TURNER'S SYNDROME AND LIVER INVOLVEMENT: PREVALENCE AND CHARACTERIZATION OF A LARGE POPULATION

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INTRODUCTION Elevated liver function tests (↑LFTs) are frequent in Turner's Syndrome (TS). The cause and clinical significance is unclear. Obesity is one of the common causes thought to contribute to this finding in TS.

Recent studies suggest that liver architectural changes described in TS may be the consequence of a primary vascular involvement[1].

OBJECTIVES In order to further elucidate the pathophysiological mechanism underlying this condition, we studied the prevalence of ↑LFTs and their relationship with karyoptype, anthropometric, metabolic and TS-related disease in a large cohort of adult TS women (n=101) from a single centre with a dedicated TS clinic and a multidiscliplinary approach to liver and cardiac conditions.

RESULTS In TS, 35% women had one or more liver biochemical parameter persistently raised (mean duration of follow-up 6.2 yrs ± 3.5 SD), with the most frequently elevated enzyme being GGT. Hepatitis serology and autoimmune-markers were negative and bilirubin was normal in all. In the normal LFTs-group no past history of ↑LFTs was reported.

There were no associations between ↑LFTs and karyotype, anthropometric values, diabetes, hypertension and autoimmunity.

Age and HRT duration was significantly higher in the↑LFTs-group. Univariate analysis of the variance revealed no significant difference between the groups for the duration of the HRT when adjusted for age. Dyslipidaemia, serum total cholesterol and LDL were significantly higher in the ↑LFTs-group (Tab. 1).

	Normal LTFs N= 66 pts (65%)	↑LFTs N= 35 pts (35%)	p value
Mean age, *yrs*	33.2 ± 12.5	41.1 ± 13.1	0.004
45 X0	38%	47%	0.57
HRT duration, *yrs*	12.3 ± 10.7	19.6 ± 12.3	0.003
GH therapy	42%	37%	0.44
Weight, *kg*	60.7 ± 13.9	63.6 ± 15.6	0.36
Height, *cm*	149.8 ± 8.5	148.7 ± 6.6	0.51
BMI, *kg/m²*	27.9 ± 6.9	28.8 ± 7.2	0.53
Diabetes	6%	17%	0.08
HbA1c, *mmol/mol*	32.8 ± 5.6	36.3 ± 13.8	0.08
Hypertension	17%	34%	0.07
Dyslipidaemia	8%	23%	0.03
Tot chol, *mmol/L*	4.8 ± 1.1	5.5 ± 1.1	0.004
LDL, *mmol/L*	2.72 ± 0.8	3.1 ± 0.8	0.015
HDL, *mmol/L*	1.63 ± 0.6	1.8 ± 0.5	0.28
TG, *mmol/L*	1.2 ± 0.7	1.4 ± 0.8	0.22
AbTPO	22%	34%	0.18
Coeliac	8%	3%	0.32

Table 1. Comparisons of anthropometric, metabolic and hormonal data between groups. HRT, estrogen replacement therapy. Continuous variables are expressed as means ±SD. p<0.05.

	Normal LFTs	↑LFTs	p value
Aortic coartation	6%	9%	0.64
Bicuspid aortic valve	13%	18%	0.49
Echo Root diameter, *cm*	2.7 ± 0.3	2.8 ± 0.4	0.14
MRI Root diameter, *cm*	2.9 ± 0.4	3.1 ± 0.2	0.27
Echo AA diameter, *cm*	2.5 ± 0.4	2.9 ± 0.5	0.002
Echo AA index	1.6 ± 0.3	1.8 ± 0.3	0.06
MRI AA diameter, *cm*	2.6 ± 0.5	3.2 ± 0.4	0.009
MRI AA index	1.7 ± 0.3	1.9 ± 0.4	0.11
MRI ASI > 2 *cm/m²*	17%	56%	0.08
Echo+MRI ASI > 2 *cm/m²*	16%	42%	0.04

Table. 2. Comparisons of cardiac and aortic evaluation between groups. AA, ascending aorta. ASI, aortic size index. Continuous variables are expressed as means ±SD. p<0.05.

91 women had cardiac transthoracic echocardiography and 27 had cardiac MRI. The aortic size index (ASI, diameter corrected for body surface area) was measured; a value greater than 2 cm/m^2 defined the presence of significant aortic dilatation in TS. The ascending aorta (AA) diameter and the ASI (combining the results from echo and MRI) were significantly greater in the ↑LFTs-group (Tab. 2).

IMAGING STUDY: Abdominal ultrasound, where performed in pts with ↑LFTs, was normal in 12 pts, suggestive of NAFLD (non-alcoholic-fatty-liver-disease) in 6 and in one (diagnosed with cryptogenic cirrhosis in childhood) it showed nodularity and hepatosplenomegaly. FibroScan was performed in 7 pts (a liver stiffness evaluation (LSE) >7 kPa suggested significant fibrosis and >11 kPa cirrhosis): 4 had LSE <6 kPa, two were 7.8 and 8.9 kPa and the LSE was 30.1 kPa in the pt with cirrhosis. Two women had a normal MRCP. Liver biopsy was performed in 5 pts: one normal, 2 NAFLD, one showed chronic hepatitis and one showed mild steatosis plus abnormal portal tract with periductal fibrosis.

CONCLUSIONS This study shows 1) for the first time the relationship between ↑LFTs and large vessel abnormalities, demostrated with aortic imaging, suggesting that liver involvement may be associated with a primary vascular involvement in TS. 2) LFT abnormalities are significantly more common in TS women with dyslipidaemia. 3) Vascular disorder rather than autoimmunity etiology may be one of the commonest underlying causes of ↑LFTs. 4) HRT can be safely continued in TS women with liver biochemical abnormalities.

References: 1. Roulot D, et al. *Vascular involvement of the liver in Turner's syndrome.* Hepatology 2004