Association Between Insulin Resistance And Diabetes Mellitus Type I in Children

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Summary:

Background: Obesity and diabetes mellitus are the common health problems,and obesity is common cause of the insulin resistance.

Aim of study: Aim of the study is to find any correlation between obesity (insulin resistance) and type I diabetes in children.

Patients and methods: This study included (40) children with type I diabetes, in addition to (40) children as control.The age of all studied groups ranged from (8-18) years.This study was attemted from Ibn Al-Balady Hospital during from 20 August to 9 Novembar, 2008.

The subjects wrer divided into (4) groups according to their BMI:-

* Obese children,diabetes,n=20 ,BMI≥30.
* Non obese children, diabetes, n=20,BMI<25.

Obese children, non diabetes, n=20 ,BMI≥30.

* Non obese children,non diabetes, n=20 ,BMI<25.

Venous blood samples were collected , 2ml parts in EDTA tube and used for HbAlc measurement by Alc variant reader and a second part in plain tube for measurement of glucose and insulin .Insulin resistance was determined by mathematic relation (HOMA).

The results: The results revealed marked increased in glucose, insulin , HbAlc and insulin resistance in obese diabetic type I patients comparing to control group they were obese and non obese found to be

within normal values for glucose , insulin , HbA1c , and insulin resistance .

Conclusion :

BMI is a factor for insulin resistance.

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* Insulin resistance is an evident observation, had a significant correlation with diabetic children type I .

* Insulin resistance reflected the degree of metabolic control so as HbA1c reflect the degree of metabolic control.

Insulin is a pancreatic peptide hormone produced in B-cells of islets of Langerhance , it plays a major role in regulation of carbohydrate , fat,and protein metabolism [1], the classical target organ for its action are muscles, adipose tissue and liver [1] .

Insulin resistance (IR) is defined as a reduced glucose response to a given amount of insulin [2], or it is a states in which a given concentration of insulin produces a less than expected biologic effect [3] .

Insulin resistance is not a new phenomenon , although media attention to rising rates of obesity and prediabetes in recent years has certainly raised awareness of the condition [4] .

In an insulin resistant person, normal levels of insulin do not trigger the signal for glucose absorption by muscle and adipose cells. To compensate for this , the pancreas in an insulin resistant individual releases much more insulin such that the cells are adequately triggered to absorb glucose [5] .

Proinsulin is normally converted to insulin by proteolytic action within the B-cells secretory granule. This conversion is usually largely complete, and in normal subjects only about 5% of the B-cells secretory product consists of proinsulin . If the conversion of proinsulin to insulin was incomplete, excess amounts of proinsulin would be

secreted into the circulation. Since this peptide has reduced biologic activity , elevated circulating proinsulin levelswould occur, leading to an apparent hyperinsulinemic state [6] .

Obesity is the most commen cause of IR. Most of people with insulin resistance and obesity do not become diabetic [7]. Insulin secretion is two to three times higher in obese subject than it is in lean .This higher insulin concentration compensates for the diminished effect of hormone (as a result of insulin resistance), and produces blood glucose levels similar to those observed in lean individuals [8].

Body mass index (BMI) or Quetelet Index is a statistical measure of the weight of a person scaled according to height. Body mass index is defined as the individual 's body weight divided by the square of their height.The formulas universally used in medicine produce a unit of measure of kg /m^2. The healthy range for BMI is between 19.5 and 25kg /m^2. Individuals with a BMI between 25 and 29.9 are considered overweight, that whos' BMI is equal to or greater than 30 are defined as obese [9].

Glycated hemoglobin (HbAlc) is the non enzymatic glycated product of the hemoglobin beta-chain at the valine N-terminal residue [10].The Alc constitutes about 60-80% of total glycated hemoglobin , this type of hemoglobin serve as the certain function of hemoglobin but it contain one molecule of sugar in its structure, therefore, it can be separated chemically [11,12].

Glycohemoglobin, measured as HbAlc or as total glycated hemoglobin provides a common means for assessing long-term glycemic control in individuals with diabetes mellitus [13].

Aim of study: Aim of the study is to find any correlation between obesity (insulin resistance) and type I diabetes in children.

Patients and methods:

Forty children with type I diabetic mellitus were enrolled in this study in addition to forty healthy children as control. The age of all studied groups range from (8-18) years. This study was attemted from Ibn Al-Balady Hospital during from 20 August to 9 Novembar, 2008.

The subjects were divided into four groups according to their BMI

* Group (1): non diabetic, non obese children, n=20 , (BMI< 25).

* Group (2): non diabetic, obese children, n=20 ,(BMI ≥ 30).

* Group (3): diabetic, non obese children , n=20 , (BMI < 25).

* Group (4): diabetic , obese chilldren , n=20 , (BMI ≥ 30).

Six milliliters (6ml) of venous blood were collected from all subjects which they asked to fast (12) hours. Two milliliters were added to EDTA tube for HbAlc determination. The rest blood was centrifuged for (15) min. at 3000 r/m.The resulting serum was separated and frozen at (-20 °c) till used for the estimation of fasting blood glucose and insulin.

Determination of Blood Glucose:

Glucose concentration was determined according to the GOD-POD enzymatic method [14].In the Frinder reaction, glucose oxidase (GOD) catalyses the oxidation of glucose to gluconic acid. The formed hydrogen peroxide (H2O2) is detected by a chromogenic oxygen acceptor phenol-aminophenazom in the presence of peroxidase (POD).The intensity of the color is proportional to the glucose concentration in the sample.

Determination of Glycated Hemoglobin (HbAlc):

The measurement of HbAlc was done by using kit from Stanibo Laboratory data (06104):No.350 according to Variant Hemoglobin Alc program [15]. The Bio-Rad Variant Hemoglobin Alc program utilizes principle of ion exchange high performance liquid chromatography (HPLC) for the automatic and accurate separation of HbAlc .

Determination of Insulin:

The levels of insulin concentrations were determined by using DSL-10-1600 ACTIVE insulin ELISA [16], which is an enzymatically amplified (one -step) sandwich- type immuno assay . The absorbance measured is directly proportional to the concentration of insulin present. A set of insulin standards is used to plot a standard curve of absorbance versus insulin concentration from which the insulin concentration in the unknown can be calculated.

Determination of Insulin Resistance:

In each subject, the degree of insulin resistance was estimated at the baseline by Homeostasis Model Assessment (HOMA) according to the method described by Matthews et al.[17]. Score were perform using fasting insulin and glucose for calculation (insulin measured in μIU/ml), glucose measured in (mmol/L) according to the following equation [18] : $HOMA = [(I^{\circ} \times G^{\circ}) / 22.5]$

I°=fasting serum insulin , G°=fasting blood glucose

Statistical Analysis:

All values were expressed as mean ± standard deviation (M±SD). Statistical analysis were performed using student 's T-Test ($p \leq 0.01$) the lowest limit of significance difference between the studied groups [19].

Results & Discussion:

Table (1) shows the levels of glucose, insulin, HbA1c, and insulin resistance in sera of children with diabetes mellitus type I and their control groups which expressed as mean ± SD.

Table (1): Distribution of levels of FBG , HbA1c , Insulin and Insulin Resistance in sera of children with Diabetes Mellitus type I and healthy children as control group.

Parameters	Control subjects No=40		Patient subjects No=40		T-Test
	Group 1 BMI<25 No=20	Group 2 BMI ≥30 No=20	Group 3 BMI<25 No=20	Group 4 BMI ≥30 No=20	
FBG (mg / dl)	81.9±19.99	90.9±9.78	174.89±65.9	227.5±96.59	P ≤ 0.01
Insulin (µmol / L)	6.83±1.93	9.6±2.51	20.46±12.90	25.53±9.45	P ≤ 0.01
HbAlc %	5.95±0.50	7.94±0.57	9.04±1.15	11.83±0.86	P ≤ 0.01
Insulin Resistance	1.36±0.09	2.13±0.06	8.74±2.07	14.19±2.23	P ≤ 0.01

The results revealed that fasting serum glucose was elevated significantly in the group (4) comparing to group (3) which the body mass index is ≥ 30 , while the two control groups (obese and non obese) found to be within normal values. Similary, HbAlc was significantly increased with the increasing of body mass index (BMI) comparing to control groups. In a healthy individual, HbAlc readings reflect the degree of glycemic control over the preceding 2-3 months, reflecting the average circulating life span of 120 days for red blood cells [20]. In the presence of plasma glucose, the hemoglobin beta-chain become increasingly glycated, making the Alc a useful index of glycemic control [20].Some researches demonstrated the relationship between ß-globin and insulin genes are present on short arm of the chromosome 11[21,22].

Table (1) shown significant elevation in the insulin hormone and insulin resistance with the body mass index. The results in agreement with the findings of [23,24].The patients respond normally to exogenously administered insulin , and since their apparent hyperinsulinemia is due to elevated levels of proinsulin rather than insulin, in a sence they are not insulin-resistance. Individuals with impaired glucose tolerance have an elevated proinsulin to insulin ratio compared to normoglycemic individuals and fasting proinsulin levels predict the development of diabetes [25].

It is now clear, there is a relation between insulin, obesity and insulin resistance and this agreed with the well known effect of obesity to amplified the IR state and increases insulin secretion to overcome the resistance [26]. Also , in obese person, too much fatty acids are released and tissues become over loaded with increase in BMI . Excess tissue fat leads to insulin resistance [27,28].

From this study, we should be concluded that BMI is a factor for insulin resistance, which is an evident observation, had a significant correlation with diabetic children type I , and each of HbA1c and insulin resistance reflected the degree of metabolic control.

Conclusion:

BMI is a factor for insulin resistance.
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* Insulin resistance is an evident observation, had a significant correlation with diabetic children type I .

* Insulin resistance reflected the degree of metabolic control so as HbA1c reflect the degree of metabolic control.

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