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OBESITY AND SERUM C-PEPTIDE LEVEL PRECEDE THE DEVELOPMENT OF INSULIN RESISTANCE IN OFFSPRINGS OF TYPE 2 DIABETIC PARENTS.

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Abstract

Objectives: Individuals with insulin resistant have higher risk of developing type 2 diabetes mellitus. Since insulin resistance tends to run in families. The present study was aimed to find out the status of serum C-peptide level in nondiabetic offsprings of diabetic parents.

Methods: Insulin resistance was studied in 127 subjects who were divided into three groups- Group I (47 biparental diabetics offsprings), group II (44 monoparental diabetics offsprings) and group III (36 nondiabetic offsprings). Fasting serum C-peptide level was assessed by standard ELISA method in all the subjects.

Results: Mean serum C-peptide level was 1.98±0.50, 1.25±0.50 ($P<0.01$) and 1.15±0.45 ng/ml ($P<0.05$) in children of biparental, monoparental & nondiabetic subjects respectively. In offsprings of biparental diabetics, serum C-peptide level were 1.75±0.53 & 2.30±0.26 ng/ml in males & females respectively ($P<0.05$). Mean serum C-peptide in normal and high BMI subjects were 1.53±0.35 & 2.29±0.27 ng/ml in biparental offsprings, 0.97±0.14 & 1.86±0.49 ng/ml in monoparental offsprings and 0.86±0.13 & 1.80±0.35 ng/ml in nondiabetic offsprings ($P<0.01$) and in normal and high waist hip ratio 1.44±3.10 & 2.29±0.25, 0.95±0.15 & 1.86±0.47 and 0.87±0.13 & 1.80±0.33 ng/ml in group I, II & III respectively ($P<0.01$).

Conclusion: Mean serum C-peptide level was significantly higher in female than male offsprings of biparental diabetics & were concomitantly increased with higher BMI indices & WHR in all three groups. Our findings suggested that female children of biparental diabetics & obese subjects with central obesity show higher incidence of insulin resistance than the other subjects.

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Introduction: Insulin resistance is a decreased ability of insulin to move glucose into fat and muscle cells and to shut off glucose release from the liver[1]. It results from a combination of genetic susceptibility and obesity[2]. Insulin resistance is now considered a cardinal feature of type 2 diabetes[3]. It is estimated that 1 in 4 people (without diabetes) has a genetic predisposition for insulin resistance.[4]

Studies[5-7] has shown that offsprings of type 2 diabetic parents have higher incidence of hyperinsulinemia that indicating insulin resistance. Offsprings of families with diabetic parents have higher incidence of altered glucose tolerance test, early chemical diabetes[8,9], higher mean concentration of blood glucose[10] hence they are more prone to higher incidence of diabetes.[11]

Early workers have shown that insulin resistance develops before onset of type 2 diabetes and early detection of insulin resistance which has benefit for long term health care for patient[12]. Therefore, simple tests for identifying insulin resistant in individuals are important for both population based research and clinical practice.

So for in most of the studies, insulin levels have been measured for diagnosing insulin resistance. In the present study, we have specially evaluated the prevalence of insulin resistance in the group which are at most risk i.e. offspring of type 2 diabetic parents. Insulin resistant was measurement in the form of serum C-peptide level because it is less susceptible than the insulin to hepatic degradation, has lower half life (about 35 min) than insulin and 5-10 times higher concentration of C-peptide persist in peripheral circulation[13]. However the estimation of serum C-peptide level have been carried out in very limited studies and hence in the present work more comprehensive study has been planned.

Material & Method: The present work was carried out in 127 subjects of variable age (between 5 years to 30 years) and either sex. Study group was divided into 3 groups, group I having 47 subjects belonging to biparental type 2 diabetics, group II having 44 subjects belonging to monoparental type 2 diabetics and group III having 36 subjects from nondiabetic parents.

Subjects were randomly selected from outpatient department of general medicine and indoor words. Written and informed consent was abstained from all the subjects before study was started. The patients having impaired glucose tolerance, pregnancy, malignancy, any significant endocrinal disorders and children of gestational diabetics were not included in this study. A detailed history was taken in regards with family history of diabetes, past history of diabetes or impaired glucose tolerance, history of prior treatment of diabetes and history of physical inactivity. All subjects were thoroughly examined for blood pressure, body mass index (BMI) and waist hip ratio (WHR).

Blood Analysis: Fasting & postprandial blood glucose level was determined to exclude the presence of any degree of diabetes in these subjects. The fasting serum C-peptide level was determined by standard ELISA kit (IBL C-peptide ELISA Kit) method.

Statistical Analysis: Data analyses were performed with the Statistical Package for the Social Sciences, version 16.0 (SPSS, Chicago, Illinois, USA). Differences in various parameters between different groups were analyzed for significance using unpaired student's 't'-test. The significance of difference was measured at 95% level of confidence ($P<0.05$).

Results: In the present study all the subjects were assessed for insulin resistance by the estimation of their fasting serum C-peptide level. Their serum C-peptide level was also correlated with their age, sex, body mass index (BMI) & waist hip ratio (WHR).

The serum C-peptide levels were significantly higher in offsprings of biparental diabetics as compared to other subjects ($P<0.01$). There was no statistically significant difference ($P>0.05$) in serum C-peptide levels of offsprings of monoparental diabetics and nondiabetics (Table 1).

The experiment was conducted in subject of age between 5 to 30 years. The mean age of the offspring of biparental diabetes, monoparental diabetics & nondiabetics was 23.1±4.56 years, 21.37±4.75 years & 21.31±4.01 years respectively. When serum C-peptide level was compared in the subjects of same age group in different groups, they were found to maximum in offsprings of biparental diabetics.

The mean serum C-peptide level was significantly higher in female than male offsprings of biparental diabetics (P<0.05) showing that female offsprings were more insulin resistant than male offsprings of biparental diabetics. However in offsprings of monoparental diabetics and nondiabetics, the serum C-peptide level was not significantly different in male and females (P>0.05) (Table 2).

It was interesting to find out that the mean serum C-peptide level concomitantly increased with higher BMI indices and WHR (P<0.01) (Table 3 & 4). It seems that serum C-peptide level was influenced by other parameters mentioned above viz. age, sex, BMI and WHR and hence the insulin resistance may also be varied by similar parameters.

Discussion: In the present study, the result suggest that the offsprings belonging to either biparental or monoparental diabetics have concommitent increase in insulin resistance. This is also has been found that the insulin resistance as judged by C-peptide levels appear to be more in the females and obese subjects. These findings are in agreements with the earlier reports[14-16] on C-peptide levels and insulin resistance in parental diabetes. The C-peptide level seemingly was higher in subjects who particularly had abdominal obesity with increased waist hip ratio. These findings are comparable with previous reports on insulin resistance and central obesity [17, 18].

In type 2 diabetes the enhanced insulin secretion is an essential failure[2]. Since the C-peptide molecule is simultaneously formed from proinsulin during the secretion of insulin molecule, its level also ought to be increase with increase formation of insulin and hence the presence of high C-peptide levels in our subjects is explainable. The increase formation of insulin and simultaneously that of the increase level of C-peptide molecule is presumably indicate reduced insulin receptor and tyrosine kinase activity in skeletal muscles of type 2 diabetics. The pathogenesis of insulin resistance is currently focused on a PI-3 kinase signaling defect, which reduces translocation of GLUT4 to the plasma membrane[2]. Adipocytes secrete a number of biologic products (leptin, TNF-a, free fatty acids, resistin and adiponectin) that contribute to the insulin resistance in obese subjects who particularly have visceral or central obesity (as evidenced by the hip waist ratio)[2]

Therefore it is concluded from the above study that C-peptide level is used as an important indicator of assessment of insulin resistance in these subjects of type 2 diabetes or those who were prone to diabetes by way of being offsprings of biparental and monoparental diabetics.

Table 1. Comparative changes of serum C-peptide level between group I, II and III subjects.

Study Group	Mean C-eptidelevels(ng/ml) (Mean ± SD)	Statistical Significance		
			r	p
Group- I(n=47)	1.98 ± 0.51	I Vs II	4.44	<0.01
Group- II(n=44)	1.25 ± 0.50	II Vs III	0.97	>0.05
Group-III(n=36)	1.15 ± 0.45	I Vs III	5.17	<0.01

Table 2. Comparative changes of serum C-peptide level in group I, II and III subjects of both sexes.

Study Group	Mean C-peptide levels(ng/ml) (Mean ± SD)		Statistical Significance		
	Male	Female		t	p
Group- I	1.75 ± 0.53	2.30 ± 0.26	Male Vs Female	2.16	>0.05
Group- II	1.16 ± 0.47	1.38 ± 0.53	Male Vs Female	0.91	>0.05
Group- III	1.06 ± 0.29	1.14 ± 0.67	Male Vs Female	0.36	>0.05

Table 3. Comparative changes of serum C-peptide level in group I, II and III subjects according to BMI.

Study Group	Mean C-peptide levels(ng/ml) (Mean ± SD)		Statistical Significance		
	Normal BMI	High BMI		t	p
Group- I(n=47)	1.53 ± 0.35	2.29 ± 0.27	Normal & High	7.60	<0.01
Group- II(n=44)	0.97 ± 0.14	1.86 ± 0.49	Normal & High	7.85	<0.01
Group- III(n=36)	0.86 ± 0.13	1.80 ± 0.35	Normal & High	10.17	<0.01

Table 4. Comparative changes of serum C-peptide level in group I, II and III subjects according to their WHR.

Study Group	Mean C-peptide levels(ng/ml) (Mean ± SD)		Statistical Significance		
	Normal WHR	High WHR		t	*p*
Group- I (n=47)	1.44 ± 0.13	2.29 ± 0.25	Normal & High	9.27	<0.01
Group- II(n=47)	0.95 ± 0.15	1.86 ± 0.49	Normal & High	7.79	<0.01
Group- III (n=47)	0.87 ± 0.13	1.80 ± 0.33	Normal & High	10.16	<0.01

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