

# ADIPOCYTE DYSFUNCTION IN PEDIATRIC OBESITY

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**Background.** Obesity is associated with adipocyte dysfunction, characterized by an impaired secretion of adipokines, which leads to a systemic inflammatory status, insulin resistance and atherogenesis.

**Aim.** To characterize adipokines serum profile in a group of obese children and adolescents.

**Method.** A case control study comparing 102 obese children (BMI  $\geq$  95<sup>th</sup> percentile) (aged 10-18 years) to a group of 43 healthy controls matched for age and pubertal status.

Adiponectin, leptin, resistin, A-FABP and lipocalin-2 were measured using ELISA method and were correlated with traditional clinical and biochemical biomarkers of the metabolic syndrome (BMI, waist circumference, blood pressure, fasting glycaemia and insulinemia, lipids profile). The BMI, waist circumference (WC), systolic and diastolic blood pressure (BP) were adjusted for age, sex and height according to WHO growth charts and the NHANES references. **HOMA-index** was calculate using the formula: **a jeun glycaemia (mg/dl) \* a jeun insulinemia  $\mu$ U/ml/405**; **insulin resistance summary score (IRS)** was calculated by adding the quartiles for systolic blood pressure, a jeun glycaemia, insulinemia and serum triglycerides (analyzed ascending) and serum HDL-cholesterol (analyzed descending).

**Results.** Obese children had significantly higher waist circumferences, BP and serum levels of triglycerides and significantly lower serum levels of HDL-cholesterol (table 1). All insulin resistance biomarkers (a jeun insulinemia, HOMA-index and IRS) were significantly higher in the obese group compared to the control group (figure 1).

Parameter	Obese group (n = 102)	Control group (n = 43)	p
BMI (Kg/sqm)	31.23 $\pm$ 5.09	19.14 $\pm$ 2.71	p<0.01
Z Score for BMI	2.17 $\pm$ 0.3	-0.21 $\pm$ 0.96	p<0.01
WC (cm)	101.57 $\pm$ 11.29	77.75 $\pm$ 10.43	p<0.01
Systolic BP (mmHg)	123.09 $\pm$ 13.26	102.67 $\pm$ 9.09	p<0.01
Systolic BP percentile	80.77 $\pm$ 21.61	30.69 $\pm$ 22.72	p<0.01
Diastolic BP (mmHg)	73.38 $\pm$ 10.34	62.09 $\pm$ 7	p<0.01
Diastolic BP percentile	72.55 $\pm$ 22.31	42.73 $\pm$ 18.86	p<0.01
Glycaemia (mg/dl)	79,87 $\pm$ 11,07	83,68 $\pm$ 8,22	0,058
Total-cholesterol (mg/dl)	166,29 $\pm$ 36,76	160,89 $\pm$ 27,23	0,392
HDL – cholesterol (mg/dl)	44,94 $\pm$ 9,55	51,72 $\pm$ 10,48	0,02
LDL-cholesterol (mg/dl)	102,73 $\pm$ 30,30	100 $\pm$ 31,93	0,69
Triglycerides (mg/dl)	108,01 $\pm$ 58,23	80,48 $\pm$ 37,6	0,005

Parameter	Obese Group (n=102)	Control Group (n = 43)	p
Adiponectin( $\mu$ g/ml)	7.52 $\pm$ 4	13.28 $\pm$ 7.94	<0.001
Leptin (ng/ml)	35.59 $\pm$ 22.15	11.95 $\pm$ 12.26	<0.001
Resistin (ng/ml)	9.62 $\pm$ 3.54	7.46 $\pm$ 2.01	<0.001
A-FABP (ng/ml)	37.89 $\pm$ 17.95	11.86 $\pm$ 5.00	<0.001
Lipocalin-2 (ng/ml)	64.3 $\pm$ 21.29	51.21 $\pm$ 14.88	0.004

The serum levels of leptin, resistin, AFABP and lipocalin-2 were significantly higher while the adiponectin serum levels were significantly lower in the obese group compared to the control group (table 2, figure 2).

All the adipokines were significantly correlated (in univariate analysis) to Z score for BMI (table 3).

Adiponectin, leptin, AFABP and resistin were significantly correlated to systolic and diastolic blood pressure (negative correlation for adiponectin, positive correlations for others adipokines); there was also a parallel variation of the previous mentioned adipokines and HDL-cholesterol, positive for adiponectin and negative for leptin, resistin and AFABP (table 3).

Adiponectin, leptin and A-FABP also correlated with various biomarkers of insulin resistance (table 3); the correlation between leptin serum levels and fasting insulinemia was kept in multivariate analysis.

## In multivariate analysis:

- Adiponectin was negatively correlated to waist circumference and serum A-FABP (R coefficient = - 0.627, p < 0.001) (fig. 3,4);
- Leptin was positively correlated to waist circumference and fasting insulinemia (R coefficient = 0.682, p < 0.001) (fig. 5,6);
- A-FABP was positively correlated to Z score for BMI and adiponectin (R coefficient = 0,700 , p < 0,001) (fig. 4,7);
- Resistin was positively correlated only to lipocalin-2 (R coefficient = 0.514, p < 0.001) (fig.8).

**Conclusions.** Pediatric obesity is already associated with an altered production of adipokines, which participates in the pathogenesis of obesity-associated comorbidities.

Figure 1. Insulin Resistance parameters (Comparison between Groups)

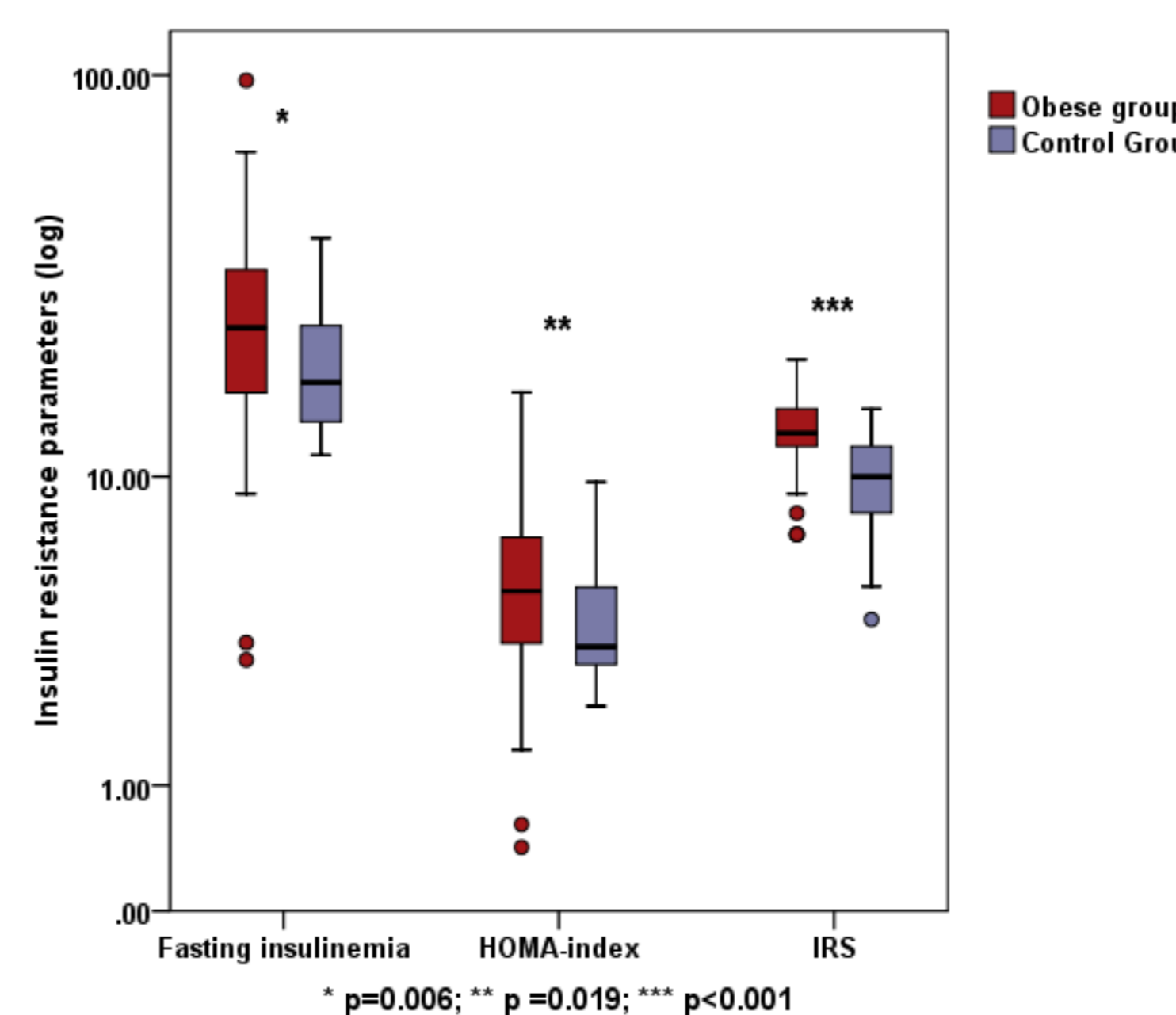


Figure 2. Serum adipokines profile in the obese group compared to the control group

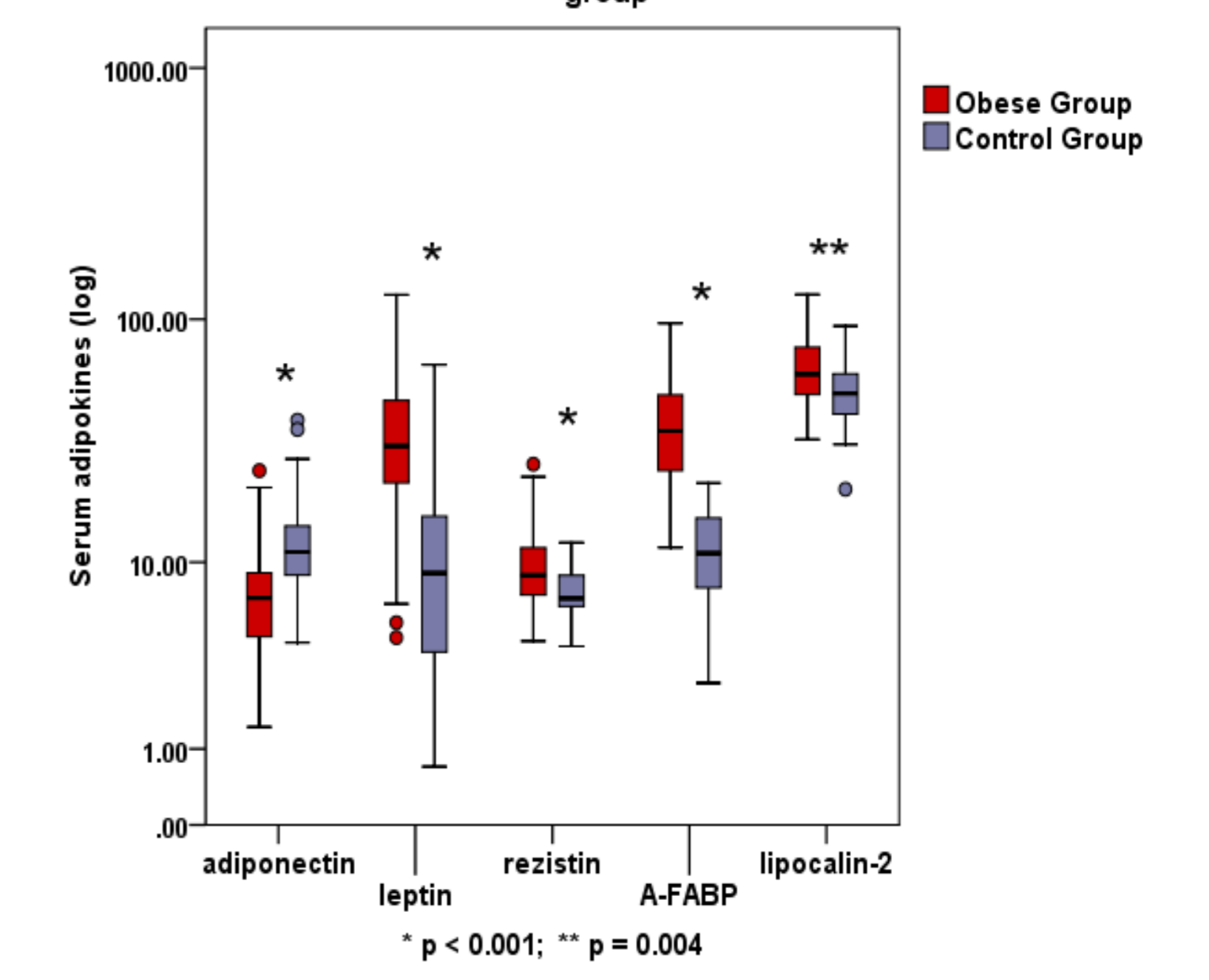


Table 3. Correlations between serum adipokines profile and clinical and biochemical parameters (rho Spearman coefficient, p for significance)

Parameter	Adiponectin	Leptin	Resistin	A-FABP	Lipocalin-2
Z score BMI	-0,486, p<0,001	0,525, p<0,001	0,296 p<0,001	0,625, p<0,001	0,295, p=0,009
WC	-0,445, p<0,001	0,407, p<0,001		0,359, p<0,001	
Sistolic BP	-0,232, p= 0,005	0,402, p<0,001	0,181, p = 0,03	0,517, p<0,001	
Diastolic BP	- 0,22, p= 0,008	0,335 p<0,001	0,176, p= 0,035	0,510, p<0,001	
HDL-cholesterol	0,453, p< 0,001	-0,223 p<0,001	-0,197, p= 0,033	-0,263, p= 0,041	
Triglycerides				0,229, p = 0,045	
Insulinemia		0,395 p<0,001			
HOMA-index		0,353 p<0,001			
IRS	-0,381, p<0 ,001	0,441 p<0,001		0,460 p<0,001	

Figure 3. Correlation between serum adiponectin and waist circumference

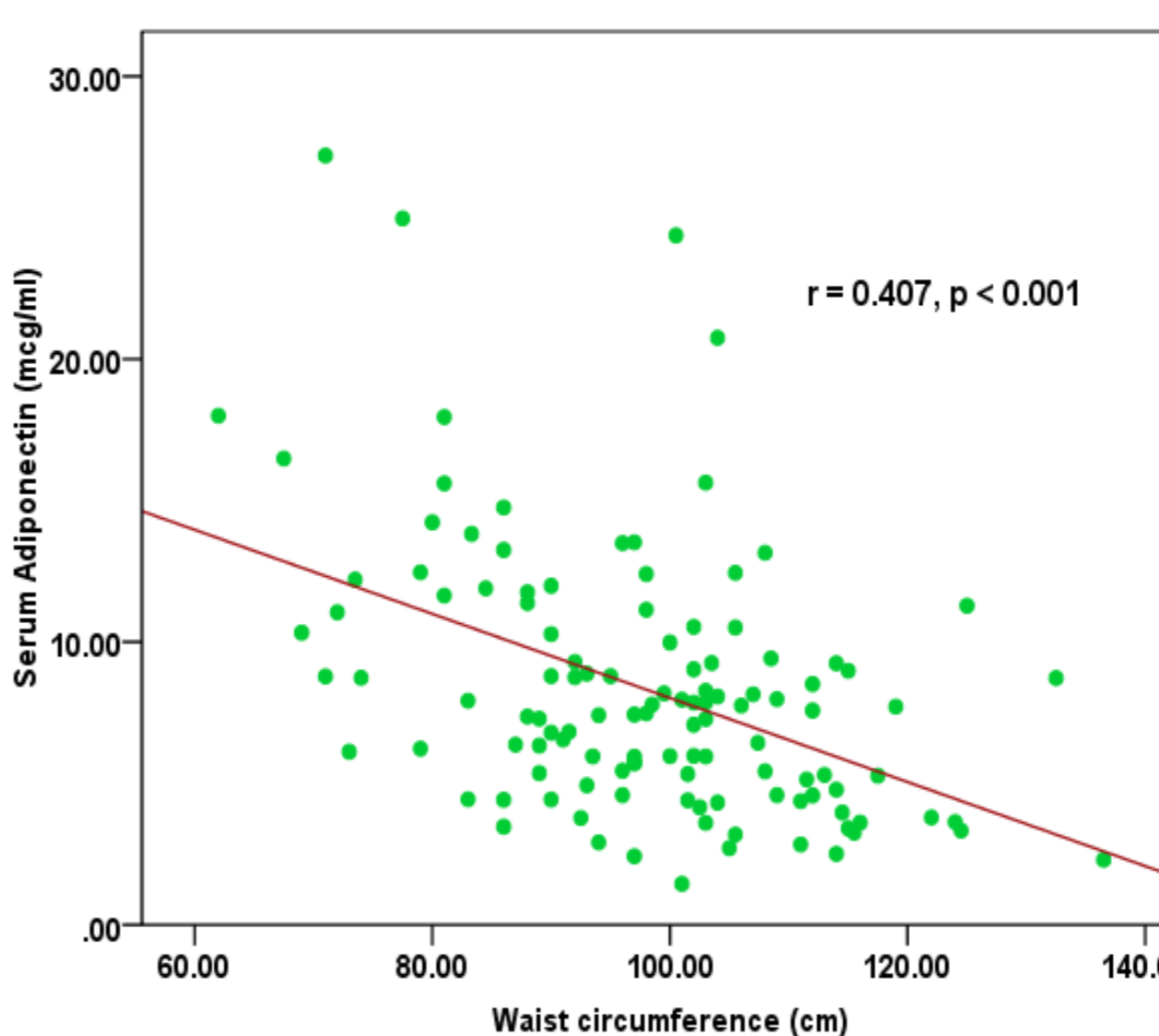


Figure 4. Correlations between serum Adiponectin and A-FABP

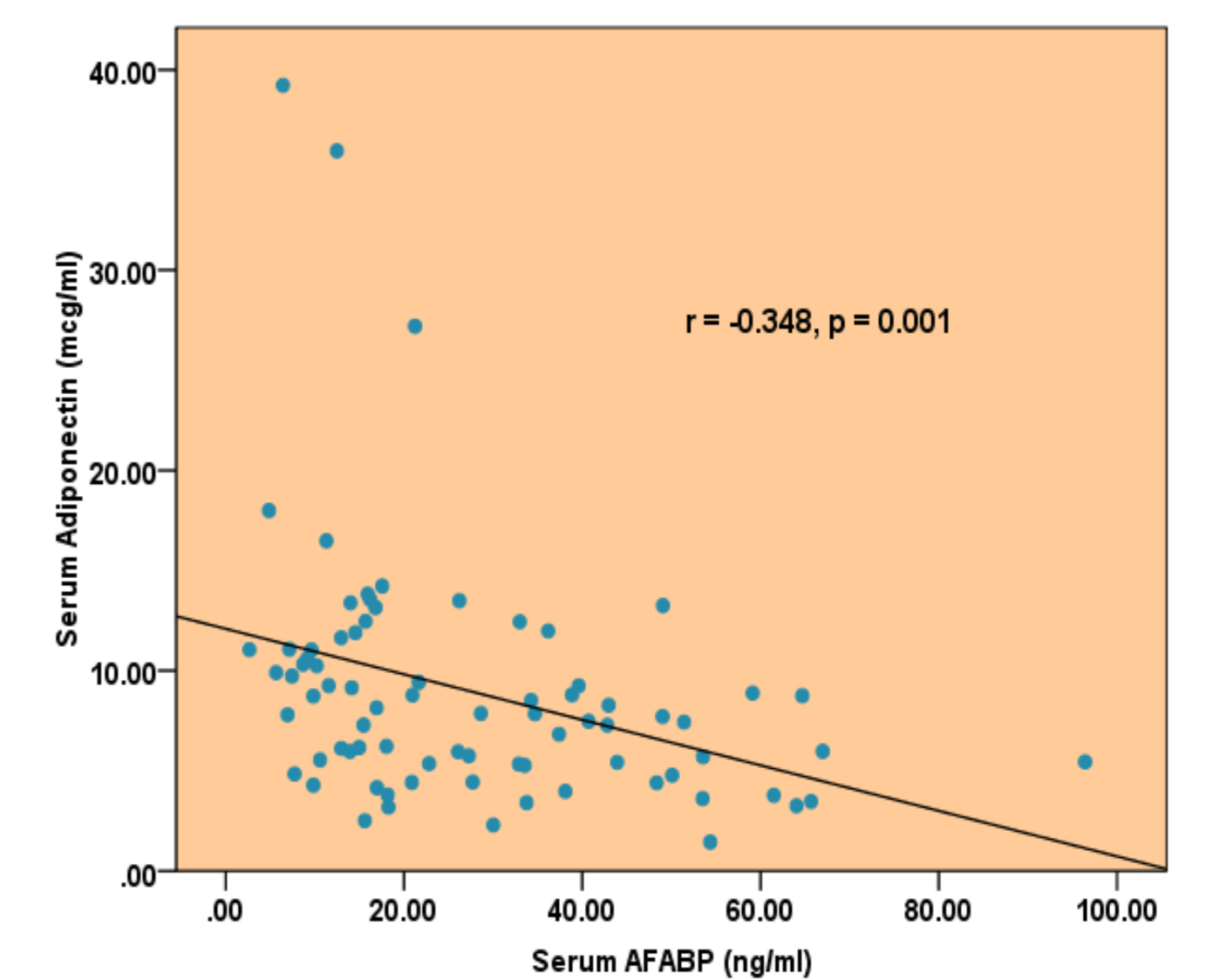


Figure 5. Correlation between serum leptin and waist circumference

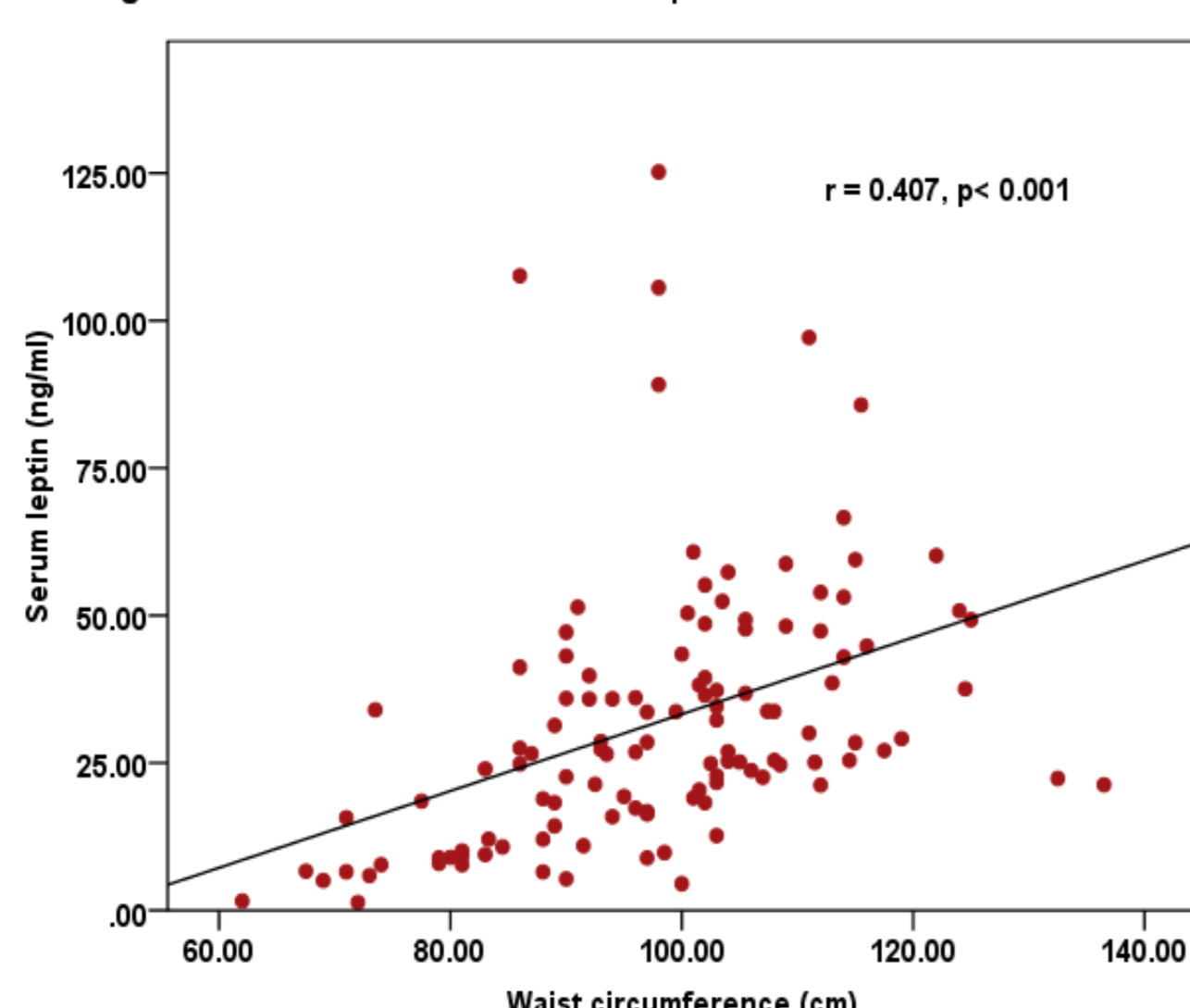


Figure 6. Correlations between serum leptin and fasting insulinemia

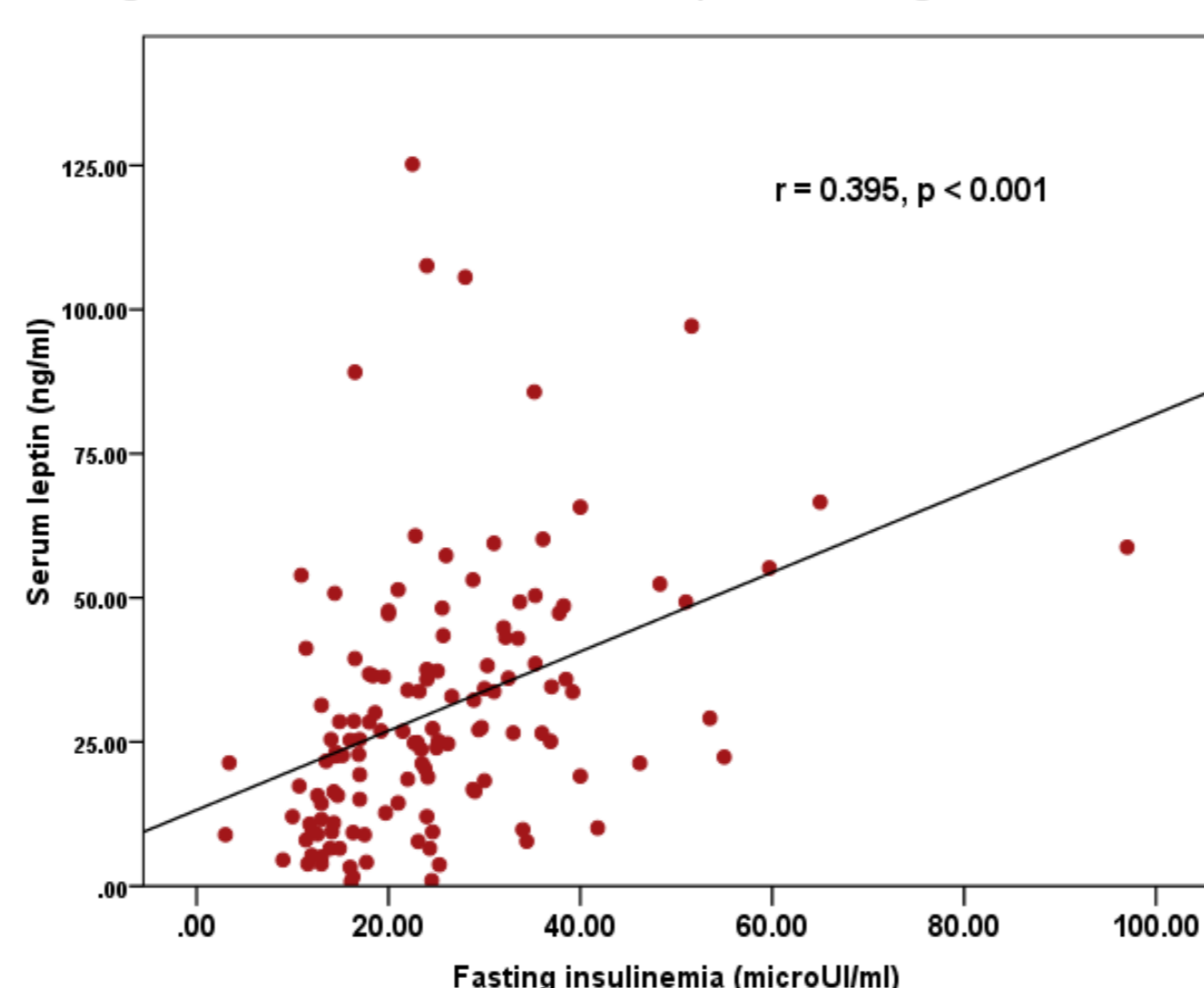


Figure 7. Correlation between serum A-FABP and Z score for BMI

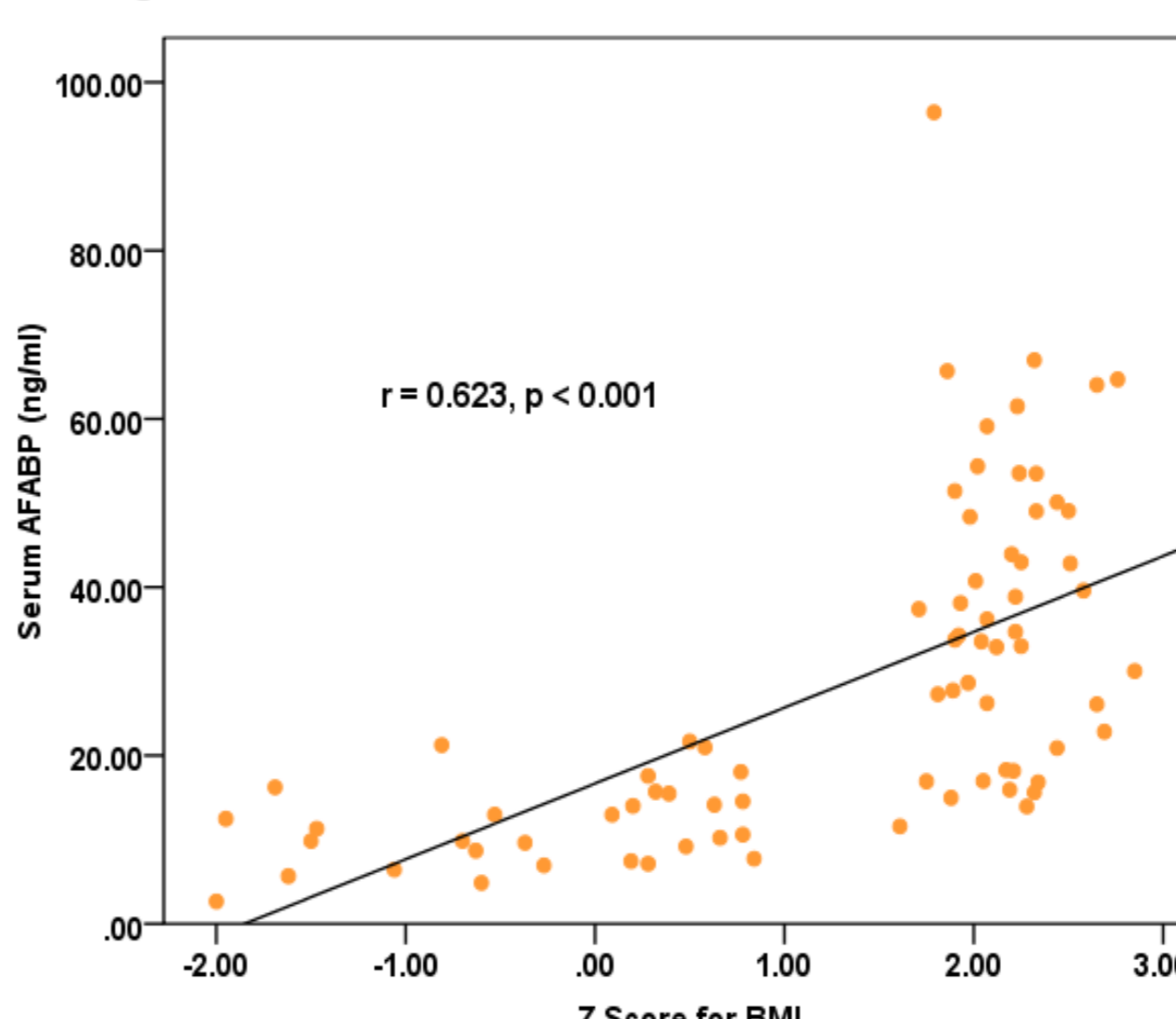


Figure 8. Correlation between serum resistin and serum lipocalin-2

