**Table S1.** Anthropometric and biochemical characteristics of girls and boys of cross-sectional study.

| | Girls | | | | Boys | | | |
|---|---|---|---|---|---|---|---|---|
| | **Lean (n= 38)** | **Obesity (n= 40)** | ***P*** | ***Test*** | **Lean (n= 35)** | **Obesity (n= 37)** | ***P*** | ***Test*** |
| Age (yr) | 10.3 (3.5) | 11.8 (3.2) | 0.06 | $ | 10.7 (3.4) | 10.5 (2.8) | 0.72 | $ |
| SD | 17:21 | 17:23 | 0.84 | | 17:18 | 21:16 | 0.49 | |
| Birth weight (kg) | 3.3 (0.4) | 3.2 (0.5) | 0.79 | $ | 3.2 (0.8) | 3.3 (0.5) | 0.74 | $ |
| **Weight (kg)** | **41.3 (16.4)** | **63.7 (17.8)** | **<0.001** | **$** | **35.9 (13.0)** | **61.4 (24.0)** | **<0.001** | **#** |
| **Height (cm)** | **141.4 (17.7)** | **149.7 (14.1)** | **0.02** | **$** | 140.2 (19.5) | 146.8 (18.0) | 0.15 | $ |
| **BMI (kg/m$^2$)** | **19.7 (4.0)** | **27.8 (4.4)** | **<0.001** | **$** | **17.5 (2.8)** | **27.2 (4.8)** | **<0.001** | **#** |
| **WC (cm)** | **69.2 (13.8)** | **91.8 (11.7)** | **<0.001** | **$** | **65.7 (10.7)** | **90.4 (15.0)** | **<0.001** | **#** |
| **Glucose (mg/dl)** | **83.9 (8.5)** | **77.2 (14.3)** | **0.01** | **$** | 83.8 (9.7) | 81.2 (7.6) | 0.21 | $ |
| **Insulin (mUI/l)** | **8.2 (8.5)** | **15.0 (9.6)** | **0.003** | **$** | **5.1 (3.4)** | **12.5 (9.7)** | **0.001** | **#** |
| **HOMA-IR** | **1.70 (1.6)** | **2.9 (2.0)** | **0.01** | **$** | **1.1 (0.8)** | **2.6 (2.2)** | **0.003** | **#** |
| IGF-1 (ng/ml) | 355.4 (186.1) | 379.6 (209.3) | 0.72 | $ | 250.5 (175.5) | 265.0 (141.7) | 0.77 | $ |
| TG (mg/dl) | 59.7 (20.3) | 65.5 (26.1) | 0.28 | $ | 50.3 (26.5) | 64.9 (37.0) | 0.06 | $ |
| FFAs (mg/dl) | 11.74 (5.3) | 10.68 (4.1) | 0.33 | $ | 13.1 (5.4) | 12.1 (3.6) | 0.40 | $ |
| TC (mg/dl) | 170.1 (32.8) | 160.2 (23.6) | 0.19 | # | 172.2 (40.1) | 160.8 (38.0) | 0.22 | $ |
| LDL-C (mg/dl) | 102.0 (27.9) | 96.5 (27.5) | 0.41 | $ | 102.5 (41.6) | 98.1 (32.3) | 0.63 | $ |
| **HDL-C (mg/dl)** | **56.7 (13.6)** | **46.5 (13.0)** | **0.002** | **$** | **62.3 (13.1)** | **46.7 (10.9)** | **<0.001** | **$** |
| **Leptin (ng/ml)** | **13.1 (17.7)** | **21.6 (12.7)** | **0.02** | **$** | **5.2 (5.8)** | **14.6 (10.7)** | **<0.001** | **#** |
| **TSH (mUI/l)** | 2.5 (1.3) | 2.5 (1.0) | 0.96 | $ | **2.3 (0.9)** | **2.9 (1.3)** | **0.04** | **#** |
| **fT4 (ng/dl)** | 1.1 (0.2) | 1.2 (0.1) | 0.40 | # | **1.0 (0.2)** | **1.2 (0.1)** | **0.02** | **#** |
| fT3 (pg/ml) | 4.2 (0.4) | 4.1 (0.4) | 0.72 | $ | 4.4 (0.5) | 4.3 (0.4) | 0.50 | $ |
| Es (pg/ml) | 45.4 (45.8) | 36.9 (42.3) | 0.43 | $ | 17.3 (14.4) | 14.1 (8.4) | 0.27 | $ |
| T (ng/ml) | 0.3 (0.2) | 0.2 (0.2) | 0.51 | $ | 1.1 (1.9) | 0.7 (0.9) | 0.32 | # |
| FSH (UI/l) | 3.4 (2.4) | 4.0 (2.6) | 0.32 | $ | 1.5 (1.3) | 1.8 (1.8) | 0.87 | # |
| **VD (ng/ml)** | **25.0 (13.8)** | **16.2 (5.7)** | **0.008** | **#** | 21.4 (10.5) | 17.7 (7.4) | 0.14 | $ |

Values are presented as mean (SD). Differences in sexual development distribution were analyzed by $X^2$ analysis. Differences between groups were analyzed by t-test ($) or Wilcoxon test (#). Bold values indicate significant statistical differences. BMI: body mass index; Es: estradiol; FFAs: free fatty acids; FSH: follicle-stimulating hormone; HDL-C: HDL-cholesterol; HOMA-IR: homeostasis model assessment of insulin resistance; IGF-1: insulin-like growth factor 1; LDL-C: LDL-cholesterol; SD: sexual development (prepuberty:puberty); T: testosterone; TC: total cholesterol; TG: triglycerides; TSH: tyroid-stimulating hormone; fT3: free triiodothyronine; fT4: free thyroxine; VD: vitamin D; WC: waist circumference.

**Table S2.** Anthropometric and biochemical characteristics of children and adolescents subjects of cross-sectional study.

| | Children | | | | Adolescents | | | |
|---|---|---|---|---|---|---|---|---|
| | **Lean (n= 34)** | **Obesity (n= 38)** | ***P*** | ***Test*** | **Lean (n= 39)** | **Obesity (n= 39)** | ***P*** | ***Test*** |
| Age (yr) | **7.7 (2.3)** | **8.7 (2.0)** | **0.04** | **$** | 13.0 (2.1) | 13.5 (1.8) | 0.27 | $ |
| Sex (girls:boys) | 17:17 | 17:21 | 0.65 | | 21:18 | 23:16 | 0.65 | |
| Birth weight (kg) | 3.1 (0.7) | 3.3 (0.4) | 0.41 | $ | 3.3 (0.4) | 3.2 (0.6) | 0.46 | $ |
| **Weight (kg)** | **26.3 (9.1)** | **46.5 (11.7)** | **<0.001** | **$** | **48.4 (11.1)** | **77.6 (15.6)** | **<0.001** | **#** |
| **Height (cm)** | **125.8 (15.5)** | **135.2 (11.7)** | **0.007** | **$** | **152.7 (10.0)** | **160.5 (7.5)** | **<0.001** | $ |
| **BMI (kg/m$^2$)** | **16.1 (1.9)** | **25.0 (3.3)** | **<0.001** | **$** | **20.6 (3.5)** | **29.9 (4.4)** | **<0.001** | **$** |
| **WC (cm)** | **58.8 (8.2)** | **82.4 (9.8)** | **<0.001** | **$** | **75.0 (10.5)** | **99.2 (10.7)** | **<0.001** | **$** |
| **Glucose (mg/dl)** | **82.4 (8.0)** | **76.9 (13.3)** | **0.04** | **$** | 85.0 (9.7) | 81.2 (9.8) | 0.08 | $ |
| **Insulin (mUI/l)** | **4.1 (3.0)** | **9.7 (7.9)** | **0.001** | **#** | **9.0 (8.1)** | **18.0 (9.6)** | **<0.001** | **#** |
| **HOMA-IR** | **0.86 (0.7)** | **1.9 (1.8)** | **0.01** | **#** | **1.8 (1.5)** | **3.6 (2.1)** | **<0.001** | **#** |
| IGF-1 (ng/ml) | 167.2 (133.2) | 221.2 (143.3) | 0.29 | $ | 381.3 (165.5) | 427.3 (173.4) | 0.37 | $ |
| TG (mg/dl) | 52.9 (26.1) | 61.0 (30.0) | 0.24 | $ | 56.9 (22.0) | 69.2 (32.8) | 0.05 | $ |
| FFAs (mg/dl) | 14.1 (6.0) | 12.7 (3.9) | 0.26 | $ | 10.8 (4.3) | 10.1 (3.5) | 0.41 | $ |
| TC (mg/dl) | 173.6 (44.9) | 161.9 (35.7) | 0.23 | $ | 169.1 (27.7) | 159.1 (26.3) | 0.10 | $ |
| LDL-C (mg/dl) | 106.0 (44.8) | 100.4 (30.9) | 0.55 | $ | 99.1 (24.8) | 94.3 (28.7) | 0.45 | $ |
| **HDL-C (mg/dl)** | **62.4 (13.6)** | **45.5 (10.3)** | **<0.001** | **$** | **57.3 (13.2)** | **47.6 (13.5)** | **0.003** | **$** |
| **Leptin (ng/ml)** | **3.0 (3.5)** | **14.1 (9.0)** | **<0.001** | **#** | **13.8 (16.7)** | **22.3 (13.7)** | **0.02** | **$** |
| TSH (mUI/l) | 2.5 (1.3) | 2.6 (1.1) | 0.54 | $ | 2.3 (1.0) | 2.7 (1.2) | 0.14 | $ |
| fT4 (ng/dl) | 1.1 (0.2) | 1.2 (0.1) | 0.07 | # | 1.1 (0.2) | 1.1 (0.1) | 0.20 | # |
| fT3 (pg/ml) | 4.3 (0.5) | 4.2 (0.3) | 0.32 | $ | 4.1 (0.4) | 4.2 (0.4) | 0.94 | $ |
| **Es (pg/ml)** | **24.7 (24.1)** | **14.3 (9.7)** | **0.02** | **#** | 35.9 (43.0) | 38.0 (43.0) | 0.83 | $ |
| T (ng/ml) | 0.2 (0.1) | 0.2 (0.4) | 0.86 | $ | 1.3 (1.9) | 0.7 (0.8) | 0.75 | # |
| **FSH (UI/l)** | 1.5 (1.5) | 1.4 (1.7) | 0.78 | $ | **3.2 (2.3)** | **4.5 (2.3)** | **0.02** | $ |
| **VD (ng/ml)** | 22.0 (12.7) | 19.3 (6.6) | 0.80 | # | **24.1 (12.3)** | **14.5 (5.7)** | **<0.001** | # |

Values are presented as mean (SD). Differences in sexual development distribution were analyzed by $X^2$ analysis. Differences between groups were analyzed by t-test ($) or Wilcoxon test (#). Bold values indicate significant statistical differences. BMI: body mass index; Es: estradiol; FFAs: free fatty acids; FSH: follicle-stimulating hormone; HDL-C: HDL-cholesterol; HOMA-IR: homeostasis model assessment of insulin resistance; IGF-1: insulin-like growth factor 1; LDL-C: LDL-cholesterol; T: testosterone; TC: total cholesterol; TG: triglycerides; TSH: tyroid-stimulating hormone; fT3: free triiodothyronine; fT4: free thyroxine; VD: vitamin D; WC: waist circumference.

**Table S3.** Specificity study of ELISA kit.

| | **Sample 1** | | **Sample 2** | |
|---|---|---|---|---|
| | Normal PL | Preadsorbed PL | Normal PL | Preadsorbed PL |
| **ANGPTL-4** | 68.89 ng/ml | < 0.51 ng/ml | 153.41 ng/ml | 1.81 ng/ml |

PL, plasma.

**Table S4.** Relationships of ANGPTL-4 with anthropometric and biochemical parameters measured in the cross-sectional study population.

| | **ANGPTL4** | |
|---|---|---|
| | r | *P* |
| **Age** | -0.01 | 0.89 |
| **Tanner state** | 0.02 | 0.83 |
| **Birth weight** | 0.16 | 0.08 |
| **Weight** | **-0.19** | **0.02** |
| **Height** | -0.07 | 0.37 |
| **BMI** | **-0.27** | **0.001** |
| **Waist circumference** | **-0.25** | **0.002** |
| **Glucose** | 0.02 | 0.77 |
| **Insulin** | **-0.26** | **0.002** |
| **HOMA-IR** | **-0.27** | **0.002** |
| **IGF-1** | -0.07 | 0.49 |
| **Triglycerides** | **-0.22** | **0.008** |
| **Free fatty acids** | **0.23** | **0.005** |
| **Total cholesterol** | 0.02 | 0.85 |
| **LDL-cholesterol** | -0.00 | 0.93 |
| **HDL-cholesterol** | 0.15 | 0.09 |
| **Leptin** | **-0.19** | **0.03** |
| **TSH** | -0.03 | 0.71 |
| **fT4** | -0.00 | 0.98 |
| **fT3** | 0.12 | 0.27 |
| **Estradiol** | 0.10 | 0.23 |
| **Testosterone** | 0.08 | 0.38 |
| **FSH** | -0.03 | 0.75 |
| **Vitamin D** | **0.24** | **0.009** |

Statistical significance is from Pearson (normally distributed data) or Spearman (non-normally distributed data) correlation tests. Bold values indicate significant statistical differences. BMI: body mass index; FSH: follicle-stimulating hormone; HOMA-IR: homeostasis model assessment of insulin resistance; IGF-1: insulin-like growth factor 1; TSH: tyroid-stimulating hormone; fT3: free triiodothyronine; fT4: free thyroxine.

**Table S5.** Relationships of ANGPTL-4 with anthropometric and biochemical parameters measured in lean and obese subjects of the cross-sectional study.

| | **ANGPTL4** | | | |
|---|---|---|---|---|
| | **Lean** | | **Obesity** | |
| | r | *P* | r | *P* |
| **Age** | 0.10 | 0.40 | -0.11 | 0.32 |
| **Tanner stage** | 0.21 | 0.09 | -0.07 | 0.57 |
| **Birth weight** | 0.21 | 0.11 | 0.10 | 0.45 |
| **Weight** | 0.14 | 0.26 | -0.04 | 0.76 |
| **Height** | 0.11 | 0.37 | -0.13 | 0.27 |
| **BMI** | 0.13 | 0.29 | -0.05 | 0.65 |
| **Waist circumference** | 0.14 | 0.26 | -0.00 | 0.96 |
| **Glucose** | -0.08 | 0.50 | -0.16 | 0.17 |
| **Insulin** | 0.13 | 0.30 | -0.06 | 0.62 |
| **HOMA-IR** | 0.09 | 0.47 | -0.09 | 0.44 |
| **IGF-1** | -0.04 | 0.84 | -0.07 | 0.56 |
| **Triglycerides** | -0.06 | 0.61 | **-0.27** | **0.02** |
| **Free fatty acids** | 0.22 | 0.06 | **0.34** | **0.002** |
| **Total cholesterol** | 0.09 | 0.47 | **-0.25** | **0.02** |
| **LDL-cholesterol** | 0.18 | 0.15 | -0.15 | 0.20 |
| **HDL-cholesterol** | -0.02 | 0.88 | -0.21 | 0.07 |
| **Leptin** | 0.22 | 0.10 | -0.13 | 0.28 |
| **TSH** | 0.09 | 0.44 | -0.01 | 0.92 |
| **fT4** | 0.23 | 0.08 | -0.10 | 0.41 |
| **fT3** | -0.13 | 0.55 | 0.20 | 0.12 |
| **Estradiol** | 0.14 | 0.29 | 0.02 | 0.84 |
| **Testosterone** | 0.11 | 0.49 | -0.00 | 0.95 |
| **FSH** | 0.18 | 0.16 | -0.13 | 0.28 |
| **Vitamin D** | -0.04 | 0.82 | 0.13 | 0.27 |

Statistical significance is from Pearson (normally distributed data) or Spearman (non-normally distributed data) correlation tests. Bold values mean significant statistical differences. BMI: body mass index; FSH: follicle-stimulating hormone; HOMA-IR: homeostasis model assessment of insulin resistance; IGF-1: insulin-like growth factor 1; TSH: thyroid-stimulating hormone; fT3: free triiodothyronine; fT4: free thyroxine.

**Table S6.** Correlations between the percent change of ANGPTL-4 and the percent change of anthropometric and biochemical characteristics in participants from interventional study.

| | **% change of ANGPTL4** | |
|---|---|---|
| | r | *P* |
| Percent change of age (%) | -0.14 | 0.56 |
| Percent change of weight (%) | 0.01 | 0.97 |
| Percent change of height (%) | -0.02 | 0.93 |
| Percent change of BMI (%) | 0.06 | 0.79 |
| Percent change of fat mass (%) | -0.13 | 0.63 |
| Percent change of non fat mass (%) | -0.00 | 0.98 |
| Percent change of % fat mass (%) | 0.45 | 0.16 |
| Percent change of waist circumference (%) | 0.18 | 0.45 |
| Percent change of glucose (%) | -0.38 | 0.10 |
| Percent change of insulin (%) | -0.08 | 0.78 |
| Percent change of HOMA index (%) | -0.41 | 0.88 |
| Percent change of IGF-1 (%) | 0.00 | 0.99 |
| Percent change of triglycerides (%) | -0.19 | 0.41 |
| **Percent change of free fatty acids (%)** | **0.67** | **0.001** |
| **Percent change of total cholesterol (%)** | **-0.45** | **0.04** |
| Percent change of LDL-cholesterol (%) | -0.25 | 0.28 |
| **Percent change of HDL-cholesterol (%)** | **-0.51** | **0.02** |
| % change of total cholesterol/HDL | 0.22 | 0.35 |
| % change of LDL/HDL | 0.26 | 0.27 |
| Percent change of leptin (%) | 0.25 | 0.37 |
| Percent change of TSH (%) | 0.15 | 0.54 |
| Percent change of fT4 (%) | 0.43 | 0.11 |
| Percent change of fT3 (%) | 0.42 | 0.12 |
| Percent change of estradiol (%) | -0.36 | 0.15 |
| Percent change of testosterone (%) | 0.37 | 0.21 |
| Percent change of FSH (%) | -0.00 | 0.99 |
| Percent change of vitamin D (%) | -0.22 | 0.35 |

Statistical significance is from Pearson correlation test. Bold values indicate significant statistical differences. BMI: body mass index; FSH: follicle-stimulating hormone; HOMA: homeostasis model assessment of insulin resistance; IGF-1: insulin-like growth factor 1; TSH: tyroid-stimulating hormone; fT3: free triiodothyronine; fT4: free thyroxine.

**Table S7.** Estimated coefficients (β) of the multivariate linear regression model of longitudinal study, with standard error (SE), t statistic and P values.

| | β (SE) | t statistic | P value |
|---|---|---|---|
| **Intercept** | 22.20 (7.93) | 2.80 | 0.01 |
| **Percent change of free fatty acids** | 0.16 (0.04) | 4.35 | 0.001 |
| **Percent change of HDL-C** | -0.35 (0.21) | -1.64 | 0.12 |
| **Percent change of total cholesterol** | -0.43 (0.40) | -1.08 | 0.30 |
| **Percent change of triglycerides** | -0.05 (0.06) | -0.89 | 0.39 |

HDL-C: HDL-cholesterol.