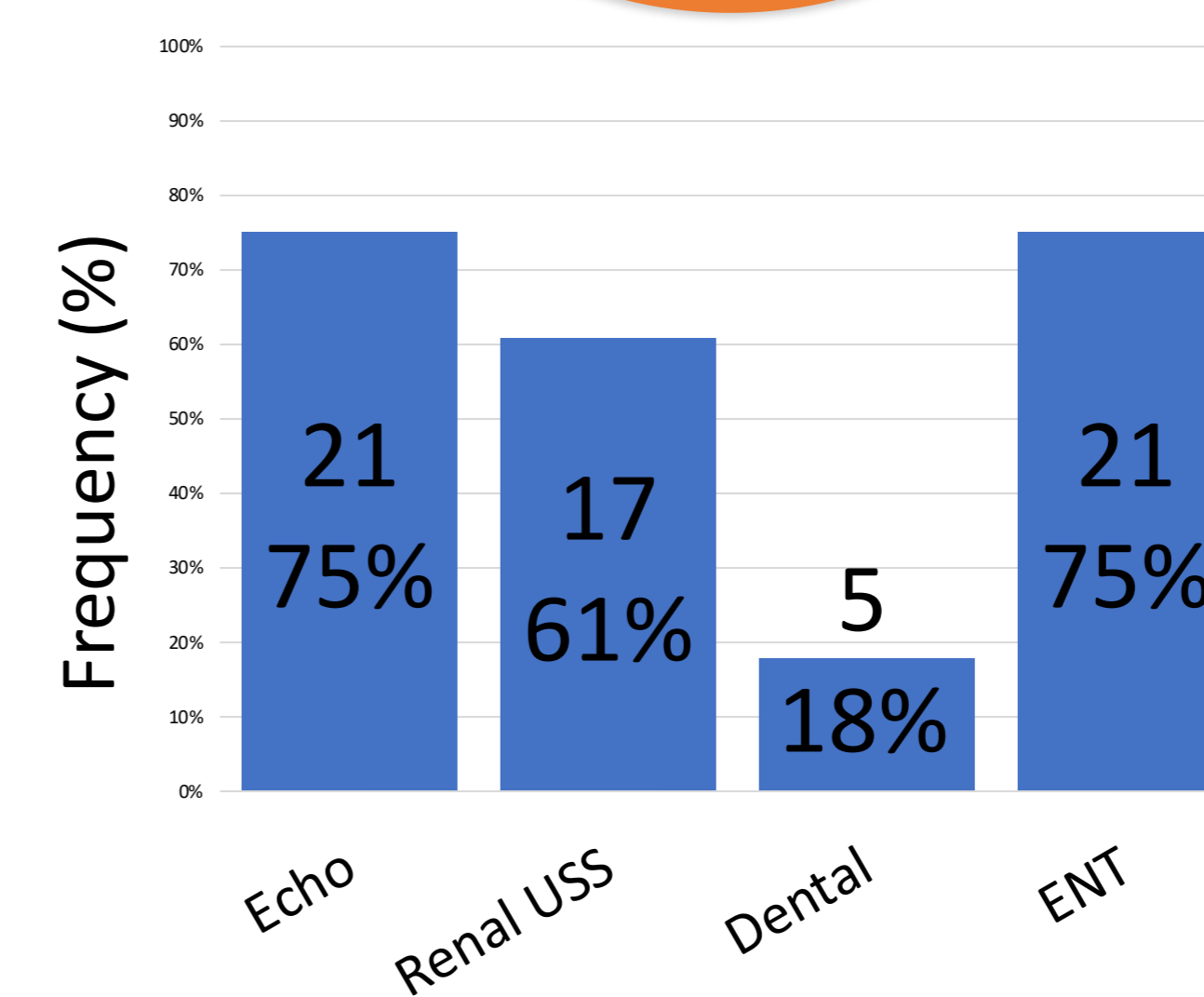


Fig. 2 Percentage of recommended referrals completed. n (%)

Comorbidity	n
ENT	12
Renal/urological	7
CHD	5
Lymphedema	5
Visual impairment	5
Psychological	3
Thyroid	3
Coeliac	1

Table 1. Comorbidities of patients. Each patient may have more than one comorbidity.

### Conclusions

Turner's syndrome is diagnosed all through childhood with typical age specific presentations. Overall short stature remains the most common presentation. Those with classic 45,X karyotype are more likely to be diagnosed early due to severe comorbidities such as congenital heart disease. Comorbidities result in a significant disease burden and ENT disorders particularly are common.

### Reference

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