Early menarche is associated with insulin resistance and non-alcoholic fatty liver disease in obese adolescents

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Background

Menarche is a significant event in the reproductive life of a woman and represents the late event in puberty indicating that a sexually immature child has become reproductively capable. Even though the timing of puberty onset is approximately conserved in different populations, the puberty starts across a wide range of ages in normal girls. However, in the last decades we are observing that girls are experiencing earlier breast development and earlier menarche, also probably due to raised obesity prevalence in youth. Although early menarche (<12 years) is not considerable as a pathological and then treatable event as precocious puberty, it is associated with increased morbidity (i.e.; obesity, diabetes, insulin resistance, metabolic syndrome, cardiovascular disease, stroke) and mortality later in life. In addiction, it has also been found an inverse association between age at menarche and non-alcoholic fatty liver disease (NAFLD) prevalence in a large population of middle-aged women.

Objective

We aimed to evaluate the impact of early menarche on metabolic parameters and NAFLD in a population of Italian obese pediatric patients.

Methods

Three-hundred eighteen young obese (mean BMI-SDS 2.91±0.81) female patients (mean age early menarche group 11.96±2.89 vs 12.85±2.97 years; mean age menarche 10.30±0.83 vs 12.64±0.80) consecutively attending our Obesity Clinic were enrolled. Anthropometric, biochemical, and metabolic evaluations were conducted in all subjects (Table 1). To detect the presence of hepatic steatosis, a liver ultrasound was also performed.

N	318
Age (years)	12.31±2.95
Menarche age (years)	11.21±1.40
BMI SDS	2.91±0.81
Waist (cm)	90.86±11.87
SBP-DS (mmHg)	0.85±1.19
DBP-DS (mmHg)	0.37±0.82
Total Cholesterol (mg /dL)	158.89±29.37
HDL-C (mg/dL)	44.01±13.02
LDL-C (mg/dL)	88.14±31.91
Triglycerides (mg/dL)	101.21±67.03
Glycaemia (mg/dL)	79.11±8.30
ALT (IU/mL)	23.97±19.07
AST (IU/mL)	21.02±8.70
gammaGT (IU/L)	16.09±7.24
HOMA-IR	5.77±4.08
Hepatic steatosis (%)	43.2

Table 1. Clinical and laboratory characteristics of the 318 patients enrolled in the study.

	Early (N=194)	N=(124)	p
Menarche age (years)	**10.30±0.83**	**12.64±0.80**	**<0.001**
Age (years)	11.96±2.89	12.85±2.97	0.75
BMI SDS	2.94±0.77	2.86±0.88	0.35
Waist (cm)	90.17±11.07	92.01±13.05	0.19
SBP-DS (mmHg)	0.92±1.14	0.73±1.27	0.17
DBP-DS (mmHg)	0.34±0.80	0.40±0.85	0.52
Total Cholesterol (mg /dL)	156.46±30.03	162.68±28.01	0.06
HDL-C (mg/dL)	42.94±12.93	45.66±13.03	0.07
LDL-C (mg/dL)	87.31±33.74	89.43±28.94	0.57
Triglycerides (mg/dL)	98.10±64.49	106.02±71.42	0.38
Glycaemia (mg/dL)	79.38±8.51	76.49±7.96	0.12
HOMA-IR	**6.10±4.36**	**5.36±3.69**	**0.02**
ALT (IU/mL)	**23.69±21.23**	**22.50±13.15**	**0.04**
AST (IU/mL)	20.50±8.99	21.83±8.19	0.18
gammaGT (IU/L)	16.01±6.58	16.20±8.20	0.51
Hepatic steatosis (%)	**67.6**	**32.4**	**0.04**

Table 2. Clinical and laboratory characteristics of the study population according to the menarche age.

Results

Patients with early menarche showed higher fasting glucose levels (p=0.003), Homeostasis model assessment of insulin resistance (HOMA-IR) (p=0.02), higher alanine transaminase (ALT) (p=0.016) values and prevalence of hepatic steatosis (67.6% vs 32.4%, p=0.04) than the other obese patients (Figure 1). The two groups showed no difference in BMI-SDS (p=0.35) (Table 2). Moreover, a higher risk to show hepatic steatosis was found in patient with early menarche (OR 1.80, CI 1.11-2.90, p value 0.016). A general linear model for ALT levels including as covariates, HOMA-IR, BMI-SDS, and menarche age (model R^2 25%; model P < .0001) was performed. It confirmed a direct association of ALT levels with early menarche age (p=0.002).

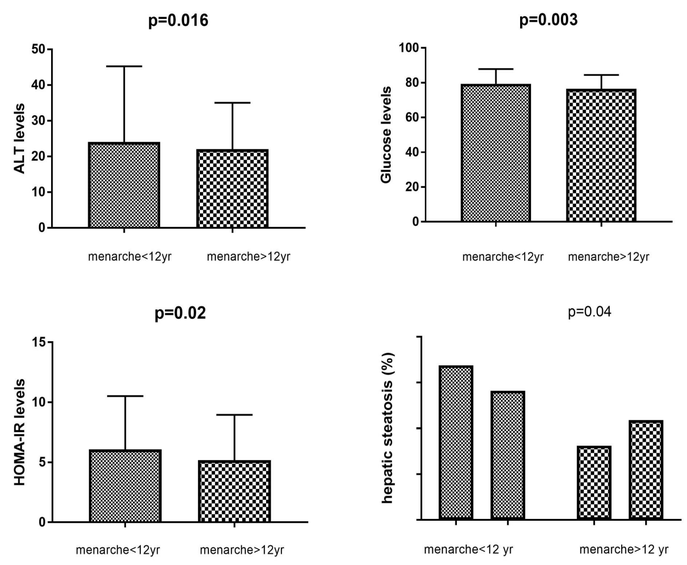

Figure 1. Significant associations between early menarche and ALT levels, glucose levels,HOMA-IR values, and prevalence of hepatic steatosis.

Conclusions

We demonstrated for the first time that obese girls with early menarche had a higher risk of NAFLD and insulin resistance already in adolescence compared to equally obese patients with regular age at menarche. Given that, early identification of these patients could be useful to carry out an adequate management in order to avoid the progression of NAFLD-related metabolic consequences.

References

1.DiVall SA, Radovick S. Pubertal development and menarche. Ann N Y Acad Sci. 2008;1135:19-28.

2.Biro FM, Greenspan LC, Galvez MP. Puberty in girls of the 21st century. J Pediatr Adolesc Gynecol. 2012;25(5):289-94.

3.Ryu S, Chang Y, Choi Y, Kwon MJ, Kim CW, Yun KE, et al. Age at menarche and non-alcoholic fatty liver disease. J Hepatol. 2015;62(5):1164-70.

4.Lim SW, Ahn JH, Lee JA, Kim DH, Seo JH, Lim JS. Early menarche is associated with metabolic syndrome and insulin resistance in premenopausal Korean women. Eur J Pediatr. 2016;175(1):97-104.

We have no conflicts of interest to declare.