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The effect of white vinegar on some blood biochemical factors in type 2 diabetic patients

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Type 2 diabetes is one of the most prevalent endocrine disorders worldwide. Traditionally, herbal plants and their derivatives are used to lessen complications of type 2 diabetes. The hypoglycemic and hypolipidemic properties have been reported for vinegar, but some cases of discrepant effects were also observed. In the current study, the impact of apple vinegar on some hematological and blood biochemical factors in type 2 diabetic patients was investigated. In this trial study, sixty patients with type 2 diabetes were divided into two groups. The first group took 15 ml of vinegar with their middle meal for one month. The second group received water as placebo. At the beginning and end of the study, blood samples were collected and biochemical factors including fasting blood sugar (FBS), glycated hemoglobin (HbA1c), triglycerides (TG), total cholesterol, low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), urea, creatinine (Cr), uric acid, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP) and complete blood count (CBC) were evaluated. Findings showed that FBS (P=0.006), HbA1c (P=0.002), MCV (P=0.0001) and mean cell hemoglobin (MCH; P=0.002) decreased where platelets (PLT) (P=0.005) increased significantly in first group. There was no significant difference in the studied parameters in placebo group. Based on the results of this study, it can be concluded that vinegar is a hypoglycemic agent that can be applied for treatment of type 2 diabetes.

Key words: Vinegar, acetic acid, type 2 diabetes, fasting blood sugar (FBS), glycated hemoglobin (HbA1c).

INTRODUCTION

Diabetes Mellitus (DM) is a globally growing health problem and has been considered as one of the five major causes of morbidity and mortality in many societies (Gispen and Biessels, 2000). According to the recent collected information worldwide, over 171 million individuals suffer from diabetes in 2000 and the number is expected to reach 366 million by 2030 (Wild et al., 2004).

Possible leading mechanisms for diabetes establishment are impaired insulin secretion, insulin resistance and overproduction of hepatic glucose (fasting hyperglycemia) (Dailey, 2004). Insulin resistance not only plays pivotal role in diabetes complications, but also involved in atherosclerosis, hypertension and dyslipidemia (Adeli et al., 2001). DM usually causes several organ damage related disorders including retinopathy, cataract, neuropathy, atherosclerosis, nephropathy, embryopathy and wound healing retardation (Diabetes Control and Complications Trial Research Group, 1994).

Although, to date, insulin and other hypoglycemia reagents

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are considered as the only medication for treatment of type 2 diabetes, but this agents have undesirable side effects. Epidemiological studies showed that application of plants and their derivatives improve chronic disease symptoms such as cardiovascular disease, cancer and diabetes (Yang et al., 2004). One of the plant derivatives is vinegar. Apple vinegar as one of the apple products contains a variety of flavonoids such as gallic acid, catechin, caffeic acid and ferulic acid (Natera et al., 2003).

Vinegar is a merged format of French words “vin aigre”, meaning “sour wine”, and can be made from almost any fermentable carbohydrate source, including dates, sorghum, apple, grapes, etc. Acetic acid, the volatile organic acid that identifies the product as vinegar consist of about 3 to 9% of vinegar content and is responsible for the tart flavor and pungent, biting odor of vinegars (Ren et al., 1997). The antiglycemic properties of vinegar were firstly reported by Ebihara and Nakajima (1988). In animal studies, it has been revealed that a diet containing acetic acid or vinegar at concentrations found in traditional diets has varying effects from enhancement of glycogen repletion (Fushimi et al., 2001), prevention of hypertension (Kondo et al., 2001) to stimulation of calcium (Ca) absorption (Kishi et al., 1999).

In a study, it was shown that white vinegar reduced both postprandial blood glucose and insulin levels. It also increased and prolonged satiety in healthy subjects (Ostman et al., 2005). The hypoglycemic impacts of acetic acid have been shown to be mediated by enhanced glycogen repletion in liver and skeletal muscles (Fushimi et al., 2001) and in the suppression of disaccharidase activity in human intestinal cells (Ogawa et al., 2000). In insulin resistant subjects, apple cider vinegar indicated to improve postprandial insulin sensitivity (Johnston et al., 2004).

In another rat model, acetic acid reduced triglycerides (TG) level in hyperlipidemic rats (Fushimi et al., 2006), in parallel risk of cardiovascular disease (Ito et al., 2001). Due to the high cost of drug remedy and their unwanted side effects, finding of some natural components for treatment of diabetes and its complications is considered.

Actually, simple, inexpensive diet strategies to help blood glucose are greatly needed to delay the progression of diabetes. Accumulating evidence indicates that a single dose of apple vinegar may attenuate postprandial glycaemia. Since postprandial glycaemia is a strong predictor of hemoglobin A1C, particularly in well controlled diabetic patients (Carol et al., 2009).

Apple vinegar is remarkably more regarded for its beneficial effects. Therefore, in the present study, the impacts of oral apple vinegar consumption on some hematological and blood biochemical factors in type 2 diabetic patients were investigated.

**MATERIALS AND METHODS**

The present study was a double-blind trial study done in 2011. Duration of treatments was one month. Type 2 diabetic patients, aging 30 to 60 years possessing the entrancing criterion (fasting blood sugar (FBS) more than 126 mg/dl, did not have any digestive, hepatic, renal, cardiovascular, asthma disease and using anti-diabetic drugs (Glibenclamide 1 daily)) were entered into the study. Also, exclusion criteria (vinegar intolerance, digestive disorder and using other drugs) were also imposed for choosing patients.

All of the enrolled patients either placebo or vinegar receiving group filled out written consent form which was designed specifically for this study. Patients with type 2 diabetes were divided into two groups. In each group, 30 persons including 15 males and 15 females were matched for body mass index (BMI).

The first group received 15 ml vinegar with middle meal for one month, without mixing with food or salad. Furthermore, they did not change their lifestyle during the study. In the second group, patients received water as placebo.

At the beginning and end of the study, blood samples were collected and hematological and blood biochemical factors including: FBS, glycated hemoglobin (HbA1c), TG, total cholesterol, low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), urea, creatinine (Cr), uric acid, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP) and hematological parameters including white blood cell (WBC), red blood cell (RBC), mean cell volume (MCV), mean cell hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), hematocrit (HCT) and platelets (PLT) were evaluated.

**Statistical analysis**

Data were expressed as mean±standard deviation of mean. Collected data were analyzed using one way analysis of variance (ANOVA) in Statistical Package for Social Sciences (SPSS) software and paired T-test. Probability level of <0.05 indicates significant difference.

**RESULTS**

The findings of this study indicate that FBS (P=0.006) and HbA1c (P=0.002) reduced significantly in the first group, while TG, total cholesterol, LDL-C, HDL-C, urea, Cr, uric acid, AST, ALT, ALP did not show significant differences. In placebo group, there was no significant difference in the studied factors (Table 1). It was also observed that the MCV (P=0.0001) and MCH (P=0.002) significantly reduced, while PLT (P=0.005) increased significantly in the first group and WBC, RBC, hemoglobin, HCT and MCHC did not change significantly. In placebo group, no significant differences were observed in the hematological parameters (Table 2).

**DISCUSSION**

The related results for biochemical factors and hematological parameters in the first (vinegar treated) and second (water treated) groups are completely illustrated in Tables 1 and 2, respectively.

In this study, it was observed that vinegar significantly reduced FBS and HbA1c in type 2 diabetic patients. Acetic acid is the active ingredient of vinegar and several
mechanisms have been suggested to explain anti-glycemic effects of vinegar. Acetic acid may control these factors via different manners like slowing down of gastric emptying (Liljeberg and Fjorck, 1998), inhibition of disaccharides activity in the small intestine, blocking the complete digestion of starch molecules (Ogawa et al., 2000) and also promotion of glucose uptake by muscle performance (Fushimi et al., 2001).

In another study performed on human subjects, the use of a starchy meal with vinegar was reported to cause suppression of postprandial increments in serum glucose and insulin by a delayed gastric emptying rate (Kondo et al., 2001). Therefore, continuous acetic acid consumption may lead to chronically decreased serum insulin level.

Several investigations examined the fact that whether delayed gastric emptying aid the hypoglycemic effects of vinegar (Liljeberg and Fjorck, 1998). Using non-invasive ultrasonography, Brighenti et al. (1995) did not observe any difference in gastric emptying rates in healthy subjects consuming bread (50 g carbohydrate) in association with acetic acid (that is, vinegar) versus sodium acetate (that is, vinegar neutralized by the addition of sodium bicarbonate); however, post-meal glycaemia was noted by the acetic acid treatment (1995).

Johnston et al. (2004) reported that vinegar could significantly improve insulin sensitivity in insulin resistant patients. There are some evidences that showed vinegar consumption can reduce postprandial glycaemia (Ostman et al., 2005). In agreement with our findings, Johnston et al. (2009) showed that regular vinegar intake by type 2 diabetic patients in a period of 12-weeks reduced HbA1c to 0.16% of its baseline as compared to a related control group.

Despite of these hypoglycemic effects, vinegar has
hypolipidemic effects as well. Although, such an effect was not observed for vinegar and cholesterol, TG, LDL-C and HDL-C levels did not change significantly in our studied patients.

More recent investigations showed that a daily diet containing vinegar induced intestinal calcium absorption (Kishi et al., 1999). Hypokalemia in parallel with hyperreninemia and osteoporosis was evidenced in a 28-year-old lady who had consumed approximately 250 ml apple cider vinegar daily for 6 years (Lhotta et al., 1998). Fushimi et al. (2006) showed that vinegar consumption with diet containing 1% cholesterol for 19 days significantly reduced TG and total cholesterol (Fushimi et al., 2006).

Several investigations revealed that vinegar positively affected lipid profile in diabetic rats, but not FBS and HbA1c (Shishehbor et al., 2007) while 10 ml/day intake of apple vinegar decreased LDL-C and cholesterol in rabbit model (Setorki et al., 2010).

The association between hepatic enzymes and some metabolic syndromes confirmed increased proportion of AST to ALT leading to atherosclerosis (Setorki et al., 2010). In this study, no significant differences were observed in ALT, AST and ALP activity in diabetic patients consuming vinegar. But the activity of liver AST and ALP in the animals treated with the vinegar decreased and elevated, respectively (Mohamed et al., 2001). No significant differences were found neither in the activity of hepatic ALT nor in hepatic acid phosphatase (ACP). Treated groups also showed statistically significant increases in both mean liver and spleen weight. Kidney weight did not show significant change. High dose of cider vinegar also induced histopathological alterations in liver, stomach and duodenum (Mohamed et al., 2001).

Current findings displayed no significant changes in the number of WBC, RBC count and its related indices such as MCHC and Hb, while MCH and MCV were reduced and the numbers of platelets were increased. In Mohammad et al. (2001), the study Hb, total RBC counts and total WBC counts were above the normal in all treated groups.

As mentioned earlier, vinegar reduced glucose level significantly as included in some previous findings and could be related to the effects of some flavonoids that are found in vinegar. Flavonoids are antioxidant components that can reduce glucose absorption and modulate the activity and expression of rate limiting enzymes involved carbohydrate metabolism (Cazarolli et al., 2008). Some studies confirmed the inhibitory effects of acetic acid on some enzymes in carbohydrates metabolism (Ogawa et al., 2000).

Considering the therapy of lipidemic disorders in diabetes, intake of vinegar affects lipid profile in diabetic patients was investigated. Evidences showed that the prevalence of type 2 diabetes is increasing globally. Simple, applicable and inexpensive diet strategies are greatly needed to help and manage blood glucose in type 2 diabetes patients for either delay or control of the progression of complications (Fushimi et al., 2001). Vinegar which is used traditionally as a folk medicine is believed to have several beneficial effects including hypoglycemic and hypolipidemic (Fushimi et al., 2001).

It is clear that these findings are consistent with previous studies in some extent and about some factor, there are contradictory results.

**Conclusion**

Conclusively, based on the previous reports and current results, it can be concluded that vinegar is useful as a therapeutic target in diabetes, but more studies are needed to explore both its advantages and disadvantages as a tool for controlling type 2 diabetes and other metabolic disorders like hyperlipidemia.

**REFERENCES**


Full Length Research Paper

Ghrelin levels in obese children of diabetic parents

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Obesity beginning in childhood often leads to hyperinsulinemic state. Ghrelin, a recently discovered growth hormone (GH) secretagogue with orexigenic effects, is proposed to be a regulator of energy balance. It is thought to be associated with obesity and metabolic syndrome. Increased abdominal fat may lead to the development of metabolic syndrome in children and has been strongly associated with insulin resistance. The aims of this study were to determine fasting ghrelin levels of obese children of diabetic parents and obese children of non-diabetic parents and to investigate possible correlations between ghrelin hormones with 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. These children were divided in two groups. Group A consists of forty obese children of diabetic parents and Group B having forty obese children of non-diabetic parents. A significant increase in the mean level of insulin, insulin resistance, triglycerides and fasting blood glucose were observed with concomitant significant decrease in the mean level of ghrelin. Fasting ghrelin levels were negatively correlated with insulin, homeostatic model assessment-insulin resistance (HOMA-IR), body mass index (BMI) and waist circumference. The results suggest that the down regulation of ghrelin secretion may be a consequence of higher insulin resistance associated with visceral fat accumulation. Ghrelin might prove to be a useful tool to identify obese children at risk for developing insulin resistance, diabetes or metabolic syndrome.

Key words: Ghrelin, obesity, insulin resistance, metabolic syndrome.

INTRODUCTION

Childhood obesity acquires its importance as a predictor of obesity in adult life. In Pakistan, where over 43% of the population comprises of children (<15 years of age), it has been observed that children are adopting more and more unhealthy eating habits and physical activities. Khuwaja et al. (2003) found that majority (58%) of the school children had at least one modifiable risk factor for cardiovascular diseases like physical inactivity, unhealthy dietary habits, overweight and obesity. The factor which gained importance regarding obesity worldwide is the ghrelin hormone. Ghrelin is a peptide hormone with activity in modulating feeding behavior and energy balance. Ghrelin is a peptide principally secreted from oxyntic cells in the stomach. It consists of 28 amino acids. Lower levels of ghrelin were found in obese individuals (Tschop et al., 2001) with the exception of patients with Prader-Willi syndrome (Haqq et al., 2003) and were found raised in anorexia nervosa (Otto et al., 2001). It is thought to play a role in causing obesity and was initially discovered as an endogenous ligand for the growth hormone secretagogue receptor (GHS-R) (Kojima et al., 1999).

Bacha and Arslanian (2005) reported an inverse relationship between fasting ghrelin level and fasting insulin
in childhood obesity. Recent literature suggests that in addition to food intake and energy balance, ghrelin also controls glucose metabolism (Poykko et al., 2003). Furthermore, current evidence suggests that ghrelin could contribute to the metabolic syndrome. It has been shown that ghrelin concentrations are reduced in different diseased conditions including obesity, type 2 diabetes and other conditions with metabolic disturbances (Østergård et al., 2003). The relationship between ghrelin secretion to insulin sensitivity and insulin secretion has been under research till present time. High levels of insulin and glucose due to insulin resistance are believed to be the origin of metabolic syndrome and type 2 diabetes (Boden et al., 2005). Clinical studies are insufficient to reveal whether ghrelin level is a physiological response or a causative factor for the insulin resistance. The aim of this study was to determine the ghrelin levels in obese children having parents with type 2 diabetes mellitus.

MATERIALS AND METHODS

In this cross sectional study, 80 obese children ranging from 5 to 18 years were included in the study. 40 obese children had diabetic parents and 40 obese children had non-diabetic parents. 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. Ghrelin, insulin, blood glucose, and lipid profile 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:

\[ BMI = \frac{Weight \ (kg)}{Height \ (m^2)} \]

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 (Han et al., 1995) with the legs close together.

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) and sera were separated. Ghrelin, insulin, and blood glucose was 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 (Matthews et al., 1985).

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), Version 16 (SPSS Inc., Chicago, IL, USA).

For each variable, mean, standard deviation (SD), and ranges were calculated. The categorical variables were expressed in frequencies. Results are given as means ± SD. Two sample t-test was applied and P values for comparison of serum ghrelin, insulin, blood glucose, lipid profiles levels, BMI, and waist circumference (abdominal obesity), and insulin resistance were determined in healthy obese children of diabetic parents and obese children of non-diabetic parents. The significance of difference between the two groups was also tested. For correlation between serum ghrelin and insulin resistance in obese children of type 2 diabetic parents and obese children of non-diabetic parents, r-values were determined 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 20 females (50%) and 20 males (50%) in both groups. Serum ghrelin levels were observed to be lower in group A as compared to group B which was statistically significant (p<0.0001). However, there was no statistically significant gender difference regarding serum ghrelin levels found between the two groups (p=0.937). Mean serum ghrelin levels in males of both groups were 8.7±6.7 pg/ml and in females of both groups were 8.8±7.0 pg/ml. The lipid profile values were on the higher side in group A as compared to group B. The differences of cholesterol, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) between the two groups were statistically significant (p<0.001). BMI had a strong positive correlation with serum insulin concentration (r=0.252, p=0.024) and insulin resistance (r=0.241, p=0.031). 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 significant negative correlation between serum ghrelin concentrations and insulin levels (r=-0.254, p=0.023). There was also significant negative correlation between serum ghrelin levels and insulin resistance (r=-0.300, p=0.007) as shown in Figure 1. There was also a significant negative correlation between ghrelin levels and age of patients (r=-0.278, p=0.013). There was also a negative correlation between ghrelin levels and waist circumference (r=-0.255, p=0.022). It was noteworthy that there was no correlation between the fasting serum ghrelin and fasting blood glucose concentrations in these groups. Waist circumference positively correlated with BMI,
Table 1. Baseline characteristics of obese subjects in groups A and B.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A (Mean±SD)</th>
<th>Group B (Mean±SD)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Obese (diabetic parents) (n=40)</td>
<td>Obese (non-diabetic parents) (n=40)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>12.4±3.5</td>
<td>11.9±2.6</td>
<td>0.438</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>150±14.6</td>
<td>149±15.1</td>
<td>0.837</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.9±4.0</td>
<td>28.1±4.4</td>
<td>0.065</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>69±19.6</td>
<td>65±19.1</td>
<td>0.328</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>91.6±12</td>
<td>91.1±11.9</td>
<td>0.878</td>
</tr>
<tr>
<td>Serum ghrelin (pg/ml)</td>
<td>4.7±1.7</td>
<td>12.8±7.6</td>
<td>0.000*</td>
</tr>
<tr>
<td>Fasting blood glucose (mg/dl)</td>
<td>105.2±8.6</td>
<td>101±12.7</td>
<td>0.079</td>
</tr>
<tr>
<td>Fasting insulin (IU/L)</td>
<td>30.5±15.0</td>
<td>22.4±11.4</td>
<td>0.009*</td>
</tr>
<tr>
<td>Insulin resistance (HOMA-IR)</td>
<td>7.8±4.1</td>
<td>5.0±2.1</td>
<td>0.000*</td>
</tr>
</tbody>
</table>

*Significant at p<0.05.

Table 2. Correlation of ghrelin with risk parameters of metabolic syndrome.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Serum ghrelin levels (r value)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>-0.366</td>
<td>0.001*</td>
</tr>
<tr>
<td>Waist circumference (&gt;90th percentile)</td>
<td>-0.255</td>
<td>0.022*</td>
</tr>
<tr>
<td>Fasting insulin</td>
<td>-0.254</td>
<td>0.023*</td>
</tr>
<tr>
<td>HOMA-IR values</td>
<td>-0.300</td>
<td>0.007*</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>-0.167</td>
<td>0.138</td>
</tr>
</tbody>
</table>

*Means statistically significant.

insulin levels (r=0.387, p=0.014), and insulin resistance (r=0.398, p=0.011) and this correlation was statistically significant. Insulin resistance also positively correlated with the triglycerides (r=0.332, p=0.036). A significant increase in the mean level of ghrelin, insulin, insulin resistance, cholesterol and triglycerides was observed in the group of children having parents with type 2 diabetes. Concomitantly, significant decrease in the mean level of ghrelin and insulin levels upon comparing the two groups was found. Ghrelin was found to correlate negatively with insulin and insulin resistance showing that ghrelin and insulin are inversely related. Also, ghrelin concentrations were lower in both obese groups and a negative relationship with BMI was found (Table 2). Only healthy obese subjects of diabetic parents were included and were compared with obese children of non-diabetic parents.

DISCUSSION

Nowadays, obesity and diabetes are considered as the twin epidemic and so are the dangers of childhood obesity and its hazardous consequences. The incidence of childhood obesity has tripled over the past three decades. Nearly 16% of children and adolescents between the ages of 6 and 19 years are currently overweight and an additional 15% are considered at risk for becoming overweight (Han et al., 2010).

The aim of the present study was to determine serum ghrelin levels in obese children of type 2 diabetic and non-diabetic parents. We also determined the correlation of ghrelin with insulin levels. This cross sectional study in 80 obese children described the significant correlation of serum ghrelin concentrations with insulin, insulin resistance and BMI.

The ghrelin levels in our study had negative correlation with age (r=-0.278, p=0.013) (Figure 2). In our study, the children with increasing age had lower ghrelin levels. These results are in accordance with Ikezaki et al. (2002) who reported that ghrelin levels are more in prepubertal age, as compared to pubertal age. Circulating ghrelin concentrations progressively increased during the first 2 years of life and then decreased during late childhood and adolescence. Secondly, ghrelin is a growth hormone secretagogue, and growth velocity decreases with rising age and puberty, so ghrelin levels decreases with increasing age (Kelishadi et al., 2008).

We found out that BMI was negatively correlated with ghrelin levels in these obese children (r=-0.366, p=0.001). This finding is consistent with the study by Zou et al. (2008),
Figure 1. Correlation of serum ghrelin and insulin resistance in obese children.

Figure 2. Correlation of serum ghrelin and age of obese children.
showing that ghrelin concentrations are lower in obese children and has a negative correlation with BMI in these obese children. 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 (Erdmann et al., 2005; Zou et al., 2009).

This study had lower serum ghrelin levels in both groups; however, it was significantly lower in the obese children of diabetic parents as compared to the obese children of non-diabetic parents (p<0.0001). Our study comprised 80 obese children with BMI more than 95th percentile, all equally obese, with central obesity (increased waist circumference). It is likely that genetic factors may be the cause of lower ghrelin levels in children of diabetic parents as compared to those having non-diabetic parents. Another factor which contributes to the down-regulation of ghrelin levels in obese subjects seems to be a consequence of elevated insulin levels, because fasting ghrelin levels were inversely correlated with fasting levels of insulin (Murphy et al., 2006). Notably, insulin could play a pivotal role in regulating body weight through its down-regulating effects on plasma ghrelin concentrations. In the present study, serum insulin levels and HOMA-IR increased significantly (p<0.0001) in the obese children of diabetic parents as compared to the obese children of non-diabetic parents. These results are in agreement with study conducted by Van Guilder et al. (2008) who mentioned that insulin resistance and hyper-insulinemia are the hallmarks of obesity, and individuals with truncal obesity exhibit the greatest degree of insulin resistance and hyper-insulinemia. In our study, genetic component is possibly involved in causing raised insulin resistance in group A.

We also found a significant negative correlation between serum insulin levels and serum ghrelin levels in the obese subjects including both groups (r=-0.254, p=0.023). The negative relationship between fasting ghrelin concentration and obesity might be explained by an inhibitory effect of insulin on ghrelin, since a higher insulin resistance is associated with visceral fat accumulation. Our findings are also in agreement with those of other studies conducted in children by Amina et al. (2011) suspecting that insulin resistance may play an important role in the release of ghrelin.

The present study showed that obesity (BMI) had a strong relation with insulin resistance (r=0.241, p=0.031), which is in accordance with the studies by Wang et al. (2001) who observed that obesity had central role in the development of insulin resistance. The selected subjects in our present study were healthy, not suffering from diabetes mellitus, cardiovascular disease, but still had high insulin resistance, which seems to be entirely related to obesity. Insulin resistance is a well recognized risk factor for the development of type 2 diabetes mellitus and cardiovascular disease (Mokdad et al., 2003). These children also had elevated triglycerides, elevated insulin levels, more of insulin resistance and low HDL levels. Work done by Hirschler 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 circumference.

This study highlighted that there was a significant increase in fasting blood glucose levels in both groups of obese children. Approximately, 63% of children of diabetic parents and 37% of children of non-diabetic parents had impaired fasting glucose, that is, >100 mg/dl (5.6 mmol/L) according to International Diabetes Federation (IDF) definition of metabolic syndrome in children (IDF, 2007). The findings were in agreement with Alberti et al. (2006) claiming obesity as the major risk factor for the development of type 2 diabetes. This moderate hyperglycemia therefore draws attention to the preclinical sign of disturbed glucose metabolism and insulin resistance. We also found no significant correlation between serum ghrelin levels and levels of fasting blood glucose in these groups. Similar results were reported in the studies conducted by Ikezaki et al. (2002) and Amal et al. (2012) who found no correlation between ghrelin and fasting glucose in obese children.

The findings of this study show that ghrelin is negatively correlated with insulin and insulin resistance. In adolescents, ghrelin is negatively correlated with insulin resistance, independent of obesity. This study also highlights that low ghrelin concentrations are associated with tendency to develop insulin resistance syndrome and its components. This can be explained by all the obese children having lower ghrelin levels and having higher BMI. Obesity influences all features of the metabolic syndrome and genetic component may play a role in causing lower ghrelin levels in obese children of type 2 diabetic parents more as compared to obese children of non-diabetic parents. This study has shown that they are more prone to develop diabetes and metabolic syndrome later in life.

Conclusion

This study will help to establish the use of ghrelin as one of the early markers to predict the onset of insulin resistance and metabolic syndrome in these children. Obese children of type 2 diabetic parents should be investigated once they start getting obese to prevent them from entering into metabolic syndrome. It also emphasize that ghrelin may be useful in risk assessment of obese children with family history of diabetes. Its levels can be used as a screening tool for developing diabetes mellitus, cardiovascular disease and it may prove an important marker for the diagnosis of metabolic syndrome. Secondly, screenings for obese children with diabetic parents should include testing for ghrelin and insulin resistance.
Early intervention by physicians should be encouraged to improve their quality of life.

Limitations of the study were that small sample size was used in this study due to budget constraints. Only healthy obese subjects of diabetic parents were included and compared with obese children of non-diabetic parents. We could not include non obese group in our study due to financial constraints. So, another study may be planned to further explore the relationship between serum ghrelin, insulin resistance (MS) and obesity in obese and non obese groups.

REFERENCES


Haqq AM, Farooqi IS, O'Rahilly S, Stadler DD, Rosenfeld RG, Pratt KL, LaFranchi SH, Purnell JQ (2003). Serum ghrelin levels are inversely correlated with body mass index, age, and insulin concentrations in normal children and are markedly increased in Prader-Willi syndrome. J. Clin. Endocrinol. Metab. 88:174-178.


UPCOMING CONFERENCES

14th Annual Scottish Conference of the Diabetic Foot

20th World congress on Parkinson's Disease and Related Disorders, Geneva, Switzerland, 8 Dec 2013
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**November 2013**
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**December 2013**
20th World congress on Parkinson's Disease and Related Disorders, Geneva, Switzerland, 8 Dec 2013
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