Correlation of serum fibroblast growth factor 21 (FGF-21) levels with metabolic parameters in Korean obese children

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Introduction

- **Serum FGF-21**
  a potential biomarker for early detection of the metabolic syndrome (MetS) and type 2 diabetes in adults.
- **A few studies about the correlation between FGF-21 levels and metabolic parameters in children**.

Objectives

This study is aimed to evaluate the relationship between serum FGF-21 & metabolic parameters in obese children

Subjects and Methods

Subjects
- 78 obese Korean children and 37 lean children
- None of children in the study suffered from any other disorder or medication known to affect the serum FGF21.

Method
- BMI was calculated as Wt(kg)/Ht(m^2)
- Reference data for 2007 Korean children were used.
- We analyzed fasting serum FGF21, adiponectin by enzyme-linked immunosorbent assays and also fasting glucose, insulin, transaminases, lipid profile were measured by standard enzymatic methods.

Statistical analyses
- analyses were performed using IBM SPSS version 22.0 (IBM Co., Armonk, NY, USA).
- Independent t-test and multiple linear regression analysis was used to evaluated the relationship between FGF21 and other clinical and metabolic parameters.
- All data were expressed as means±standard deviation. The P-value of <0.05 was considered as statistically significant.

Table 1. Composition of subjects

	Normal	Overweight or obese
Male, n=50	14(5:5:4)	36(16:10:10)
Female, n=65	23(5:16:2)	42(6:19:17)

()= Prepuberty(Tanner I): early puberty(Tanner II-III): late puberty(Tanner IV-V)

Results

- Serum FGF-21 were significantly increased in the obese children compared to those of normal-weight children.
- Obese children demonstarated significantly increased insulin, total cholesterol, LDL-C, triglycerides, liver transaminase(AST, ALT).
- Serum adiponectin and HDL-C were significantly decreased in obese children than in controls.
- Serum FGF21 levels were positively correlated with insulin (r=0.341, p<0.001), triglycerides (r=0.451, p<0.001) and ALT (r=0.285, p=0.002). But serum FGF21 levels were negatively correlated with HDL-C (r=-0.347, p<0.001).
- After multicollinearity checking among explanatory variables (BMI, Triglyceride, HDL-cholesterol, fasting insulin, ALT), a multivariate analysis using multiple linear regression revealed fasting insulin levels were only independently and significant correlated with serum FGF21 levels

Conclusions

Serum FGF21 was higher in obese children and significantly correlated with metabolic parameters. Our results suggest that FGF-21 may be potentially used as early biomarker for obese children with metabolic disorders. .

Table 2. Clinical parameters of all study subjects

Parameters	Subjects
N	115
Gender (Male:Female)	(50:65)
Puberty (Pre-: early: late puberty)	(32:50:33)
Age(years)	10.8±2.0
BMI(kg/m^2)	22.0±4.3
Systolic BP(mmHg)	113.5±13.6
Diastolic BP(mmHg)	62.7±8,7
Triglyceride(mg/dL)	110.4±64.3
Total cholesterol(mg/dL)	169.6±30.8
LDL-cholesterol(mg/dL)	102.4±45.0
HDL-cholesterol(mg/dL)	48.5±9.8
FBS(mg/dL)	94.6±6.0
Fasting Insulin(mU/L)	14.3±10.0
FGF21(pg/mL)	142.3±150.9
Adiponectin (μg/mL)	8.8±3.0
AST(U/L)	27.0±6.9
ALT(U/L)	23.6±21.1

Data are expressed as mean±S.D.
Abbreviation:
BMI, body mass index; BP, blood pressure;
LDL, low-density lipoprotein;
HDL, high-density lipoprotein;
FBS, fasting blood glucose;
FGF21, fibroblast growth factor 21

Table 3. Baseline characterstics in male and female subjects

Parameters	Male (n=50)	Female (n=65)	*P* value
Puberty (Pre-: early: late puberty)	(21:15:14)	(11:35:19)	
Age(years)	11.8±2.3	10.1±1.4	<0.001
BMI(kg/m^2)	23.3±4.5	21.0±3.9	0.005
Systolic BP(mmHg)	118.0±15.6	110.1±10.8	0.003
Diastolic BP(mmHg)	64.8±10.3	61.1±7.0	0.027
Triglyceride(mg/dL)	99.2±48.5	119.1±73.3	0.100
Total cholesterol(mg/dL)	169.5±32.1	169.6±30.1	0.974
LDL-cholesterol(mg/dL)	97.4±31.1	106.2±53.3	0.304
HDL-cholesterol(mg/dL)	50.4±9.3	47.0±10.0	0.071
FBS(mg/dL)	96.0±6.1	93.6±5.8	0.044
Fasting Insulin(mU/L)	13.5±9.6	14.9±10.4	0.468
FGF21(pg/mL)	119.1±134.9	160.1±160.9	0.150
Adiponectin (μg/mL)	8.6±2.6	9.0±3.3	0.510
AST(U/L)	27.4±8.5	26.7±5.4	0.452
ALT(U/L)	26.4±24.5	21.3±18.0	0.645

Men and women did not differ significant according to FGF21, adiponectin, lipid profile, fasting insulin, or AST/ALT levels .

Table 4.
Metabolic characteristics in subjects with normal-weight and obese group

Parameters	Normal	Obese	*P* value
N	37	78	
Gender (Male:Female)	(14:23)	(36:42)	
Puberty (Pre-:early: late puberty)	(10:21:6)	(22:29:27)	
Age(years)	11.1±1.9	10.7±2.1	0.260
BMI(kg/m^2)	17.2±2.3	24.2±3.0	<0.001
Systolic BP(mmHg)	108.3±12.1	115.8±13.6	0.005
Diastolic BP(mmHg)	59.2±5.9	64.3±9.4	0.001
Triglyceride(mg/dL)	86.7±35.5	121.7±71.6	0.001
Total cholesterol(mg/dL)	155.2±32.1	176.4±27.9	<0.001
LDL-cholesterol(mg/dL)	85.7±25.8	110.2±49.9	0.006
HDL-cholesterol(mg/dL)	52.1±10.0	46.8±9.2	0.005
FBS(mg/dL)	96.1±6.5	94.0±5.7	0.076
Insulin(mU/L)	8.8±4.7	16.9±10.8	<0.001
FGF21(pg/mL)	91.7±123.7	166.2±157.3	0.013
Adiponectin (μg/mL)	10.1±3.1	8.3±2.7	0.002
AST(U/L)	24.7±4.1	28.1±7.7	0.003
ALT(U/L)	13.5±4.4	28.4±24.1	<0.001

All the metabolic parameters without fasting glucose were significantly higher in obese children compared with lean children

Table 5. Factors associated with serum FGF21 levels

Parameters	All Subjects (n=115)		Normal (n=37)		Obese (n=78)	
	r	*P*	*r*	*P*	*r*	*P*
Age(years)	0.081	0.389	-0.050	0.769	0.190	0.096
BMI(kg/m^2)	0.291	0.002	-0.120	0.478	0.189	0.098
Systolic BP(mmHg)	0.083	0.379	-0.116	0.499	-0.006	0.960
Diastolic BP(mmHg)	0.147	0.119	0.055	0.750	0.001	0.994
Triglyceride(mg/dL)	0.451	<0.001	0.359	0.029	0.403	<0.001
Total cholesterol(mg/dL)	0.164	0.079	0.123	0.467	0.017	0.883
LDL-cholesterol(mg/dL)	0.131	0.164	0.148	0.383	-0.068	0.557
HDL-cholesterol(mg/dL)	-0.347	<0.001	-0.151	0.373	-0.394	<0.001
FBS(mg/dL)	-0.031	0.743	-0.137	0.419	0.014	0.901
Fasting Insulin(mU/L)	0.341	<0.001	0.051	0.767	0.366	0.001
Adiponectin (μg/mL)	-0.113	0.228	0.135	0.427	-0.133	0.246
AST(U/L)	0.068	0.475	-0.232	0.167	0.102	0.378
ALT(U/L)	0.285	0.002	-0.106	0.532	0.284	0.012

Spearman's correlation analysis was used to examine an association between serum FGF21 and other factors
r is a correlation coefficient and a *P* value less than 0.05 was considered statically significant.

Figure 1.
FGF21 positive correlation with insulin

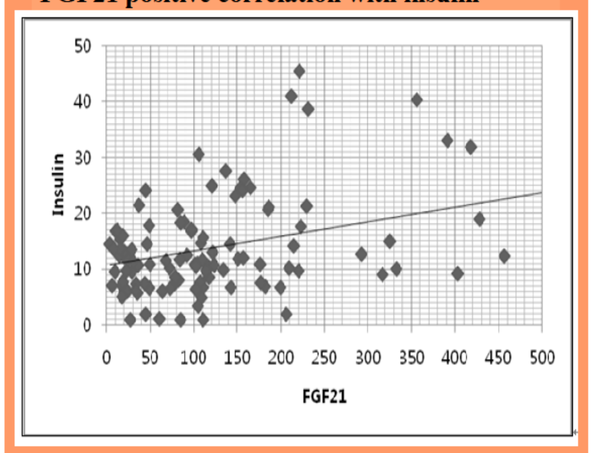

Table 6.
The correlation between serum FGF21 & multiple variables (by multiple linear regression)

	FGF21 in all subjects(n=115)			FGF21 in obese subjects(n=78)		
Variable	Coefficient	SE	*P*-value	Coefficient	SE	*P*-value
BMI(kg/m^2)	-0.038	3.870	0.736			
Triglyceride(mg/dL)	0.149	0.251	0.164	0.119	0.298	0.381
HDL-cholesterol(mg/dL)	0.015	1.636	0.888	0.014	2.411	0.920
Fasting Insulin(mU/L)	0.361	1.819	0.004	0.379	1.886	0.005
ALT(U/L)	0.008	0.729	0.936	-0.014	0.790	0.910

SE: Standard error

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