Early life programming of abdominal adiposity in adolescents; The HELENA study

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Aim: To examine the relationship between birth weight (BW) and abdominal adiposity in adolescents.

Research Design and Methods: A total of 284 adolescents (49.3% females) aged 14.9±1.2 years were included in the study. BW and gestational age were obtained from parental records. Abdominal adiposity (in three regions: R1, R2, and R3), trunk and total body fat mass (FM) were measured by DXA. Regional FM indexes (FMI=FM/height$^2$) were thereafter calculated (Trunk FMI and abdominal FMI R1, R2, and R3).

Results: BW was negatively associated with abdominal FMI R1, R2 and R3 independently of total FM, gestational age, gender, breastfeeding duration, pubertal stage, physical activity and socioeconomic status (all $P<0.01$).

Conclusions: Our study shows an inverse association between BW and abdominal adiposity in adolescents, independently of total FM and other potential confounders. These findings suggest that fetal nutrition, as reflected by BW, may have a programming effect on abdominal adiposity later in life.
Low birth weight (BW) seems to increase the risk of type 2 diabetes and cardiovascular disease by programming a more central fat deposition (1). However, the association between BW and fat distribution remains controversial (2-4). Studies using advanced methods to assess body composition such as Dual Energy X-ray Absorptiometry (DXA) may help to better describe these associations.

The aim of this study was to examine the relationship between BW and abdominal adiposity measured by DXA in Spanish adolescents participating in the Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional study (HELENA-CSS).

SUBJECTS AND METHODS
The HELENA study was designed to examine the interactions between personal, environmental and lifestyle influences on the risk factors for future cardiovascular diseases (5).

The present study comprises 284 healthy Caucasian adolescents (140 females, 144 males) aged 14.9±1.2y from Zaragoza (Spain) with complete data on BW, gestational age and abdominal fat measured by DXA. To be born at more than 37 weeks of gestation (95.1%) was an additional inclusion criterion. The study was approved by the Human Research Ethics Committee of Aragon. Written informed consent to participate was obtained from both parents and adolescent. BW and duration of gestation were obtained from the health booklets (6).

Body composition and abdominal fat distribution: Body weight and height, waist circumference and subscapular to tricipital skinfold thicknesses were measured in triplicate (7). Waist circumference, waist to height ratio and subcapular to tricipital skinfold (StT) were used as surrogate markers of central body fat.

We measured fat mass (FM) with DXA using an extended research model (pediatric version of the software QDR-Explorer, Hologic Corp., Software version 12.4, Waltham, MA, USA). Abdominal adiposity was assessed at three different regions, R1, R2, and R3 (8, 9). A rectangle was drawn on the digital scan image to establish every region. All of them have the lower horizontal border on the top of iliac crest. For R1 the upper border was established parallel to the end of the lowest rib. The upper border of the R2 was parallel to the junction of the T12 and L1 vertebrae, and for the R3 was parallel to the middle of the costo-vertebrae articulation of the last rib. The lateral sides were adjusted to include the maximal amount of abdominal tissue within each region. Trunk FM and abdominal FM R1, R2 and R3 were used as surrogates of abdominal adiposity.

Confounders: Several factors potentially related to BW or fat distribution were investigated. Pubertal status was evaluated by trained physician (6, 10). Physical activity (PA) was objectively assessed by accelerometry (Actigraph MTI) (11). Socioeconomic status (SES) was assessed via questionnaire and defined by maternal and paternal educational status (1=lower education; 2=lower secondary education, 3=higher secondary education and 4=higher education or university degree). Exclusive breastfeeding duration was coded as follows: 0=never; 1 <3 months; 2=3-6 months; 3=>6 months (6).

Pubertal status was obtained in 97.9% of adolescents (96.4% of males, 97.9% of females), PA in 94.7% (95% of males, 94.4% of females), SES in 97.9 (99.3% of
males, 98.6% of females) and information on breastfeeding duration in 98.9% (99.6% of males, 99.3% of females).

**Statistical analysis:** Statistical analyses were performed using SPSS software 16.0 and the level of significance was set at 0.05. We adjusted abdominal fat deposition variables by height squared. Regional FM indexes (FMI=FM/height^2) were then calculated (Trunk FMI and abdominal FMI R1, R2, and R3).

The association of BW with fat distribution was analyzed by linear regression in an extended model approach: Model 1 included the predictor (BW) and the dependent variable (trunk FMI, abdominal FMI R1, R2 and R3, waist circumference, waist to height or StT) adjusted for gestational age. For model 2, total FM was entered into the model. For model 3, a set of confounders (gender, pubertal stage, breastfeeding duration and PA) was added. For model 4, SES was added to the model. We also tested the interaction effect between gender and BW. Pubertal stage, SES and breastfeeding duration were entered as dummy variables.

**RESULTS**

BW was 3.31±0.44 kg (3.36±0.50 in males and 3.26±0.39 in females). As there was no evidence that the associations of BW with trunk FMI and abdominal FMI R1, R2 and R3 differed between females and males (P for interaction, 0.256, 0.301, 0.243 and 0.304, respectively) the results are presented jointly for males and females (Table 1).

BW adjusted for gestational age was negatively associated with trunk and abdominal FMI, R1 and R2 (all P<0.05). When total FM was entered into the model (model 2), these relationships were strengthened (P<0.01). The results did not change after further adjustment for potential confounders (models 3 and 4). A decrease of 1 Kg in BW predicted an increase of ≈ 50g/m^2 in abdominal FMI. The adjustment for age instead for pubertal stage did not substantially change the results (data not shown).

**DISCUSSION**

The present study shows a negative association between BW and central and abdominal fat deposition independently of total body FM in adolescents. These associations were independent of gestational age, pubertal stage, PA, breastfeeding duration and SES.

Although our sample size was not comparable to that of larger epidemiological studies, the main strength was the use of DXA in an extended model which is a very accurate technique to measure abdominal adiposity (9). Results from the limited number of studies that have investigated this issue using direct measures of central fat in adolescents are controversial. Our findings are in agreement with those of Dolan et al (2) in a study conducted in 101 young adolescents. One other report found no relationship between BW and central fat deposition, but included children and adolescents with a very large range of age (from 4-20y) (3).

In conclusion, our findings give further support to the concept that fetal undergrowth, as reflected by lower BW, may have a programming effect on increased abdominal adiposity later in life. These results may contribute to explain the relationship between low BW and later metabolic disorders as diabetes or cardiovascular disease.
ACKNOWLEDGMENTS

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REFERENCES
Table 1 - Unstandardized regression coefficients ($\beta$) and standard errors (SE) showing the association between birth weight and abdominal fat deposition indexes in adolescents.

<table>
<thead>
<tr>
<th></th>
<th>Model 1 (n=284)</th>
<th>Model 2 (n=258)</th>
<th>Model 3 (n=258)</th>
<th>Model 4 (n=252)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\beta$</td>
<td>SE</td>
<td>$P$</td>
<td>$\beta$</td>
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<tr>
<td>Trunk FMI (kg/m$^2$)</td>
<td>0.317</td>
<td>0.158</td>
<td>0.045</td>
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<tr>
<td>Abdominal R1 FMI (kg/m$^2$)</td>
<td>-0.055</td>
<td>0.032</td>
<td>0.091</td>
<td>-0.037</td>
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<td>Abdominal R2 FMI (kg/m$^2$)</td>
<td>-0.090</td>
<td>0.043</td>
<td>0.036</td>
<td>-0.060</td>
</tr>
<tr>
<td>Abdominal R3 FMI (kg/m$^2$)</td>
<td>-0.104</td>
<td>0.048</td>
<td>0.031</td>
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<td>Waist (cm)*</td>
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<td>0.007</td>
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<td>Waist to height</td>
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<td>-0.008</td>
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<td>Subscapular SFT (mm)</td>
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<td>0.534</td>
<td>0.001</td>
<td>-1.601</td>
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</tbody>
</table>

Analysis was performed on log-transformed data.
†Birth weight controlling also for tricipital skinfold thickness.
FMI: fat mass index (FM/height$^2$); R1, R2 and R3: abdominal regions 1, 2 and 3; SFT: skinfold thickness.
Model 1: BW adjusted for gestational age.
Model 2: model 1 + total body fat.
Model 3: model 2 + gender, breastfeeding duration, pubertal stage and physical activity.
Model 4: model 3 + socioeconomic status (mother and father educational levels).