ORIGINAL ARTICLE

Insulin and leptin levels in overweight and normal-weight Iranian adolescents: The CASPIAN-III study

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Background: In this study, we aim to compare insulin and leptin levels in adolescents with or without excess weight and in those with or without abdominal obesity. **Materials and Methods**: This case-control study was conducted among 486 samples. We randomly selected 243 overweight and an equal number of normal-weight adolescents from among participants of the third survey of a national surveillance program entitled "Childhood and Adolescence Surveillance and PreventIon of Adult Non-communicable diseases study." Serum insulin and leptin were compared between two groups and their correlation was determined with other variables. **Results:** The mean age and body mass index (BMI) of participants were 14.10 ± 2.82 years and 22.12 ± 6.49 kg/m^2, respectively. Leptin and insulin levels were higher in overweight than in normal-weight adolescents ($P < 0.05$). Leptin level was higher in children with abdominal obesity than in their other counterparts ($P < 0.001$). Leptin level was correlated with age, fasting blood glucose, BMI, and insulin level. **Conclusion:** Insulin and leptin levels were higher among overweight and obese children, which may reflect insulin and leptin-resistance. Given the complications of excess weight from early life, prevention and controlling childhood obesity should be considered as a health priority.

Key words: Children, insulin, leptin, obesity, overweight

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INTRODUCTION

Alarming increase in childhood obesity is one of the major health concerns due to its long-term health consequences as cardiovascular disease, type 2 diabetes, hypertension, fatty liver etc.[1] High prevalence rate of overweight and obesity is reported in many studies in Iranian pediatric population.[2,3]

Biophysiological factors might play a role in the pathogenesis of excess weight during childhood. The relationship of obesity and insulin resistance is well-established. Although, the risk of insulin resistance is higher in overweight persons, but all overweight persons are not insulin resistant.[4,5]

Leptin is a biomarker, which physiologically regulates fat and glucose metabolism. It modulates long-term energy intake and might identify children at risk of obesity.[6] Leptin-resistance state is reported among obese children.[7] By secreting leptin, fatty mass might influence plasma leptin concentrations. Thus, in spite of high leptin levels, its metabolic actions might face resistance. Moreover, other effects, as sympathetic overactivity, might exist.[8] Association of leptin and insulin resistance is documented.[9,10] Although, some animal studies reported insulin as a potent regulator of leptin expression, but such experience is limited from human studies.[9]

Some studies have evaluated the leptin or insulin levels and their associations among adults, but few studies are conducted in the pediatric age group. In addition, the effects of ethnic differences and diverse lifestyles on levels of insulin and leptin levels are reported.[11-13] This study aims to compare insulin and leptin levels, as well as their correlations in a nationally representative sample of overweight and normal-weight Iranian adolescents.

MATERIALS AND METHODS

This study was conducted as a sub-study of the third survey of a national surveillance program entitled

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"childhood and adolescence surveillance and prevention of adult non-communicable diseases study." After obtaining the ethical confirmation from national and provincial committees, the study was conducted in 2009-2010 among 5528 school students, aged 10-18 years. Participants were selected by random cluster sampling from urban and rural areas of 27 provinces in Iran. Those students with any chronic disease and long-term medication use were not included to the study. Physical examination and laboratory tests were conducted under standard protocols using calibrated instruments. We have previously described its detailed methodology.[14]

The current case-control study was conducted among a randomly selected sample of 486 adolescents, i.e., 243 with overweight and 243 with normal-weight. The cut points suggested by the World Health Organization were used to categorize these groups. Abdominal obesity was defined as waist-to-height ratio more than 0.5. We used the demographic and anthropometric data and lipid profile and fasting blood sugar obtained in the main study; for measuring leptin and insulin, we used the serum subsamples that were kept frozen at −70°C.

Serum leptin levels were measured by ELISA method using DueSet ELISA Development Kit (R and D Systems, Abingdon, UK), and serum Insulin levels were measured by ELISA method (Monobid, California, USA) according to manufacturer's protocols and recommendations.

Statistical analysis

We used the Statistical Package for the Social Sciences, version 17.0 (SPSS Inc., Chicago, USA). The normality of distribution of variables was confirmed by the Kolmogorov–Smirnov test. Mean ± standard deviation of descriptive variable. The mean of variables studied in the case and control groups were compared by independent *t*, Chi-square, and Mann-Whitney U-tests, where applicable. Pearson correlation was used to determine the association of insulin and leptin levels with other variables.

RESULTS

The mean age and body mass index (BMI) of participants were 14.10 ± 2.82 years and 22.12 ± 6.49 kg/m^2, respectively. The characteristics of the overweight and normal-weight participants are presented in Table 1. Insulin and leptin levels were significantly higher in obese adolescents than in their normal-weight counterparts.

Leptin concentration and most cardiometabolic risk factors were higher in participants with abdominal obesity than in those without it [Table 2]. Leptin level had significant correlation with age, fasting blood glucose, BMI, and insulin level [Table 3].

DISCUSSION

In this study, we investigated the difference and correlations of leptin and insulin levels in overweight and normal-weight adolescents, as well as in those with and without abdominal obesity. The main finding of this study is significant high level of insulin and leptin in obese children in compared with normal weights. Leptin level was correlated to BMI and insulin level.

It is documented that both concentration of insulin and insulin resistance might contribute to variations in leptin levels in individuals with similar BMI. Moreover, leptin may have a role in the etiology of insulin resistance. Several studies among adults showed that leptin level is higher in obese than in non-obese individuals.[10,11] Likewise, a study

Table 1: Characteristics of overweight and normal-weight adolescents

Variables	Case		Control		*P* value*
	Mean ± SD	Median	Mean ± SD	Median	
Insulin (μU/ml)	23.10±42.08	11.50	16.32±28.48	11.11	0.040
Leptin (pg/ml)	13148±14292	7619	2795±3523	1136	<0.001
FBS (mg/dl)	86.47±21.84	85.00	88.07±12.88	88.00	0.016
BMI (kg/m^2)	26.23±6.76	25.81	18.02±2.23	17.59	<0.001
Cholesterol (mg/dl)	155.29±29.65	152.00	149.66±32.43	147.00	0.081
HDL (mg/dl)	43.68±12.83	42.00	46.96±13.98	44.00	0.014
LDL (mg/dl)	91.48±25.95	91.00	84.97±30.16	83.00	0.048
TG (mg/dl)	109.90±61.13	96.50	88.81±43.63	81.00	<0.001
Sex *N* (%)					
Male	142 (57.3)		106 (42.7)		0.001
Female	103 (42.6)		139 (57.4)		
Abdominal obesity (%)					
No	99 (31.2)		218 (68.8)		<0.001
Yes	146 (84.4)		27 (15.6)		

FBS = Fasting blood sugar; BMI = Body mass index; HDL=High density lipoprotein; LDL = Low density lipoprotein; TG = Triglycerides; SD = Standard deviation

Table 2: Characteristics of adolescents with or without abdominal obesity

Variables	Abdominal obesity				*P* value*
	No		Yes		
	Mean ± SD	Median	Mean ± SD	Median	
Insulin (μU/ml)	20.17±39.51	11.32	18.90±28.83	11.20	0.816
Leptin (pg/ml)	6018±9872	1845	11529±13584	5206	<0.001
FBS (mg/dl)	88.04±20.77	86.00	85.86±10.90	86.00	0.302
BMI (kg/m^2)	20.15±6.27	18.82	25.74±5.21	26.39	<0.001
Cholesterol (mg/dl)	149.96±30.19	148.00	157.75±33.18	154.50	0.027
HDL (mg/dl)	45.74±13.71	43.00	44.51±13.08	42.00	0.499
LDL (mg/dl)	86.92±28.50	87.00	91.25±27.53	91.00	0.219
TG (mg/dl)	93.12±50.15	83.00	111.42±58.81	97.50	0.001
Sex *N* (%)					
Male	178 (64.7)		70 (28.2)		0.001
Female	139 (57.4)		103 (42.6)		

FBS = Fasting blood sugar; BMI = Body mass index; HDL = High density lipoprotein; LDL = Low density lipoprotein; TG = Triglycerides; SD = Standard deviation

Table 3: Pearson correlation of insulin and leptin with other variables

Variables	Insulin		Leptin	
	Correlation	*P* value	Correlation	*P* value
Age	−0.057	0.205	0.101	0.026
FBS (mg/dl)	−0.008	0.852	−0.096	0.035
BMI (kg/m^2)	−0.016	0.723	0.272	<0.001
Cholesterol (mg/dl)	−0.004	0.941	−0.033	0.517
HDL	0.053	0.319	−0.059	0.272
LDL (mg/dl)	0.020	0.732	−0.025	0.677
TG (mg/dl)	0.004	0.938	0.066	0.205

FBS = Fasting blood sugar; BMI=Body mass index; HDL = High density lipoprotein; LDL = Low density lipoprotein; TG = Triglycerides

among adolescents found higher levels of leptin in obese than in non-obese subjects.[15] In a study, among 7-12-year-old children in Iran, leptin was associated to obesity indexes such as BMI and waist circumference.[16] Our findings are consistent with these studies conducted in the pediatric age group. It might be attributed to leptin secretion by fat tissue.[6] The relationship of leptin level and BMI is well-documented.[7,15,16]

Our study showed higher levels of insulin in overweight children. This finding was in line with previous studies.[7,10,17-19]

We did not find any correlation between insulin or leptin level with lipid profile. It is inconsistent to a previous study.[17] In another study, among 6-13-year-old children in Kuwait, fasting insulin level had a positive correlation with serum triglycerides (TG) and very low density lipoproteins, as well as negative correlation with high density lipoprotein-cholesterol (HDL-C), and no correlation with total cholesterol.[18] Some studies in other countries have documented the correlation of leptin and insulin with lipid profiles. Parts of inconsistencies between the study findings might be because of ethnic differences.

Study limitations

In this study, we did not determine the pubertal stage of participants. In a study among prepubertal children in the obese group, leptin showed a positive correlation with BMI, insulin, TG, and correlated negatively with HDL-C.[20] Moreover, we did not consider the effect of physical activity on insulin and leptin levels, as found in a previous study.[21]

CONCLUSION

In summary, this study has confirmed the significant difference in leptin and insulin levels among overweight and normal-weight children, as well as among those with or without abdominal obesity. Further studies are recommended in different ethnicities.

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