

Fetuin-A as an Alternative Marker for Insulin Resistance and Cardiovascular Risk in Prepubertal Children

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Introductions

- Childhood obesity has become a major health concern in recent decades since it was known as an independent predictor of short-term and long-term metabolic and cardiovascular morbidities.
- Insulin resistance is common feature of childhood obesity and also a key therapeutic target for cardiovascular risk reduction.
- Fetuin-A, called α 2-Heremans-Schmid glycoprotein (AHSG) in human, is a multipotent glycoprotein produced predominantly in liver.
- Previous preclinical and clinical researches have shown that Fetuin-A may act as an endogenous inhibitor of the insulin receptor tyrosine kinase, therefore, could be a surrogate index for insulin resistance.

Objectives

- In present study aimed to evaluate whether there were 1) differences in serum fetuin-A level in overweight and obese prepubertal children compared to normal-weighted prepubertal children and 2) relationships between fetuin-A levels and metabolic and cardiovascular risk factors.

Methods

- 99 prepubertal Korean children (59 males) with ages ranging from 6 to 10 years were included in this study.
- Subjects were analyzed after stratified into 2 groups: normal-weighted and overweight/obese groups.
- Serum fetuin-A levels were measured using an enzyme-linked immunosorbent assay.
- Insulin resistance was determined from basal fasting plasma glucose and insulin levels by the homeostasis model assessment for insulin resistance (HOMA-IR) and quantitative insulin sensitivity check index (QUICKI).
- HOMA-IR and QUICKI were calculated as follows:
 - HOMA-IR = [fasting insulin (μ U/ml) \times fasting glucose (mmol/l)]/22.5
 - QUICKI = 1/[log(fasting glucose (mg/dL)) + log(fasting insulin (μ U/ml))]

Results

Table 1. Basal characteristics of subjects (n = 99)

	Normal weight (n = 52)	Overweight/Obesity (n = 47)	P
Age (year)	8.02 \pm 1.14	8.36 \pm 1.08	0.132
Sex (M:F)	29:23 (55.8%)	30:17 (63.8%)	0.539
Height SDS	0.28 \pm 1.39	0.96 \pm 0.89	0.005
Weight SDS	-0.06 \pm 1.0	1.64 \pm 0.51	< 0.001
BMI SDS	-0.29 \pm 0.83	1.66 \pm 0.47	< 0.001
WC SDS	-0.54 \pm 1.10	1.29 \pm 0.67	< 0.001
Systolic BP (mmHg)	99.00 \pm 9.37	101.64 \pm 9.78	0.174
Diastolic BP (mmHg)	62.79 \pm 4.89	65.45 \pm 6.89	0.031
Bone age (year)	7.34 \pm 1.76	8.82 \pm 1.76	< 0.001
Glucose (mg/dL)	103.35 \pm 15.78	100.72 \pm 9.48	0.314
Total-C (mg/dL)	168.19 \pm 25.13	170.96 \pm 25.02	0.585
TG (mg/dL)	64.46 \pm 25.69	80.64 \pm 32.00	0.006
LDL-cholesterol (mg/dL)	96.33 \pm 20.51	102.53 \pm 22.75	0.157
HDL-cholesterol (mg/dL)	63.73 \pm 12.83	56.79 \pm 10.98	0.005
AST (IU/L)	25.96 \pm 6.70	25.57 \pm 6.66	0.774
ALT (IU/L)	14.79 \pm 9.54	20.60 \pm 11.66	0.008
Insulin	4.72 \pm 2.18	7.42 \pm 3.55	<0.001
Ln insulin	1.45 \pm 0.47	1.88 \pm 0.54	<0.001
HOMA-IR	1.22 \pm 0.63	1.83 \pm 0.87	< 0.001
QUICKI	0.382 \pm 0.033	0.357 \pm 0.035	0.001
Fetuin-A	119.89 \pm 86.54	203.21 \pm 254.54	0.029
Ln Fetuin-A	4.66 \pm 0.52	4.79 \pm 0.71	0.013

Table 2. Correlations between Fetuin-A and clinical parameters

	Ln Fetuin-A	
	r	P
Age	0.192	0.057
BMI SDS	0.239	0.017
WC SDS	0.154	0.127
SBP (mmHg)	0.274	0.006
DBP (mmHg)	0.304	0.002
Glucose (mg/dL)	-0.170	0.093
Total-C (mg/dL)	-0.264	0.008
TG (mg/dL)	0.285	0.004
LDL-C (mg/dL)	-0.378	<0.001
HDL-C (mg/dL)	-0.236	0.019
Ln insulin	0.377	<0.001

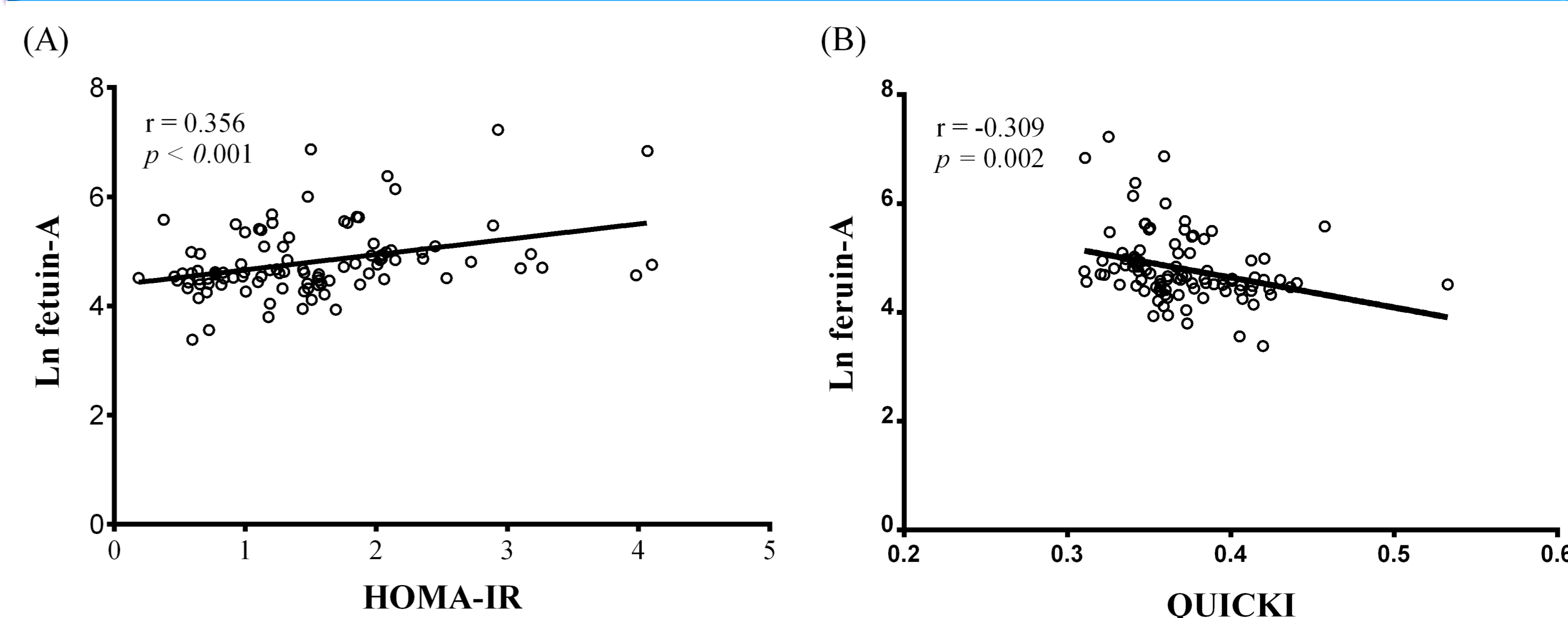
Table 3. Univariate linear regression analyses of HOMA-IR and QUICKI

	HOMA-IR		QUICKI	
	R	P	r	P
Age	0.263	<0.001	-0.192	0.057
BMI SDS	0.439	< 0.001	-0.384	< 0.001
WC SDS	0.387	< 0.001	-0.358	< 0.001
SBP (mmHg)	-0.034	0.738	0.075	0.460
DBP (mmHg)	0.194	0.055	-0.099	0.331
Glucose (mg/dL)	0.200	0.047	-0.225	0.025
Total-C (mg/dL)	-0.081	0.428	0.074	0.469
TG (mg/dL)	0.395	< 0.001	-0.341	0.001
LDL-C (mg/dL)	-0.048	0.638	-0.009	0.933
HDL-C (mg/dL)	-0.274	0.006	0.288	0.004
Ln insulin	0.915	<0.001	-0.964	<0.001
Ln fetuin-A.	0.356	< 0.001	-0.309	0.002

Table 4. Stepwise multivariate regression analyses of HOMA-IR and Ln insulin

	HOMA-IR			QUICKI		
	β	SE	P	β	SE	P
AGE	0.134	0.062	0.032	-0.004	0.003	0.177
BMI SDS	0.209	0.061	0.001	-0.008	0.003	0.005
TG	0.006	0.002	0.012	0.000	0.000	0.041
Ln fetuin-A	0.229	0.114	0.048	-0.010	0.005	0.054

Figure. Correlation between serum Fetuin-A and insulin resistance indices



Conclusions

- Fetuin-A levels were significantly higher in overweight and obese prepubertal children than in normal-weighted children.
- Among baseline demographic and clinical parameters, Fetuin-A was associated with BMI SDS, blood pressure, TG, total cholesterol, LDL, and HDL.
- There were significant correlations between fetuin-A and insulin resistance indices (positively with HOMA-IR and negatively with QUICKI), and observed associations remained significant after correction for baseline covariates.
- The present study supported that fetuin-A could be regarded as an alternative marker for insulin resistance in children with prepuberty.

Disclosure of conflict of interest

None to declare