Is the insulin secretion in pancreatic beta cells related with IGF-1/IGFBP-1 axis in Korean children?

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OBJECTIVES

Recent studies have revealed that type 2 diabetes, including impaired glucose tolerance are associated cross-sectionally with altered circulating level of IGF-I and its binding proteins (IGFBPs). The aim of this study was to investigate

1.Is there difference of serum IGF-I and IGFBP-1 in subjects grouped by glucose tolerance state and BMI.

2. Are there significant correlations between serum IGF-I and IGFBP-1 and clinical variables in children.

METHODS

Selection of subjects

- Evaluation of diabetes in the 36 students with glucosuria detected by school urinary screening test and obesity at Chonbuk National University Children Hospital
- **2013. 3 – 2014. 8**
  - **Age : 10-18 years old**
  - Diabetes mellitus (-), Chronic disease (renal disease, hypertension, metabolic disease, growth retardation, etc) (-), Medication history (-)
- **By oral glucose tolerance test**
  - Normal glucose tolerance (NGT), Impaired glucose tolerance (IGT)
  - Diabetes Mellitus (DM)
- **By body mass index (BMI)**
  - Normal : BMI< 85 percentile, Overweight : 85 ≤ BMI < 95 percentile
  - Obesity : BMI≥ 95 percentile
- **Data from review medical records retrospectively**
- **Demographic findings :** Gender, Age, Body mass index (BMI, kg/m^2)
- **Laboratory data**

IGF-I, IGFBP-3 (IRMA kit (Immunotech, Cobra, France)), IGFBP-1 (ELISA Kit, Abnova, USA), HbA1c, serum fasting plasma glucose level (FPG)
Oral glucose tolerance test (OGTT), Serum c-peptide, serum insulin level
Cholesterol, triglyceride, HDL, LDL, HOMA-IR (homeostasis model of assessment-insulin resistance)

RESULTS

Table 1. Demographic features of 36 studied subjects

Characteristic		Total	NGT	IGT	DM	*P*
Number (%)		36 (100.0)	23 (63.9)	8 (22.2)	5 (13.9)	
Age (yr)		11.66±3.16	11.37±3.39	11.52±2.62	13.21±2.94	0.506
Gender (%)	Male	23 (63.9)	15 (65.2)	3 (37.5)	5 (100.0)	0.480
	Female	13 (36.1)	8 (34.8)	5 (62.5)	0 (0.0)	
BMI (kg/m^2)		24.94±5.41	23.03±3.98	27.94±4.58	28.57±8.64	0.019
HbA1c (%)		5.94±1.29	5.46±0.18	5.73±0.28	8.52±2.15	<0.001
FPG (mg/dL)		96.72±28.64	87.70±6.77	91.25±8.26	147.00±55.82	<0.001
OGTT 120min (mg/dL)		176.08±180.22	113.83±18.42	151.38±16.94	502.00±354.30	<0.001
Serum c-peptide (ng/mL)		3.01±2.04	2.56±1.81	3.31±1.40	4.56±3.15	0.127
HOMA-IR		5.16±5.79	3.93±4.48	5.29±6.30	10.44±8.43	0.071

Table 3. The clinical characteristics 36 by BMI

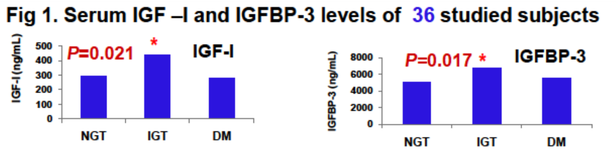
Characteristic	Normal	Overweight	Obesity	*P* value
Number (%)	10 (27.8)	10 (27.8)	16 (44.4)	
NGT number (%)	8 (80.0)	7 (70.0)	7 (43.8)	0.089
Age (yr)	12.85±3.70	11.50±2.37	11.20±3.25	0.428
BMI (kg/m^2)	18.57±3.56	24.08±1.77	28.20±5.46	<0.001
HbA1c (%)	5.97±1.70	5.53±0.18	6.25±1.51	0.469
FPG (mg/dL)	97.56±36.69	93.00±8.29	99.93±34.69	0.866
OGTT 120min (mg/dL)	133.00±107.67	246.63±351.00	173.87±92.51	0.479
Serum c-peptide (ng/mL)	1.44±0.54	3.70±2.31	3.07±0.93	0.018
HOMA-IR	1.67±0.84	6.99±6.82	6.04±6.04	0.095

Table 2. Correlation (γ) between serum IGF-I / IGFBP-1 and clinical variables

		Total		NGT		Glucose intolerance (IGT, DM)	
		p	γ	*p*	γ	*p*	γ
IGF-I	Age	0.084	0.305	0.104	0.340	0.432	0-.281
	BMI	0.813	0.043	0.406	-0.178	0.680	-0.150
	FPG	0.879	0.028	0.612	0.109	0.323	-0.349
	OGTT 120min	0.322	-0.181	0.510	0.145	0.098	-0.552
	Cholesterol	0.958	-0.009	0.860	-0.038	0.671	-0.154
	Triglyceride	0.600	0.095	0.570	0.122	0.397	-0.301
	HDL	0.255	-0.204	0.628	-0.104	0.742	-0.120
	LDL	0.956	-0.010	0.681	-0.089	0.700	-0.140
	HOMA-IR	0.455	0.139	0.570	0.125	0.912	0.047
	HbA1c	0.925	0.017	0.208	0.267	0.085	-0.571
	Serum C-peptide	0.244	0.209	0.401	0.179	0.599	0.190
	IGFBP-3	0.001	0.543	0.001	0.654	0.527	0.228
	IGFBP-1	0.023	-0.396	0.062	-0.386	0.345	-0.334

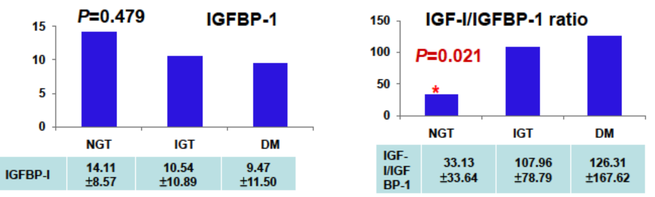
		Total		NGT		Glucose intolerance (IGT, DM)	
		p	γ	*p*	γ	*p*	γ
IGFBP-1	Age	0.006	-0.427	0.029	-0.398	0.124	-0.469
	BMI	0.000	-0.548	0.019	-0.449	0.032	-0.620
	FPG	0.939	0.013	0.456	-0.150	0.606	0.166
	OGTT 120min	0.179	-0.229	0.344	-0.193	0.604	0.167
	Cholesterol	0.778	-0.047	0.950	-0.012	0.937	-0.027
	Triglyceride	0.287	-0.180	0.806	-0.049	0.769	-0.100
	HDL	0.080	0.291	0.346	0.185	0.071	0.564
	LDL	0.210	-0.221	0.362	-0.190	0.589	-0.184
	HOMA-IR	0.001	-0.560	0.005	-0.539	0.056	-0.655
	HbA1c	0.894	-0.023	0.191	-0.260	0.705	0.122
	Serum C-peptide	0.000	-0.550	0.005	-0.505	0.003	-0.798
	IGF-I	0.023	-0.396	0.062	-0.386	0.345	-0.334
	IGFBP-3	0.000	-0.628	0.000	-0.616	0.007	-0.758

Fig 1. Serum IGF –I and IGFBP-3 levels of 36 studied subjects



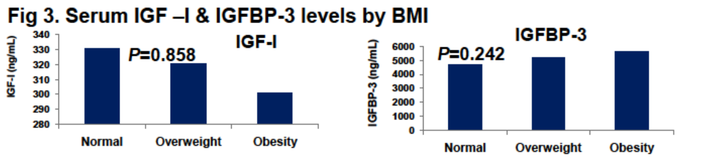
	NGT	IGT	DM
IGF-I	295.41 ±124.29	442.41 ±124.29	275.18 ±73.65
IGFBP-3	4989.55 ±1012.36	6711.43 ±1911.80	5468.00 ±1482.40

Fig 2. Serum IGFBP-1 and IGF-I/IGFBP-1 ratio of 36 studied subjects



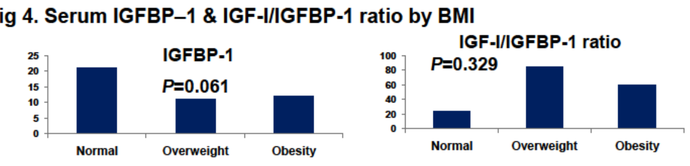
	NGT	IGT	DM
IGFBP-I	14.11 ±8.57	10.54 ±10.89	9.47 ±11.50
IGF-I/IGFBP-1	33.13 ±33.64	107.96 ±78.79	126.31 ±167.62

Fig 3. Serum IGF –I & IGFBP-3 levels by BMI



	Normal	Overweight	Obesity
IGF-I	330.95 ±90.41	321.11 ±129.60	301.36 ±141.90
IGFBP-3	4678.00 ±1288.31	5209.00 ±1145.275	5661.25 ±1630.173

Fig 4. Serum IGFBP–1 & IGF-I/IGFBP-1 ratio by BMI



	Normal	Overweight	Obesity
IGFBP-1	20.70 ±10.48	10.97 ±9.46	12.06 ±9.86
IGF-I/IGFBP-1	24.28 ±14.58	85.30 ±126.53	60.40 ±69.51

CONCLUSIONS

- **Serum IGF-I, IGFBP-3 and IGF-I/IGFBP-1 ratio levels were significantly higher in glucose intolerance group than NGT. Serum IGFBP-1 level showed the negative correlation with BMI, HOMA-IR, serum c-peptide, IGF-I and IGFBP 3 in studied subjects. In glucose intolerance group, serum IGF-I level was no significantly association, but IGFBP-1 was negative correlation with BMI and serum c-peptide. Serum IGF-I/IGFBP-1 ratio was significantly associated with HOMA-IR, serum c-peptide and IGFBP-3. According to BMI, serum IGF-I and IGFBP-1 levels were not significantly different within each group.**
- **These findings suggest that the alteration of serum IGF-I/IGFBP-1 axis in glucose intolerace state is due to disease itself rather than obesity, and IGF-I/IGFBP-1 ratio, especially IGFBP-1, are related to insulin secretion in pancreatic beta cell .**
- **Further studies investigating the relationship between IGFBP-1 and type 2 diabetes in children and adolescents will be needed.**

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