The Association Between IGF-1 levels and Nonalcoholic Fatty Liver Disease (NAFLD) in adolescents with type 2 Diabetes.

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INTRODUCTION & OBJECTIVES

Type 2 diabetes (T2D) is an emerging disease in pediatric population. The association between T2D and non-alcoholic fatty liver disease (NAFLD) has been described. The mechanisms responsible for the development of NAFLD and progression to nonalcoholic steatohepatitis (NASH) in these patients are incompletely understood. Low serum insulin-like growth factor-1 (IGF-1) levels are associated with increased histologic severity of NAFLD. Growing evidence suggests that growth hormone (GH) and IGF-1 may have roles in the development and progression of NAFLD.

This study was designed to evaluate the association between serum IGF-1 levels with the percentage of liver fat in T2D youths.

METHODS

The protocol was approved by the local Ethics and Research Committees. This Cross-sectional study included a total of 70 adolescents, 47 adolescents with T2D and 23 healthy adolescents. The characteristics of the study were explained to all the participants; Informed consent and teenager assent were requested. A complete clinical history, anthropometry and physical examination were performed.

To evaluate the average of liver fat, the imaging estimated proton density fat fraction (PDFF) was determined by magnetic resonance (MR). The serum IGF-1 levels were analyzed by chemiluminescent immunometric assay.

RESULTS

TABLE 1. Clinical and anthropometric characteristics in healthy adolescents and patients with T2D

	HEALTHY ADOLESCENTS n = 23	T2D WITHOUT NAFLD n = 16	T2D WITH NAFLD n = 31	P Value
Sex (M/F)	11 / 12	6 / 10	6 / 25	0.080 §
Age (years)	13.4 ± 2.4	15.1 ± 1.8	15.9 ± 1.6 β	<0.001*
Weight (kg)	51.6 ± 10.4	66.6 ± 15.3 α	64.6 ± 14.4 β	<0.001*
Height (m)	1.58 ± 0.08	1.64 ± 0.12	1.58 ± 0.08	0.106*
BMI (Kg/m²)	20.3 ± 2.9	24.1 ± 3.4 α	25.6 ± 5.0 β	<0.001*
BMI (score z)	0.4 (-1.9 - 1.7)	1.1 (-1.2 - 2.1)α	1.2 (-1.0 - 4.1)β	0.015 δ
Waist circumference (cm)	71.2 ± 6.8	84.0 ± 10.5 α	86.6 ± 13.7 β	<0.001*
Waist/height ratio	0.44(0.37-0.50)	0.48(0.40-0.61)α	0.66(0.43-0.81)β	<0.001 δ
SBP (mmHg)	103.9 ± 6.0	102.5 ± 10.6	105.2 ± 9.0	0.617 *
DBP (mmHg)	63.1 ± 3.1	65.5 ± 9.0	68.8 ± 7.3 β	0.011*
Tanner 3-5 (%)	74.0	88.0	96.0	0.046§
Duration of diabetes (months)	N/A	40.0 ± 24.1	54.6 ± 28.6	0.001 μ
Metformin treatment (%)	N/A	100	100	0.999 §
Insulin treatment (%)	N/A	64.8	66.7	0.892 §
Insulin dose (U/Kg/day)	N/A	0.42 ± 0.26	0.64 ± 0.25	0.028 μ

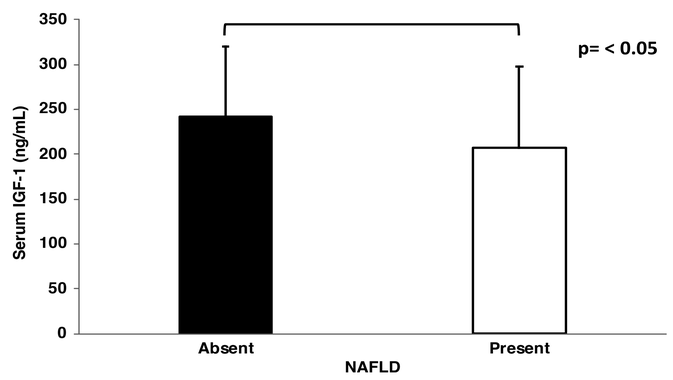
** ANOVA αP <0.05 Control vs T2D without EH βP <0.05 Control vs T2D with EH(Bonferroni-Dunn's Test)*
δ Kruskal-Wallis Test § x² μ U de Mann-Whitney

TABLE 2. Metabolic characteristics in healthy adolescent and patients with T2DM

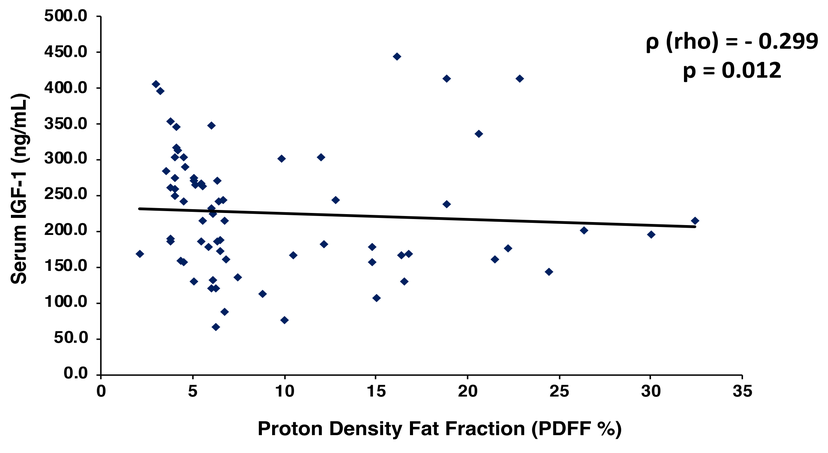
	HEALTHY ADOLESCENTS n = 23	T2D WITHOUT NAFLD n = 16	T2D WITH NAFLD n = 31	P Value
HbA1c average (%)	N/D	7.3 ± 1.0 γ	8.2 ± 2.2	0.032 ξ
Glucose (mg/dL)	80.6 ± 4.4	190.0 ± 121.6 α	203.0 ± 97.0 β	<0.001 *
Total Cholesterol (mg/dL)	152.1 ± 20.4	168.7 ± 36.7	171.2 ± 45.5	0.157 *
Triglycerides (mg/dL)	86.4 (43 - 184)	139.6 (47- 317)	189.5 (55 - 1041) β	0.001 δ
C-HDL (mg/dL)	51.9 ± 10.9	43.3 ± 6.9 α, γ	38.5 ± 9.1 β	<0.001 *
C-LDL (mg/dL)	86.6 ± 18.0	103.0 ± 32.9	102.4 ± 26.9 β	0.005 *
ApoB (mg/dL)	78.5 ± 13.5	99.3 ± 28.1 α	107.0 ± 32.2 β	0.001 *
ApoA (mg/dL)	141.6 ± 25.5	136.0 ± 13.8	130.7 ± 19.4	0.160 *
Uric Acid (mg/dL)	5.3 (3 - 7.5)	5.5 (2.5 - 8.6)	4.3 (2.4 - 8.7)β	0.037 δ
Creatinine (mg/dL)	0.6 (0.4 - 1.1)	0.6 (0.4 - 1.0)	0.6 (0.4 - 0.8)	0.234 δ
GOT (U/L)	19.6 (13.2 - 28.5)	19.7 (9.0 - 40.5)	24.3 (9.2 - 115.1)	0.108 δ
GPT (U/L)	14.4 (6.5 - 30.8)	21.4 (7.1 - 73.3)	26.4 (3.8 - 143.4)	0.747 δ
ALP (U/L)	207.7 (57.2 - 401.0)	139.6 (56.9 - 227.3)	132.0 (69.4 - 377.9)	0.070 δ
GGT (U/L)	16.17 (7.8 - 39.3)	27.45 (7.0 - 84.5)	34.0 (8.7 - 177.7) β	0.015 δ

** ANOVA αP <0.05 Control vs T2D without EH βP <0.05 Control vs T2D with EH (Bonferroni-Dunn's Test)*
γP <0.05 T2D without EH vs T2D with EH δ Kruskal-Wallis Test ξ t de Student

Mean serum IGF-1 in subjects with NAFLD vs ("present") vs. controls without NAFLD ("absent")



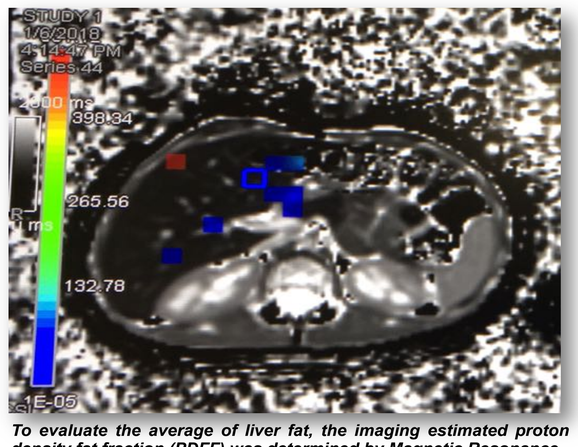
Correlation analysis between liver fat percentage (PDFF%) and serum IGF-1 levels .



Effects of liver fat percentage (% PDFF) on serum IGF-1 levels in adolescent patients with T2D.

	IGF-1 (mg/dL)	
	R^2=0.05	p
PDFF (%)	*-0.299*	*0.012*
Age (years)	-0.177	0. 071
Sex (F)	-0.175	0.074
Tanner Score	-0.034	0.060
IBM (Kg/m²)	-0.105	0.194
HbA1c (%)	*-0.343*	*0.002*
Severity of NAFLD	-0.072	0.139

** It was considered a statistically significant value with a p <0.05. The values were obtained by multiple linear regression analysis, adjusting for age, sex, Tanner stage, BMI, HbA1c levels Severity of NAFLD.*



To evaluate the average of liver fat, the imaging estimated proton density fat fraction (PDFF) was determined by Magnetic Resonance.

CONCLUSIONS

In adolescents with T2D, low serum IGF-1 levels are associated with increased of the percentage of liver fat (PDFF). Further investigation is warranted to determine the differential effects of GH and IGF-1 on the development and progression of NAFLD in adolescents with T2D, which could further elucidate pathophysiology and identify therapeutic targets.

ESPE European Society for Paediatric Endocrinology

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Diabetes and insulin

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