Hospital Infantil Universitario Niño Jesús — SaludMadrid — INSTITUTO DE INVESTIGACIÓN SANITARIA IIS·P·M — Comunidad de Madrid

excelencia UAM CSIC+

ciberobn — Centro de Investigación Biomédica en Red Fisiopatología de la Obesidad y Nutrición

INTRAUTERINE GROWTH RESTRICTION IS ASSOCIATED WITH GREATER SEVERITY IN CHILDHOOD OBESITY-ASSOCIATED METABOLIC IMPAIRMENT AND POORER ADULT HEIGHT PREDICTION

Rocío González-Leal[1], Julián Martínez-Villanueva[1], Jesús Argente[1,2,3], Gabriel Á. Martos-Moreno[1,2,3].

[1]Department of Endocrinology, Hospital Infantil Universitario Niño Jesús, IIS La Princesa. [2]Universidad Autónoma de Madrid [3]CIBERobn, Instituto de Salud Carlos III; Madrid, Spain.

The authors have nothing to disclose.

Introduction:

• Restricted intrauterine growth is known to increase the risk of childhood obesity and its associated metabolic derangement; however, the existence of eventual differences in the severity of obesity and its associated comorbidities among obese children upon the background of their newborn anthropometry is insufficiently explored.

• Similarly, obesity in children is assumed to be associated to increased prepubertal growth rate along with accelerated skeletal maturation but without impairment of final height. Having been born small for gestational age could affect this growth pattern in obese children.

Objective:

• To investigate the effect of intrauterine growth (as shown by newborn anthropometry) on physical and metabolic features in obese children and adolescents.

Patients and methods:

• A retrospective study was conducted on a cohort made up of 1049 obese children and adolescents (46.8% females / 53.2% males; mean age: 10.31 ± 3.23 years; BMI: +4.00 ± 1.95 SDS; 54.9% prepubertal / 45.1% pubertal).

• Comparison groups were established according to the patients´ newborn anthropometry standardized for gestational age (GA) as: adequate for GA (AGA, n=810), small for GA (SGA, n=73) or large for GA (LGA, n=166).

• **Studied variables:**

- **Timing and severity of obesity:** Age at the onset of obesity, age and BMI-SDS at their first visit.
- **Growth:** Bone age (Greulich & Pyle), adult height prediction (Bailey & Pinneau), IGF-I and IGFBP-3 serum levels.
- **Metabolic:** - Fasting glucose, insulin, cholesterol (total, HDL, LDL, VLDL) and triglyceride serum levels.
  - HOMA index, Area under the curve (AUC) for glucose and for insulin in the OGTT (n=638)
  - LDL/HDL and triglyceride/HDL ratios.

Results:

• SGA prevalence was 6.3%. None of these patient received rGH treatment as all of them had presented with spontaneous catch-up growth. No inter-group differences were observed in age (at obesity onset or 1st visit), BMI-SDS, sex or pubertal distribution.
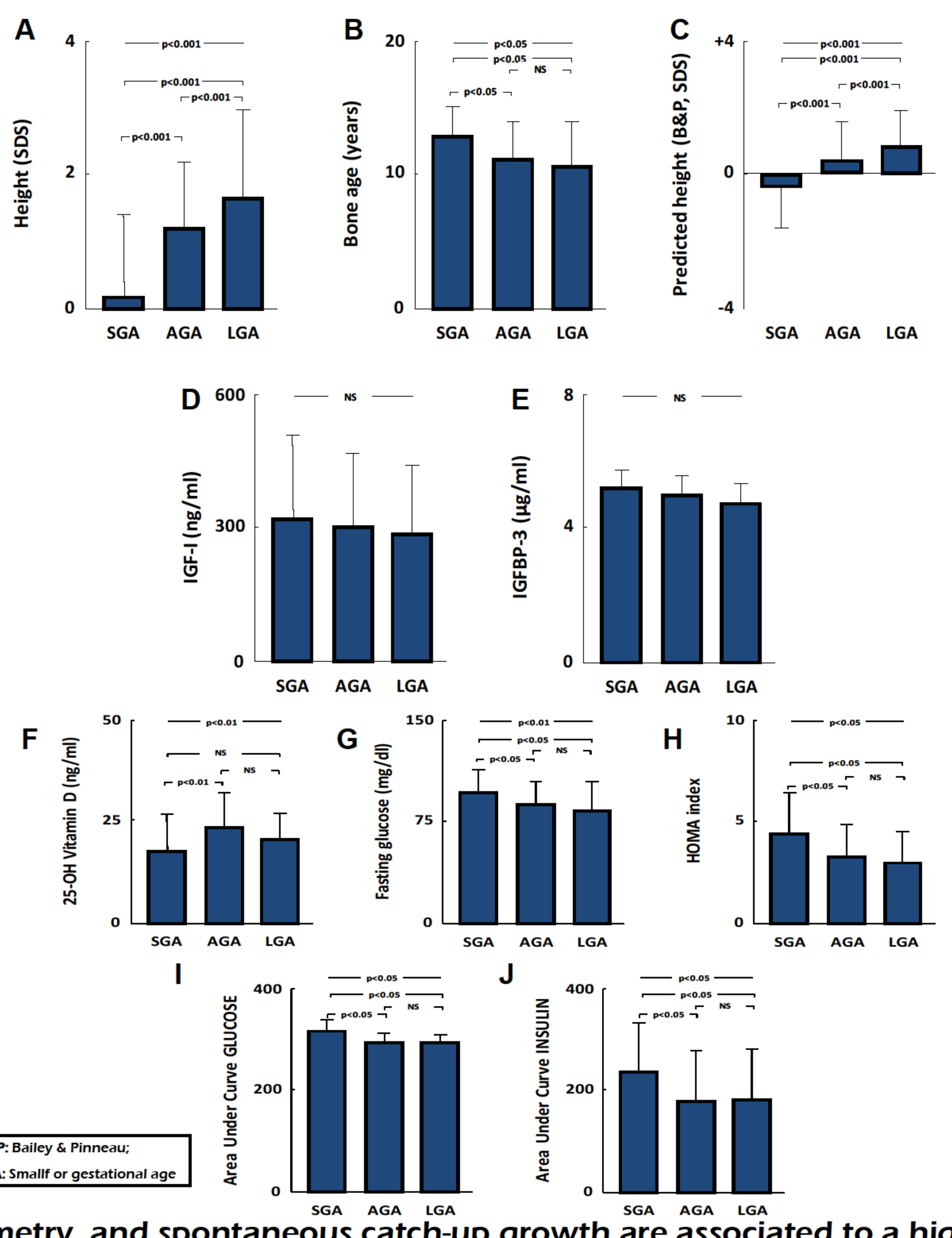
• LGA were taller and SGA shorter than AGA ($p<0.001$, Figure A) with SGA showing more advanced skeletal maturation ($p<0.05$, Figure B) that resulted in a poorer adult height prediction ($p<0.001$, Figure C), despite similar IGF-I and IGFBP-3 levels (Figures D & E).

• No other differences were found between LGA and AGA.

• In contrast, SGA had lower 25-OH-vitamin D levels ($p<0.01$, Figure F) and more severe impairment of carbohydrate metabolism with higher fasting glucose ($p<0.01$, Figure G), HOMA and AUCs for glucose and insulin in the OGTT than the two other groups (all $p<0.05$, Figures H to J).

• **When compared exclusively with AGA,** SGA patients also had higher triglycerides and triglyceride/HDL ratio (both $p<0.05$), as well as a higher prevalence of increased levels of VLDL cholesterol (25.0% in SGA vs. 10.3% in AGA (χ^2 13.10; $p<0.01$).

Additionally, prevalence of insulin resistance (as estimated by insulin levels in the OGTT [fasting > 15; peak > 150 and/ or insulin at 120 minutes > 75 µU/ml]) was significantly higher in SGA (57.0%) than in AGA (44.6%; χ^2 3.65; $p<0.05$).

Figures A–J: A. Height (SDS); B. Bone age (years); C. Predicted height (B&P, SDS); D. IGF-I (ng/ml); E. IGFBP-3 (µg/ml); F. 25-OH Vitamin D (ng/ml); G. Fasting glucose (mg/dl); H. HOMA index; I. Area Under Curve GLUCOSE; J. Area Under Curve INSULIN. Groups: SGA, AGA, LGA.

Abbreviations: AGA: Adequate for gestational age; B&P: Bailey & Pinneau; LGA: Large for gestational age; NS: non significant; SGA: Smallf or gestational age

Conclusions:

1) Restriction of intrauterine growth, as shown by SGA anthropometry, and spontaneous catch-up growth are associated to a higher frequency and severity of obesity-associated metabolic comorbidities.

2) Obese children born SGA with spontaneous catch-up growth exhibit poorer adult height prediction than those born AGA or LGA.