LIVER STEATOSIS IN OBESE CHILDREN COURSES WITH ENHANCED INSULIN RESISTANCE AND DYSLIPIDEMIA, WHICH ARE INFLUENCED BY GENDER, PUBERTY, RACE AND BODY FAT DISTRIBUTION.

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Introduction:

The authors have nothing to disclose

- Obesity, insulin resistance (**IR**) and dyslipidemia are major predisposing factor for the development of liver steatosis (**LS**), although severity of **LS** is not exclusively related to the degree of overweight.
- The observed increase in obesity prevalence and severity in children in the past decades has turned it into the main cause of **LS** in children and adolescents, even above drug side effects or biliary diseases.

Objective:

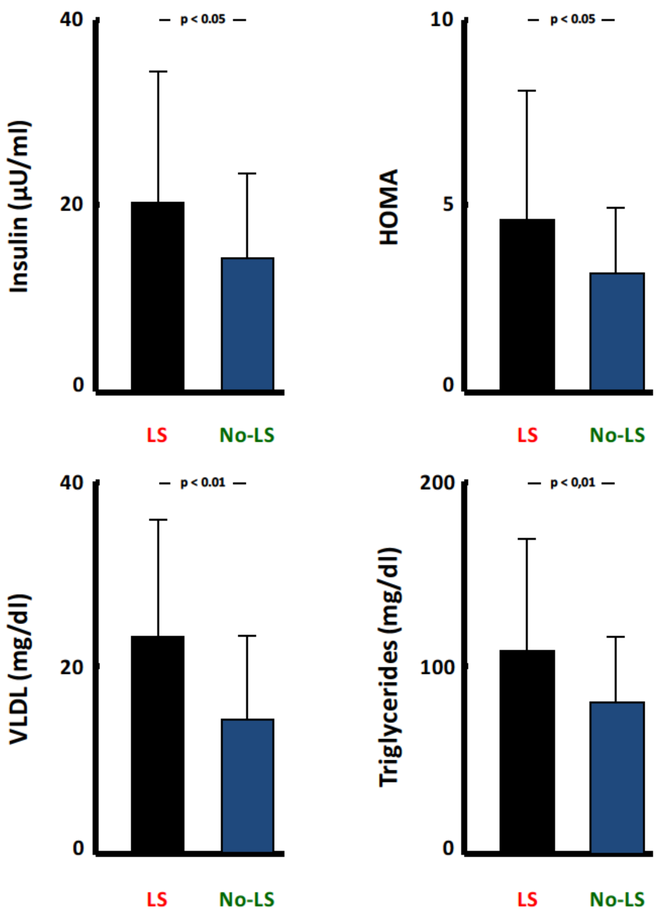
- To investigate the differential features of patients diagnosed with obesity associated LS (as diagnosed by ultrasonography).

Patients and methods:

- We retrospectively studied 88 obese children with **LS** (**LS-OB**: mean age 12.07 2.81 years and BMI 4.60 2.30 SDS) and 88 obese children without LS (**no-LS-OB** : mean age 11.91 2.76 years and BMI 4.46 3.43 SDS).
- Both groups were age, BMI, gender, race and puberty matched and their composition was: 71.6% males / 28.4% females; 56.5% Caucasians / 41.2% Latinos; 60.2% pubertal/39.8% prepubertal.
- *The analyzed variables included:* ***Anthropometric:*** Body mass index (BMI-SDS). ***Metabolic:*** Baseline and after OGTT (1.75 g/kg, maximum 75g) glucose and insulin levels and derived indexes (HOMA, WBISI); HbA1c; lipid profile, apoprotein-A1 and B, liver enzymes (AST/ALT) and uric acid in both groups. Additionally, body composition measured by Dual energy X-ray absorptiometry (DXA) and abdominal fat distribution measured by magnetic resonance imaging (MRI) were studied in 27 **LS-OB**.

Results:

- Obesity associated **LS** was mainly diffuse (97.7%, only 4 cases of focal LS) and mild (Stage I / III, 65.9%). **LS-OB** showed a prevalence of IR of 65.8% (as estimated by insulin levels in the OGTT); mean HOMA 4.62 3.36 and HbA1c levels were >5.7% in 35.9% of them. In **LS-OB,** the prevalence rate for dyslipidemia (low HDL, high LDL, VLDL or triglycerides), 25-OH-vitamin D insufficiency (< 20 ng/ml) and IR were 30%, 79.4% y 65.8%, respectively.
- **LS-OB** showed higher AST/ALT ($p<0.001$), insulin/HOMA ($p<0.05$) and triglycerides/VLDL ($p<0.01$) than **no-LS-OB** (FIGURE).
- Among diffuse OB-LS, those moderate-severe (Stage II-III; 31.8%) associated lower WBISI and HDL levels ($p < 0.05$) and higher AST ($p < 0.05$), ALT ($p < 0.01$), apoprotein-B ($p < 0.05$) and LDL/HDL ratio ($p < 0.05$). Their trunk to lower limb (DXA) and visceral/subqutaneous (RM) fat ratios were higher ($p < 0.05$) than those in patients with mild LS (Stage I, 65.9%) (TABLE).
- Among **LS-OB,** increased serum liver enzyme levels (AST/ALT) was observed in 40.5% patients (lower levels in prepubertals and females [$p < 0.05$]). Compared to those patients with LS but without increased serum liver enzymes, they showed higher glucose and insulin at 30 minutes in the OGTT ($p<0.05$ and $p<0.01$), cholesterol, apoprotein-B, cholesterol/HDL and LDL/HDL-ratios ($p<0.05$) and higher trunk to lower limb (DXA) and visceral/subqutaneous (RM) fat ratios ($p<0.05$).
- Latinos showed higher rates of dyslipidemia (decrease in HDL and increased LDL/HDL ratio), 25-OH-vitamina D insufficiency ($p < 0.05$ and $p<0.001$, respectively) and *acantosis nigricans* ($p < 0.01$) (TABLE).



Comparison according to ethnic backgroundc	Latino	Caucasian	Significance level
Chronological age in years (mean± SDS)	11.57 ± 2.90	12.61 ± 2.70	NS
SEX (%) *FEMALE* *MALE*	 37 63	 25 75	NS
PUBERTY (%) *Prepubertal* *Pubertal*	 35.3 64.7	 39.6 60.4	NS
BMI-SDS	4.14 ± 1.59	4.88 ± 2.62	NS
HDL (mg/dl)	38.55 ± 11.20	44.63 ± 11.06	p <0.05
LDL/HDL ratio	2.78 ± 0.96	2.33 ± 0.94	p<0.05
25-OH-vitamin D (ng/ml)	12.30 ± 4.96	22.36 ± 7.71	p<0.001
Comparison according to LS severity (ultrasonography)	**Moderate-Severe (Stages II-III)**	**Mild (Stage I)**	**Significance level**
WBISI	0.78 ± 0.32	1.10 ± 0.64	p<0.05
HDL (mg/dl)	38.10 ± 10.00	44.59± 11.24	p<0.05
LDL/HDL ratio	2.82 ± 1.03	2.32 ± 0.90	p<0.05
AST (U/l)	42.61 ± 19.22	33.72 ± 14.62	p<0.05
ALT (U/l)	60.93 ± 35.03	38.59 ± 24.39	p<0.01
Apoprotein-B (mg/dl)	90.02 ± 26.31	77.39 ± 17.02	p<0.05
Trunk to lower limb fat ratio (DXA)	1.58 ± 0.33	1.32 ± 0.17	p<0.05
Visceral to sunqutaneous fat ratio (MRI)	0.28 ± 0.08	0.22 ± 0.05	p<0.05

Abbreviations: **BMI:** Body mass index; **HDL**: high density lipoprotein; **LDL**: low density lipoprotein; **LS**: Liver steatosis; **NS**: non significant; **VLDL**: Very low density lipoprotein; **WBISI**: Whole body insulin sensitivity index.

Conclusions:

1. Liver steatosis in obese children courses with enhanced insulin resistance and dyslipidemia.
2. Severe obesity associated liver steatosis is associated with greater visceral adiposity and metabolic impairment, which are also influenced by race, sex and pubertal stage.

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