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Comparative Study of Insulin Resistance in Healthy young Adults with and without Family History of Diabetes Mellitus

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Abstract
Family history of diabetes is an important risk factor for diabetes mellitus. Insulin resistance (IR) is central feature in the natural history of Impaired glucose tolerance (IGT) and Type-2 DM. we studied occurrence of insulin resistance in healthy young adults and subjects with family history of diabetes. Subjects with F/H of DM had higher levels of fasting plasma insulin and Insulin Resistance compared to those without F/H of DM Recognition of IR in the pre-disease state would be beneficial, as it affords, potential implementation of interventions designed to reduce such disease development.

Keywords: *Insulin Resistance; Metabolic syndrome; FPI; HOMA_IR; Diabetes mellitus.*

Introduction

The clinical profile of average Indian type 2 diabetic patients is different from that of a white Caucasian. At diagnosis Indian patients are a decade younger, despite their thinness Indians are more insulin resistant and hyperinsulinemic. Family history of diabetes is more common in Indians[1]. Studies have also shown that low insulin sensitivity tends to cluster in families. In addition, individuals with this genetic predisposition to IR and type 2 diabetes have even greater level of obesity induced IR than do individuals from non-diabetic families.

Very few studies have specifically evaluated for the presence of insulin resistance in younger age group with normal glucose tolerance and its association with family history of diabetes[2].

Objectives

- To detect early occurrence of insulin resistance in healthy young adults, age 18-25 years.

- To study the impact of family history of diabetes and its possible early impact on insulin resistance.

Materials and Methods

In this study 100 normal young adult volunteers, 50 subjects with and 50 subjects without family history of diabetes, in the age range of 18 to 25 years were evaluated for insulin resistance.

Inclusion Criteria

1. The subject between the age 18years and 25 years without any apparent disease.
2. Subject with family history of diabetes.

Exclusion Criteria

1. Known case of diabetes mellitus.
2. Use of corticosteroids.
3. Pregnancy.
4. Infections or severe illness.
5. Any medical conditions that would interfere with OGTT (e.g. frequent vomitin, partial bowel obstruction).

A detailed physical examination and measurement for Blood Pressure, Body weight, height, Hip & waist circumference was done.A standard (75 g) Oral Glucose Tolerance Test (OGTT) was performed on all thestudy subjects.Fasting serum insulin concentration was determined by radioimmunoassay (RIA). Insulin resistance calculated using Homeostatic model assessment calculator using fasting plasma insulin and fasting plasma glucose parameters.

Results

Table: 1 Age and sex wise distribution of all subjects in the study

Age	Sex		Total
	Male	Female	
18-19	16	29	45
19-20	16	14	30
20-21	11	5	16
21-22	2	1	3
22-23	1	0	1
23-24	0	1	1
24-25	3	1	4
Total	49	51	100

There were 49 male subjects and 51 female subjects with mean age of19.08 years

Table 2 Distribution of subjects with FH of DM into 1st& 2nd degree FH subject

Number of Persons with DM in a family(n=50)	First Degree (Parents)		Number of Persons with DM in a family(n=50)	Second Degree (Grand Parents)	
	Number	%		Number	%
Father	18	66.67%	Paternal Grand Parents	18	41.86%
Mother	3	11.11%	Maternal grand Parents	15	32.55%
Both	6	22.22%	Both	11	25.58%
Total	27	100%	Total	44	100%

50 Subjects with positive F/H had the Subjects with 1st degree relatives with diabetes (Parents) = 27 (54%) and 2nd degree relatives (Grand Parents) = 44 (88%) and 20 (40%) of the subjects had both 1st and 2nd degree relations with diabetes in the family

Table 3 Correlation of HOMA_IR & clinical parameters with & without family history of diabetes

Correlation of HOMA_IR	With Family history			Without family history		
Clinical parameters	Pearson's correlation	P value	Inference	Pearson's Correlation	P value	Inference
BMI	+0.397	0.004	Significant	+0.196	0.17	NS
Waist circumference in cm	+0.31	0.027	Significant	+0.085	0.55	NS
W/H ratio	-0.07	0.62	NS	+0.082	0.57	NS

Comparison of clinical parameters in subjects with and without F/H of DM: Statistical analysis found BMI to be significant (p = 0.04) on comparing healthy young adults with and without family history of diabetes & other clinical parameters revealed no statistical significance.

Table 4- Comparison of FPG, FPI, HOMA_IR, HOMA_ B% in subjects with without family history**.**

Lab parameters	With Family history		Without family history		Statistical analysis		
	Mean	SD	Mean	SD	T	P	Inference
FPG (mmol)	4.58	0.47	4.40	0.59	1.70	0.09	NS
FPI(mU/l)	10.24	8.29	6.19	3.93	3.12	0.002	Significant
HOMA_IR	2.05	1.57	1.24	0.89	3.16	0.002	Significant
HOMA _Beta%	227.63	272.60	179.67	162.76	1.06	0.28	NS

Comparison of Insulin levels and insulin resistance parameters in subjects with & without F/H of DM revealed statistically significant higher values of FPI 10.24 v/s 6.19 (p-0.002) & the HOMA_IR 2.05(±1.57) in v/s 1.24 (± 0.089) [p-value = 0.002]in subjects with family history of diabetes mellitus

Discussion

The maintenance of normal glucose tolerance in healthy subjects is achieved mainly by three important factors, Insulin secretion, Tissue glucose uptake in Peripheral (primarily muscle) & Splanchnic (liver and gut) andSuppression of hepatic glucose production.

Both insulin resistance and beta-cell dysfunction occur during the development of type 2 DM[4,5]

Guzzaloni G et al[6] studied a total of 405 prepubertal and pubertal obese subjects to verify whether the data from fasting samples were enough for evaluating IR and insulin secretion or if OGTT was mandatory. IGR and HOMA IR increased in both sexes during puberty, HOMA beta cell did not show any variation. In our study to eliminate the effect of puberty on IR, the study subjects were in the age range of 18 to 25 yrs.

An analysis of the patients' records at the Diabetes Research Centre, Madras, has shown that out of a total of 70,000 patients registered at the centre, 25, 182 have at least one diabetic parent[7]. A cross sectional analysis of patient population showed a prevalence of diabetes as follows: First-degree relatives -53% and Second degree relatives - 9%. In our study of 50 subjects with a family history of DM we observed the following pattern: 1st degree relatives- 54% and 2nd degree relatives- 86.0%. This pattern indicates the strong familial aggregation of diabetes.

In our study we have establishedthe insulin resistance by HOMA method for our sub-population with normal OGTT in the age range of 18-25 years, HOMA_IR =1.64 (0.30-6.91) SD-1.33, HOMA_% BETA = 203.65(21.00- 1809.52) SD-224.66.

In subjects with IR, normal glucose tolerance is accompanied by hyperinsulinemia (> 50mU/l fasting; >300mU/l stimulated), due to insensitivity of target tissue to insulin or secondary to reduced number of insulin receptor at the target cell surface.In our study of 100 subjects with normal OGTT we observed a fasting insulin of 8.22 µIU (1.6 to 40.0) and fasting glucose of 81.14 mg/dl (64-108). Subjects with F/H of DM had higher basal insulin value of 10.24 v/s 6.19 for subjects without F/H of DM (p - 0.002) and baseline glucose of 82.44 v/s 79.2 respectively.

Both Indian and western population studies have shown that predicting individuals insulin sensitivity and ß - cell function from BMI is possible. It was found that BMI was the most important determinant of IR. It was also seen that a positive family history of diabetes and obesity were independent risk factors for development of type 2 diabetes. In our study, we observed a statistically significant correlation between HOMA_IR with increasing BMI and waist circumference in subjects with F/H of DM.[BMI ; Pearson's correlation = + 0.397, (p = 0.004) & Waist circumference ; Pearson's correlation = + 0.31, (p = 0.027) respectively].

Conclusion

It can be seen from our study that IR exists at a much younger age (18 –25 yrs) in our population. It was also evident that siblings of diabetic parents and grandparents were at higher risk of having IR. Among these subjects, those who had had higher BMI had higher IR values when compared to subjects without family history of diabetes with similar BMI.

This paves the way for implementation of interventional programmes at a much younger age in siblings of diabetic parents and grandparents to delay and prevent the onset of metabolic syndromes and its complications.

Subjects with F/H of DM had detectable IR at younger age and are at risk for future development of metabolic syndromes and its complications. Recognition of IR in the pre-disease state would be beneficial, as it affords, potential implementation of interventions designed to reduce such disease development.

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