Autoimmune diseases and metabolic outcome in Turner syndrome – comparison between 45,X0 and other X chromosome abnormalities

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BACKGROUND

Turner syndrome (TS) is a genetic disorder caused by X chromosome monosomy (45,X0) or partial absence of the second sex chromosome, with or without mosaicism. An increased frequency of autoimmune diseases and metabolic disorders has been observed in Turner patients.

OBJECTIVE

To compare Turner monosomy (45,X0) to the other X chromosome abnormalities with regards to occurrence of autoimmune diseases and metabolic disorders.

METHODS

Retrospective study of 103 TS patients followed at the Institute for Endocrinology and Diabetes, SCMCI during 1960-2013.

RESULTS

Monosomy was diagnosed in 30% of the cohort.

Age at genetic diagnosis was younger in 45,X0 compared to the other X chromosome abnormalities (6.2 ± 5.5 vs. 4 ± 4.8 years, *P* =.004)

Duration of follow-up - 14.0 ± 8.8 years

Age at last visit - 21.9 ± 9.6 years

Autoimmune diseases

Prevalence of [autoimmune thyroiditis (45.6%) and positive celiac serology (7.1%)] and age at onset of autoimmune co-morbidities were similar in both groups.

Metabolic disturbances

Weight status:

- **BMI-SDS (TS charts)** increased during follow-up
- Obesity at young adulthood was more prominent in girls with 45,X0 (*P* = .013).

Impaired glucose metabolism:

Percentage of patients with impaired glucose metabolism increased from adolescence to young adulthood:

- IFG (>100mg/dL) from 10.6% to 17.9%
- IGT (140-199mg/dl) from 23.8% to 30.5%
- elevated HbA1c (>5.8%) from 12% to 16.7%.

Lipid profile levels at young adulthood

Percentage of patients with lipoprotein levels above the 90th centile:

- TC - 29.1%
- LDL-c - 23.5%
- TG - 30.1%

- **Elevated blood pressure** at young adulthood
  - Systolic blood pressure increased in 52.3%
  - Diastolic blood pressure in 18.2%

The prevalence of metabolic disturbances (impaired glucose metabolism, dyslipidemia, and hypertension) were similar in both groups

Karyotype distribution in patients with Turner syndrome

Karyotype distribution	Number (%)
Monosomy 45XO	31 (30.1)
Mosaicism normal cell line 45X, 46XX	11 (10.7)
Mosaicism with isochromosomes	10 (9.7)
Mosaicism with ring chromosomes	5 (4.8)
Mosaicism with fragments	0
Mosaicism with Y chromosome	8 (7.8)
Deletion	8 (7.8)
Translocation	1 (1)
Mosaicism normal cell line 45X, 47XXX	5 (4.8)
Isochromosome	8 (7.8)
Mosaic other	14 (13.6)
Other	2 (1.9)

Glucose metabolism in patients with Turner syndrome – Comparison between 45,X0 and other X chromosome abnormalities

	Turner cohort	45, X0	Other X	*P*
BMI-SDS	0.54 ± 1.73	1.24 ± 1.74	0.26 ± 1.66	.013
Fasting glucose	*(n = 95)*	*(n = 30)*	*(n = 65)*	
Age, years	24.0 ± 11.2	22.4 ± 9.3	24.7 ± 12.0	.356
Normal (< 100 mg/dl), %	82.1	86.7	80	
Impaired (100-125 mg/dl), %	12.6	10	13.8	.718
Diabetes (> 125 mg/dl), %	5.3	3.3	6.2	
OGTT	*(n = 36)*	*(n = 12)*	*(n =24)*	
Age, years	22.9 ± 5.4	23.9 ± 5.7	22.3 ± 5.3	.476
Glucose 120 min				
Normal (<140 mg/dl), %	69.4	66.7	70.8	
Impaired glucose tolerance (IGT) (140-199 mg/dl), %	30.5	33.3	29.2	.798
Diabetes (> 199 mg/dl), %	0	0	0	
HOMA-IR index				
Abnormal (≥ 3), %	12.5	9.1	14.3	.673
HbA1c				
Mean	5.5 ± 0.9	5.3 ± 0.6	5.5 ± 0.6	
Normal ≤ 5.7%, %	83.3	81	84.6	
Pre-diabetes 5.8-6.4%, %	10	19	5.1	.09
Diabetes ≥ 6.5%, %	6.7	0	10.3	

Blood pressure distribution in young adults (age>18 years) with Turner syndrome – Comparison between 45,X0 and other X chromosome abnormalities

	Turner syndrome (n =44)	45, X0 (n =13)	Other karyotypes (n =31)	*P*
Age, years	24.2 ± 6.6	25 ± 6.2	23.8 ± 6.6	.862
Systolic blood pressure				
Normal, %	47.7	46.2	48.4	
Pre-hypertension, %	45.5	46.2	45.2	.842
Stage 1 hypertension, %	4.5	7.6	3.2	
Stage 2 hypertension, %	2.3	0	3.2	
Diastolic blood pressure				
Normal, %	81.8	76.9	83.9	
Pre-hypertension, %	9.1	15.4	6.5	.638
Stage 1 hypertension, %	9.1	7.7	9.7	
Stage 2 hypertension, %	0	0	0	

CONCLUSIONS

In TS, an increased risk of autoimmune diseases and metabolic disorders were found regardless of the karyotype.

Careful surveillance and early intervention in patients with 45, X0 and increased weight gain are warranted in an attempt to prevent obesity and thereby the risk for development of metabolic disorders.

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