Research Article

The relationship between fasting serum glucagon and insulin resistance in obese and non-obese individuals

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ABSTRACT

Background: Obesity is a condition manifested by an abnormal distribution of adipose or fatty tissue or excessive accumulation of fat in the body that may lead to many serious health problems such as type 2 diabetes mellitus, cardiac disease, cancers, joint problems, and respiratory and neurological problems. **Methodology:** One hundred people were included in this study: Classified according to their body mass index (BMI), 50 obese patients and 50 non-obese individuals. **Exclusion Criteria:** History of diabetes mellitus, finding of high blood glucose on biochemical examination, history of taking drugs that cause obesity or an increase in body weight, and patients with diseases of high growth hormone and pregnant women were excluded from the study. Investigations including: Fasting blood sugar, fasting serum glucagon, and fasting serum insulin were used. Insulin resistance (IR) was measured using homeostasis model of assessment IR module. **Results:** The mean age for the study group was 34.00 ± 9.43 years old while that of the control group was 34.50± 7.40 years old. The mean BMI for cases was 39.23 ± 6.71 kg/m² and 23.08 ± 1.19 kg/m² for the control individuals. There is association between IR and obesity as it well known and a non-significant relationship between fasting serum glucagon and obesity/IR ($P > 0.05$). **Conclusions:** Obesity is associated with IR without a high level of fasting serum glucagon.

KEY WORDS: Glucagon, Insulin resistance, Obesity

INTRODUCTION

Obesity is a condition manifested by an abnormal distribution of adipose or fatty tissue or excessive accumulation of fat in the body that may lead to impairment of health.[1] An accumulation of fatty tissue results from a disturbance in the balance between energy intake and expenditure which is too big to be regulated by the hypothalamus regulatory mechanism represented by basal metabolic rate.[2] The causes for obesity are usually related to many factors such as genetic factors, consumption of high-calorie food and/or poor or lack of practicing of physical exercise, diseases of the endocrine system, medications, or psychological disorders.[3] Globally, the adult proportion with a body mass index (BMI) of 25 kg/m² or greater had amplified from 28.8% to 36.9% between 1980 and 2013 in males and from 29.8% to 38.0% in females.[1] Obesity leads to many serious health problems such as type 2 diabetes mellitus, cardiac disease, cancers, joint problems, and respiratory and neurological problems.[4] Glucagon is an amino acid polypeptide composed of 29 amino acids with a molecular weight of 3485 daltons, it is produced by the alpha cells of the pancreas, its effect is the opposite of insulin by raising the level of glucose in the circulation. It raises the blood glucose level through its effect on the liver cells (hepatocytes) which have glucagon receptors; thus, it stimulates these cells to form glucose through glycogenolysis and gluconeogenesis. It is one of the so-called counterregulatory hormones that respond to stress.[5,6] Regulation of glucagon secretion: Glucagon secretion stimulated by hypoglycemia which is the main factor, epinephrine through alpha-1, alpha-2, and beta-2 adrenergic receptors, arginine, alanine, acetylcholine, and cholecystokinin.[7-9] Glucagon secretion inhibited by insulin, free fatty acids, somatostatin, and high blood urea. However, its production seems to be independent of central nervous system and regulated mainly by blood glucose level.[10,11]

Insulin resistance (IR) is a state in which cells fail to respond normally to the actions of insulin. The pancreas makes insulin when glucose level is raised in the bloodstream after the digestion of the carbohydrates

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from the food. In normal condition, insulin makes glucose to be being taken into the cells, to be used for energy utilization, and inhibits cells from utilizing fat as a source of energy. When the cells produce insulin in patients with IR, the cells do not respond normally to its action and are unable to use it in an effective way, leading to high level of glucose in the circulation. Beta cells have subsequently raised their release of insulin, further increasing the blood insulin concentration. Usually, this remains undetected and can help the diagnosis of type 2 diabetes.

MATERIALS AND METHODS

Inclusion Criteria

A convenience sample of 100 individuals is included in this study (50 individuals were classified as obese and 50 individuals with normal BMI), with an age range from 20 to 50 years old. Individuals with BMI above 30 kg/m² are considered as obese patients. Individuals with a BMI of <25 kg/m² are considered normal.

Exclusion Criteria

The study excludes any participant with a history of diabetes mellitus, finding of high blood glucose on biochemical examination, history of taking drugs that cause obesity or an increase in body weight such as antiepileptic drugs, steroids, and chemotherapy also excluded from the study, and patients with diseases of high growth hormone level such as acromegaly plus any congenital abnormality and postmenopause women and/or pregnant women. Individuals with BMI between 25 and 30 were excluded from the study.

Laboratory Analysis

Fasting serum glucagon was measured with ELISA.

IR was measured with homeostasis model of assessment IR model:

$$IR = FBS \times \text{fasting insulin concentration}/22.5$$

Insulin was measured by ELISA. A result above 2.5 is considered as IR.

RESULTS

The results revealed a significant difference between patients and control in all parameters except glucagon [Table 1]. There is a significant positive correlation between BMI and IR ($r = 0.268$, $P = 0.010$) [Figure 1]. There is a non-significant negative correlation between IR and glucagon ($r = 0.032$, $P = 0.801$) [Figure 2]. There is a non-significant positive correlation between BMI and glucagon ($r = 0.077$, $P = 0.472$) [Figure 3].

DISCUSSION

IR

There is a significant difference in proportion between cases and controls, and data showed that 32% of cases having IR with mean of 3.54 ± 5.508 and 10% of

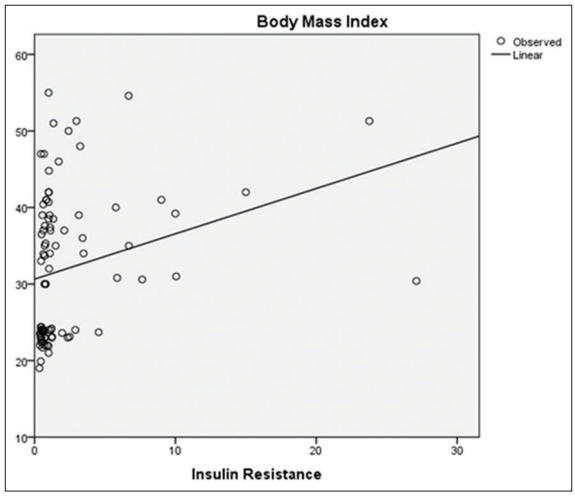

Figure 1: Correlation between insulin résistance and body mass index

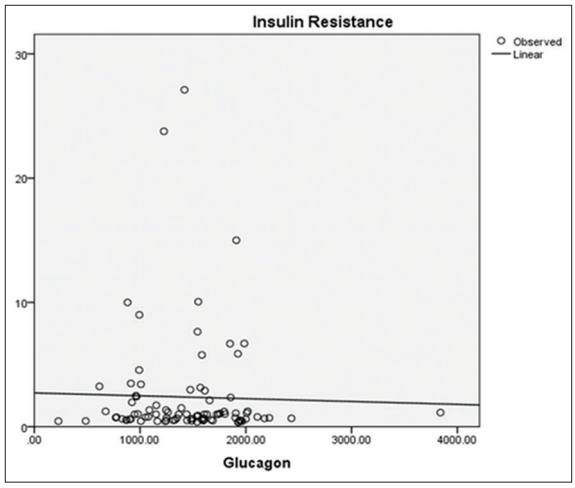

Figure 2: Correlation between insulin résistance and glucagon

Table 1: Concentration of the study parameters among patients and control

Parameter	Study groups		*t*-test	*P* value
	Patient (%)	Control (%)		
Homeostasis model of assessment insulin resistance	3.54±5.51	0.93±0.84	3.3	0.002*
Glucagon (pg/ml)	1500.41±540.97	1397.82±462.80	0.95	0.34
Insulin (ng/ml)	14.13±21.45	4.48±4.64	3.09	0.003*
Fetal bovine serum (mg/ml)	5.57±0.90	4.77±0.82	4.31	<0.001*

*$P \leq 0.05$ is statistically significant

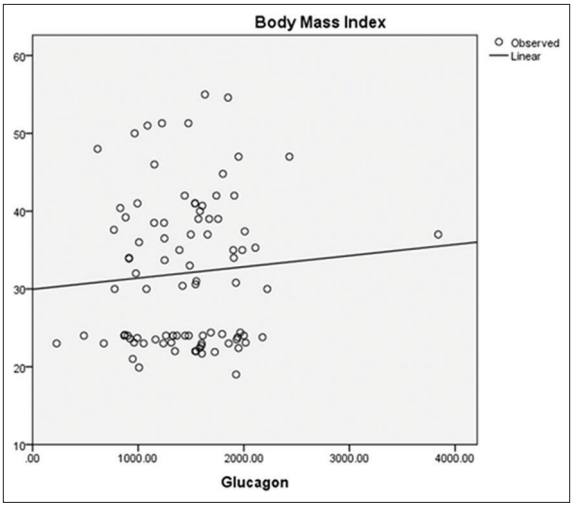

Figure 3: Correlation between glucagon and body mass index

control group having IR with mean of 1.47 ± 2.660; $P = 0.022$, this relation has been long established such as with Bastard *et al*.[12] who asserted that obesity is associated with a low-grade inflammation of white adipose tissue resulting from chronic activation of the innate immune system which can subsequently lead to IR, impaired glucose tolerance, and even diabetes mellitus. It is established that this link might also lead to CV disease.[13]

Fasting Serum Glucagon

There is no significant difference in percentage between cases and controls, and the data showed that 12% of cases have abnormal fasting serum glucagon with mean of 1500.408 ± 540.96917 pg/ml and 5% of the subjects in the control group have normal level of fasting glucagon with mean of 1397.8225 ± 462.79522 pg/ml; $P = 0.344$, this goes with Ahrén who found that serum fasting glucagon in obese non-diabetic patients with IR does not differ from non-obese, non-diabetic patients and explains it by that high insulin concentrations play a negative feedback on alpha cells of the pancreas and thus suppress glucagon secretion. However, in our study, glucagon mean was higher in obese patients in comparison to control group but not to a statistically significant degree which can be explained by what Ahren concluded that IR modifies the physiology of alpha cells to which it starts to increase glucagon secretion.[14] Færch and her colleagues[14] contradicts with the results of this study and the possible explanation may be this study is made on large population over 1300 patients.[15]

CONCLUSIONS

Obese people are high risk for IR, type 2 diabetes mellitus, and CV diseases. Measuring serum glucagon might not give a clear picture of IR and more studies with larger population are needed.

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