ORIGINAL ARTICLE

Ghrelin Levels are Negatively Correlated with Waist Circumference, in Obese Children and Adolescents

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ABSTRACT

Increased abdominal fat may lead to the development of metabolic syndrome in children and has been strongly associated with insulin resistance. Ghrelin hormone plays an important role in the regulation of food intake and body weight. Ghrelin levels are influenced by body fat and possibly insulin resistance (IR). The aims of this study were to determine fasting ghrelin levels of obese children and to investigate possible correlations between ghrelin hormones with waist circumference and insulin levels. This was a cross sectional study. Eighty obese children ranging from 5 to 18 years of age were recruited from the Pediatric Clinic of Shalamar Hospital, Lahore. Fasting ghrelin levels were negatively correlated with waist circumference, insulin, homeostatic model assessment-insulin resistance (HOMA-IR), and BMI. The results suggest that negative correlation of ghrelin secretion with waist circumference may lead to higher insulin resistance in these children associated with increased abdominal fat accumulation.

Key words: Ghrelin, obesity, insulin resistance, metabolic syndrome, waist circumference

INTRODUCTION

Obesity, emerging more as a global epidemic is rampant in the younger age group. Eating habits of consuming more 'refined and junk food' induces weight gain at an early age[1]. Eating habits of consuming more 'refined and junk food' induces weight gain at an early age. Waist circumference (WC) of greater than 40 inches or 102 cm and in females with a waist circumference greater than 35 inches or 88 Cm. Normal waist-hip ratio (WHR) is less than 1.0 in men and 0.8 in women. Cut-off value for BMI in males with WC >120 Cm and females with WC >88 Cm was 30.7. The health risks associated with an excessive abdominal fat distribution in children, however, are unclear. The Bogalusa Heart Study showed that an abdominal fat distribution determined by WC in children aged 5 to 17 years was associated with abnormal concentrations of triglycerides, low-density lipoprotein and high-density lipoprotein cholesterol, and insulin[2-3].

MATERIALS AND METHODS

In this cross sectional study, 80 obese children ranging from 5 to 18 years were included in the study. Ethical approval was obtained from the Ethical Committee of University of Health Sciences, Lahore. A written consent was obtained from all the parents of children included in this study. All study cases were recruited from Pediatric Clinic of Shalamar Hospital, Lahore. The children enrolled in this study were classified according to their body mass index (BMI) which was ≥95th percentile. Their anthropometric measurements mainly waist and hip circumference measurements were taken. All the obese children were screened on the basis of medical history and physical examination. Insulin, blood glucose, lipid profile and Ghrelin levels were then performed on their blood samples. Insulin resistance was calculated by using homeostatic model assessment (HOMA) model. The obese children of diabetic parents were labeled as group A, and obese children of non-diabetic parents were labeled as group B. Height (cm) was measured using wall-mounted stadiometer and weight (kg) was measured using a weighing balance to calculate BMI (as an expression of obesity). All the subjects were lightly clothed and without shoes. BMI was calculated by the following formula: BMI=Weight(kg)/Height (m2)

Waist Circumference: The waist circumference was measured at a level midway between the lowest rib and the iliac crest, in the standing position, using a non elastic flexible tape and recorded to nearest centimeters and the hip circumference at the level of the greater trochanters with the legs close together[4]. Waist circumference was plotted on waist percentile centile charts by Fernandez et al. (2004). IDF has also chosen to use the 90th percentile as a cut-off for waist circumference[5,6]. The waist-hip ratio was also calculated which equals the waist circumference divided by the hip circumference.

Laboratory investigations: After 10 to 12 h fasting, samples were drawn from all subjects in the study. All the samples were centrifuged (10 min at 3000 rpm)

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and sera were separated. Ghrelin, insulin, were performed on the same day. Serum for lipid profile was stored at -20°C until assayed. Fasting blood glucose level was performed using GOD-pap method. The quantitative determination of serum ghrelin was conducted by enzyme-linked immunosorbent assay (ELISA) technique, using commercially available reagent kit (IBL Ghrelin Sandwich by SPI BIO) with ELISA having Catalogue number A05106. Insulin was assessed using chemiluminescence method. Insulin resistance (IR) was assessed using the HOMA-IR according to the formula of fasting insulin (µIU/ml) × fasting glucose (mmol/L)/22.5[7]

Statistical analysis: All statistical analyses were performed using the SPSS Version 16. For each variable, mean, standard deviation (SD), and ranges were calculated. For correlation between serum ghrelin and waist circumference in obese children r-values were deter-mined by Pearson's correlation test. A p value <0.05 was taken as statistically significant.

RESULTS

Demographic data is presented in Table 1. There were 40 females (50%) and 40 males (50%) included in the study. Mean serum ghrelin levels in males were 8.7±6.7 pg/ml and in females were 8.8±7.0 pg/ml. There was no statistically significant gender difference regarding serum ghrelin levels found between the two groups (p=0.937).

BMI had a significant negative correlation with ghrelin levels (r=-0.366, p=0.001). BMI positively correlated with waist circumference (r=0.769, p<0.001). There was also a negative correlation between ghrelin levels and waist circumference (r=-0.255, p=0.022). Waist circumference positively correlated with BMI, insulin levels (r=0.387, p=0.014), and insulin resistance (r=0.398, p=0.011) and this correlation was statistically significant.

Table 1: Correlation of Ghrelin with different metabolic parameters

Parameters	Serum Ghrelin Levels R value	P value
BMI	-0.366	0.001*
Waist circumference (>90th centile)	-0.255	0.022*
Fasting insulin	-0.254	0.023*
Homa-ir values	-0.300	0.007*
Triglycerides	0.076	0.501

Ghrelin was found to correlate negatively with waist circumference and insulin resistance showing that ghrelin and insulin are inversely related. Also, ghrelin concentrations had a negative relation-ship with BMI (Table 1).

DISCUSSION

This cross sectional study in 80 obese children described the significant correlation of serum ghrelin concentrations with waist circumference, insulin resistance and BMI. The aim of the present study was to determine serum ghrelin levels in obese children and adolescents. We also determined the correlation of ghrelin with insulin levels.

Waist circumference positively correlated with BMI, Insulin levels (r=0.387, p=0.014), and insulin resistance (r=0.398, p=0.011). Waist hip ratio WHR correlated positively with the insulin resistance (r=0.256, p=0.022), and with the triglycerides (r=0.463, p=0.003) and this correlation was statistically significant.

We found a negative correlation between ghrelin and waist circumference (r=-0.255, p=0.022) which is in conformity with the study of Fagerberg, B et al. (2003). They reported that negative association between ghrelin and waist circumference that is high levels of WC and low ghrelin levels can be a consequence for development of metabolic syndrome in obesity[8-10].

In the present study there existed a positive correlation between waist hip ratio and HOMA-IR (r=0.256, p=0.022), explaining that with increasing WHR, insulin resistance increases. In our study it was observed that children with increased waist circumference had lower ghrelin levels, elevated triglycerides, elevated insulin levels, more of insulin resistance and low HDL levels. Work done by Hirschler V et al., (2005) showed that in obese youth with similar BMI, insulin sensitivity is lower in those with high visceral adipose tissue and high waist/hip ratio. Another research by Inge TH, Garcia V and Daniels S et al. (2004) recognized that insulin levels increases with increasing waist circumference percentiles, which leads to insulin resistance syndrome[11].

In simpler explanation a child having obesity, with more waist circumference (more of abdominal fat), when develops hyperinsulinemia, becomes insulin resistant leading to down regulation of ghrelin, and then ending up in to development of metabolic syndrome. All these scenarios then lead to impairment of his quality of life.

We measured waist circumference (WC) in these children as an important diagnostic parameter for metabolic syndrome. WC in children is an independent predictor of insulin resistance, lipid levels and blood pressure which are the components of metabolic syndrome[12-13]. In our study we found a significant positive correlation between BMI and waist circumference (r=0.769, p□ 0.001) which are in agreement with the findings of Hirschler, V et al showing that WC is a valuable tool for identifying overweight and obese children who are at risk of developing metabolic complications.

We found that ghrelin levels was negatively correlated with BMI in these obese children (r=-.366, p=0.001). As ghrelin secretion induces the accumulation of lipids in visceral fatty tissue, located in the abdominal zone and thus leads to increase in obesity and BMI. It has been shown in research that with increasing obesity ghrelin levels decrease and with the loss of weight, ghrelin levels increase[14].

CONCLUSION

Waist circumference is a predictor of insulin resistance syndrome in children and adolescents and could be included in clinical practice as a simple tool to help identify children at risk. The present study showed that children with abdominal obesity, as determined by WC, have increased metabolic risk factors for CVD and T2DM. Because this study is cross sectional, longitudinal studies will be needed to determine the significance of our observations.

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