Nationwide Study of Turner Syndrome during Childhood in Turkey: Evaluation of Associated Problems

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Introduction

Turner syndrome (TS), one of the most common chromosomal disorders, can manifest with various clinical features depending on the karyotype. There are a few large demographic studies on TS in childhood related to frequency of associated problems and their distribution among different karyotypes. In the present study we aimed to define the frequency of associated problems in TS patients during childhood and the distribution of these clinical features according to karyotype and age.

Material and Method

In this retrospective study, 842 patients with TS between aged between 0 and 18 years who were followed in 35 different centers from different regions of Turkey were recruited.
A common case recording form (CRF) was created after literature review by four physicians (FD, EY, ES, and PC) experienced on TS and an expert on electronic CRF preparation (CA). The CRF consisted of demographic features, clinical and laboratory findings of TS. The CRF was uploaded to the website of FAVOR Web Registry System (www.favorsci.org).

Results

In our population, the frequency of 45,X monosomy was 50.7% (n=427), and the mosaicism was 35.4%. The most frequent mosaic patterns were 45,X/46,XX (10.8%) and 45,X/46,X,i(Xq) (9.5%).

Mean age at diagnosis was 10.2±4.4 years. Majority of our patients (86.3%) had short stature and/or delay in puberty. Patients with karyotype 45,X or isochromosome Xq were diagnosed earlier than those with other karyotypes.

Cardiovascular Pathologies: The frequency of cardiac abnormality in TS patients between 0-18 year-old was 25%. We found less bicuspid aortic valve (n=61; 8.6%) compared to literature, but the frequency of coarctation of the aorta (n=46; 6.5%) and aortic stenosis (n=38; 5.4%) were consistent with the literature. In our study cardiac malformations were significantly more common in patients with 45,X karyotype compared to other karyotypes.

Renal Pathologies: The most frequent ones were horse-shoe kidney (9.0%) followed by double collector duct system (2.7%) and rotation anomalies (1.3%) and others (renal agenesis, renal ectopia etc.). There was no difference between karyotypes with regard to renal abnormalities.

Thyroid Pathologies: A striking increase was observed in the frequency of thyroid autoantibody positivity by age; 74% of the patients with positive thyroid autoantibodies were over 10 years, 24% of them were between 5-9.99 years and 2% were below 5 years. Thyroid autoimmunity was more common in patients with isochromosome karyotype.

Gastrointestinal Pathologies: In the present study 62 out of 698 patients (8.9%) had gastrointestinal pathologies. Transaminases were elevated in 24 (3.4%) patients, of whom 5 were younger than ten years of age. Celiac disease was detected in 18 (2.5%) and celiac antibody positivity in 32 (4.5%) patients. Prevalence of celiac disease in our cohort was higher than in healthy Turkish school children that have prevalence of 0.47%.

Ear Pathologies: Recurrent otitis media was the most common finding encountered in 77 patients (14.3%), followed by hearing loss in 54 (10.0%) patients of whom 44 had conducting type and 10 sensory-neural type hearing loss. The frequency of ear problems did not differ among karyotypes.

Orthopedic Problems: The frequency of scoliosis was 3%. Scoliosis was more prevalent above 10 years compared to 5-10 years of age and not seen in patients younger than 5 years. Osteoporosis and osteopenia were the most common findings in 63 (15.3%) and 49 (11.1%) patients, respectively.

Metabolic Problems: 69 were obese (9.5%), 40 were overweight (5.5%). 24 (3.3%) patients had insulin resistance, 16 patients had impaired fasting glucose levels, 6 patients had glucose intolerance and 3 patients had Type 2 diabetes. Insulin resistance (p=0.042) and glucose intolerance (p=0.003) were more common in patients with isochromosome X.

Table 1: Distribution of patients according to karyotype (n= 842)

Numeric (n= 538)		n (%)
Pure	45,X	427 (50.7)
Mosaic (n= 111)	45,X/46,XX	91 (10.8)
	45,X/47,XXX	13 (1.5)
	Others	7 (0.8)
Structural (n= 120)		
Pure (n= 117)	46,X,i(Xq)	85 (10.1)
	46,X,del(Xp)	16 (1.9)
	Others	16 (1.9)
Mosaic (n= 3)	46,XX/46,X,i(Xq)	2 (0.2)
	46,XX/46,X,del(Xq)	1 (0.1)
Numeric/Structural (n: 184)		
	45,X/46,X,i(Xq)	82 (9,5)
	45,X/46,X,r(X)	29 (3.4)
	45,X/46,XY	23 (2.7)
	45,X/46,X,idic(Y)	11 (1.3)
	45,X/46,X,+mar	10 (1.2)
	Others	29 (3.4)

Table 2: Distribution of pathologies in TS according to karyotype

	45,X (%)	Mosaic (%)	Structural (%)	Isochromosome (%)	Total (%)
Cardiovascular Pathologies					
Bicuspid Aortic Valve	9.5	9.1	6.9	5.7	8.6
Coarctation of Aorta	10.8	1.2	2.1	1.4	6.5
Renal Pathologies					
Horseshoe Kidney	10.0	8.2	10.5	7.1	9.0
Rotational abnormalities	1.8	0.4	1.3	0.7	1.3
Thyroid Pathologies					
Hypothyroidism	9.8	12.4	14.7	14.6	11.2
Positive Anti-TPO	6.6	11.3	13.6	14.0	10.4
Positive Anti-Tg	6.1	11.3	12.8	14.0	8.6
Ear Pathologies					
Recurrent middle ear infections	15.0	14.9	14.4	15.3	14.3
Conduction hearing loss	8.1	7.1	6.3	7.1	8.1
Sensorineurol hearing loss	1.5	3.0	2.3	1.0	1.9
Orthopedic Problems					
Osteopenia-Osteoporosis	24.6	23.0	26.0	26.1	25.3
Scoliosis	2.7	2.6	4.0	5.7	3.0
Metabolic Problems					
Obesity	8.6	11.4	11.6	9.8	9.5
Overweight	6.3	5.3	4.9	6.9	5.5
Insulin resistance	3.2	2.8	4.5	4.9	3.4

Conclusion

The present study describes general demographic data and frequency of associated problems in TS during childhood in Pediatric Endocrinology centers in Turkey. It has been observed that some of the associated problems are not thoroughly searched in all patients. In those with complete evaluation, frequency of associated problems and their relationship with the karyotype groups are similar to that found in the other populations.

Aknowledgement
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