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Study of insulin resistance in offspring of type 2 diabetes mellitus and obese persons

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ABSTRACT

Introduction: Insulin resistance always associate pancreatic β-cell dysfunction in type 2 diabetes mellitus. Obesity is strongly associated with type 2 diabetes mellitus. Therefore screening to evaluate the status of insulin resistance in offspring of type 2 diabetes mellitus to identify risk of further metabolic complications is important.

Aims and objectives: The aim of the study is to find out the correlation between insulin resistance in control with genetic inheritance and obesity.

Materials and Methods: It was a Case control Study carried out on 120 apparently healthy, non-diabetic people were included in the study. The age of these people lies between 20 to 40 years. The following anthropometric measurements were done in the above 120 patients. These people were classified depending upon BMI.

Body Mass Index (BMI) Categorym 18.5–29.99 Non obese 30.0 Obese

Further these people were categorized on the basis of detailed family history of diabetes mellitus to their parents into 4 different groups and each group contain 30 people as a

a) Group-I (Control): Includes 30 people who were non-obese, off-springs of non-diabetic persons.

b) Group-II (Cases): Includes 30 people who were non-obese, offsprings of type 2 diabetes mellitus patients.

c) Group-III (Cases): Includes 30 people who were obese, off-springs of non-diabetic persons.

d) Group-IV (Cases): Includes 30 people who were obese, offsprings of type 2 diabetes mellitus.

Conclusion: The purpose of our study was to identify insulin resistance individuals even before appearance of diabetes mellitus in the above groups by HOM-IR method. So that they can be targeted for aggressive lifestyle interventions and subsequent morbidity can be prevented.

1. Introduction

Diabetes mellitus (DM) is a chronic disorder that can alter carbohydrate, protein, and fat metabolism

Type 2 diabetes mellitus is caused by the relative insulin deficiency or in majority of cases due to decreased sensitivity of target tissue to insulin, which is called an insulin resistance.[1] Insulin resistance always associate pancreatic β-cell dysfunction in type 2 diabetes mellitus.

Obesity is strongly associated with type 2 diabetes mellitus.[2] Obesity is a highly heterogeneous disorder characterized by a state of excess adipose tissue mass. This excessive deposition of fat particularly its central or visceral component is responsible to develop insulin resistance.[3] Obesity is said to be an insulin resistant state[4] and insulin resistance with common pathophysiological factor together called a "syndrome" of cardio metabolic disturbances, affecting adiposity, glucose intolerance, dyslipidemia and altered blood pressure control.[5]

1.1. Insulin resistance

Is defined where a normal or elevated insulin level produces an attenuated biological response, this refers to impaired

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sensitivity to insulin mediated glucose catabolism. While insulin resistance runs in families and may have a genetic basis, it is often lifestyle factors that trigger cardio metabolic disease processes.[2] Thus insulin resistance said to predicts type 2diabetes mellitus and is strong risk factor for the disease.

Therefore screening to evaluate the status of insulin resistance in offspring of type 2 diabetes mellitus to identify risk of further metabolic complications is important. Because insulin resistance usually develops long before metabolic complications of obesity. Therefore dentifying and treating insulin resistant individuals at an earlier stage can have potentially great preventive value. Identifying patients with insulin resistance before appearance of any cardio metabolic complications

2. Aims and Objectives

The aim of the study is to find out the correlation between insulin resistance in control with genetic inheritance and obesity.

The objectives of our study are-

1. Estimation of fasting plasma glucose in study groups.
2. Estimation of fasting insulin level in study groups.
3. Estimation of insulin resistance in study groups.
4. Comparison of insulin resistance between various groups.

3. Materials and Methods

It was a Case control Study carried out in department of Biochemistry of Grant Government Medical College Mumbai during period from March 2016 to June 2017. After a written consent, total 120 apparently healthy, non-diabetic people were included in the study. The age of these people lies between 20 to 40 years. Detailed history of people including age, sex, history of any medications, addictions, physical activities, any surgery, eating habits and lifestyle was taken.

The following anthropometric measurements were done in the above 120 patients.

These people were classified depending upon BMI.

3.1. Bodymass index (BMI) category

18.5 – 29.99 Non obese $>$ 30.0 Obese

Further these people were categorized on the basis of detailed family history of diabetes mellitus to their parents into 4 different groups and each group contain 30 people as a

1. Group-I (Control): Includes 30 people who were non-obese, off-springs of non-diabetic persons.
2. Group-II (Cases): Includes 30 people who were non-obese, off-springs of type 2 diabetes mellitus patients.
3. Group-III (Cases): Includes 30 people who were obese, off-springs of non - diabetic persons.
4. Group-IV (Cases): Includes 30 people who were obese, off-springs of type 2 diabetes mellitus.

3.2. Inclusion criteria

1. All people of age group between 20-40 years.
2. Persons with normal fasting and post meal plasma Glucose level.
3. Persons with history of type 2 diabetes mellitus to their parents or obese or both.

3.3. Exclusion criteria

1. People of age group less than 20 year and above 40 years.
2. People of known diabetic mellitus.
3. Patients with chronic liver disease, pancreatic disease, renal diseases, cardiovascular diseases and endocrine disorders.
4. Patients with history of chronic alcoholism.
5. Patients on statin therapy, oral contraceptive pills, steroids etc

3.4. Clinical examination

3.5. Anthropometry

1. Height (meters): Measured by standing erect against wall without shoes by fixing tape on wall.
2. Weight(Kg): Measured by weighing pan at nearest Kg
3. Body Mass Index (BMI)

3.6. Biochemical investigations

The 12 hour fasting venous blood samples were collected from all people in Fluoride and plane bulbs. Serum was separated after 1 hour by centrifugation at 3000 rpm for 10 minutes, and was tested for following parameters.

1. Fasting plasma glucose
2. Fasting plasma insulin level.
3. Serum cholesterol.
4. Serum Triglycerides
5. Serum HDL
6. Serum LDL
7. Serum VLDL
8. Serum insulin resistance was calculated by HOMA-IR(102)

HOMA-IR index = Fasting blood glucose (mg/dl) x fasting serum insulin (μU /ml)/405

The second blood sample is collected in the fluoride bulb after 2 hours for postprandial plasma glucose.

Table 1: Results showing average BMI index among the various groups

Parameters	Group I	Group II	Group III	Group IV
BMI	23.22±17.5	20.41±1.53	31.14±1.89	31.86±2.40

Table 2: Results showing average values of all the biochemical parameters among the various groups

Parameters	Group I	Group II	Group III	Group IV
Fasting plasma glucose (Mg/dl)	85.03±10.54	89.6±8.37	90.9±8.76	94.03±9.3
Fasting serum insulin (μIU/ml)	5.84±1.43	5.13±1.85	9.55±13.18	8.04±3.30
Serum cholesterol (mg/dl)	168.2±14.73	177.1±30.62	205±21.49	203.5±13.38
Serum triglyceride (mg/dl)	103.4±22.83	94.37± 13.55	119.3±12.45	80.97±11
Serum HDL (mg/dl)	51.57±8.73	44.6±7.54	48.2±6.9	46.47±4.08
Serum LDL (mg/dl)	163.6±18.52	146.4±37.7	132.9±21.81	140.8±15.48
Serum VLDL (mg/dl)	20.3±4.46	18.81±2.75	23.86±2.49	16.19±2.2
Post prandial plasma glucose (mg/dl)	112.2±14.49	114.1±10.95	115.2±10.47	143.8±18.22
HOMA IR	1.2±0.33	1.13±0.41	2.1±2.79	1.85±0.75

4. Observations and Results

5. Discussion

As all the persons are non-diabetics their fasting and post prandial plasma glucose level is in the normal range. But the obese persons (Group-III and IV) have their fasting plasma glucose level significantly higher as compared to non-obese. Similar results are found by Aslam M, Obaidullah S, Haider Z in which fasting plasma glucose is significantly increased in obese persons than non-obese persons.[6]

We have found non-significant difference in fasting insulin between Group-I and Group-II. As persons in the Group I (control) are non-obese and off-springs of non-diabetic persons whereas the person in the Group II are non-obese but off springs of type 2 diabetes mellitus persons. From this it shows that heredity alone is not responsible in the increase in fasting insulin level. But our study results do not correlate with the study of Strączkowski M, Kowalska I, Stępień A et al. According to them Persons with positive family history of type 2 diabetes associate with decreased stimulation of insulin receptor substrate (IRS)-associated with tyrosine phosphorylation and association of phosphatidylinositol 3-kinase activity with IRS-1.[7]

Also we have found non-significant difference in fasting insulin between Group-I (control) and Group-III which are obese but off-springs of non-diabetics patients. So we can conclude from the above results that obesity does not affect the fasting insulin level. Thus similar results are given by Lillioja S, Bogardus C. They suggest that at maximum plasma insulin concentration there is a significant, negative linear relationship between the degree of obesity and insulin resistance in males. The relationship is much weaker at these higher insulin concentrations than at physiologic insulin concentrations.[8] However, Paulsen EP, Richenderfer L, Ginsberg- Fellner F. et al. in their study about 1968, 66 black, Puerto Rican, and white obese children between 4 and 16 years of age were studied, so the Fasting glucose level and insulin were similar in children with and without a positive family history of diabetes.[9]

We have found significant difference in fasting plasma insulin between Group-I and Group-IV which are obese and off-springs of type 2 diabetes mellitus. It shows that when obesity and heredity factor combines in the persons then it affect the fasting insulin level significantly as observed from above results. Similar results are found in the studies performed by Petersen KF, Dufour S, Befroy D et al.[10]

We have found non-significant difference in fasting insulin between Group-II and Group-III. This suggest again that hereditary factor alone does not have influence in increasing the serum insulin level. So our study correlate with Morris RD, Rimm DL, Hartz AJ et al. They found increased prevalence of diabetes with obesity or family history. According to them obesity and family history represent independent risks for daibetes.[11]

We have found significant difference in fasting insulin between Group-II and Group-IV. These results suggest obesity plays an important role in the rise in the fasting insulin level in Group IV. So the results are contradictory to the results which we have found previously Bogardus C, Lillioja S, Mott D et al also found the similar results. They have reported decreased in vivo maximal insulin-stimulated glucose utilization rates in obese compared with lean subjects.[12] In contrast, DeFronzo reported that in vivo maximal insulin-stimulated glucose utilization rates were similar between lean and obese subjects. A possible explanation for the different results was that Kolterman et al. studied obese subjects with or without glucose intolerance, whereas DeFronzo studied only glucose-tolerant subjects. Olefsky et al. have also reported a significant association between decreased maximal insulinstimulated glucose utilization rates in vivo and in vitro in isolated abdominal adipocytes from obese subjects with and without glucose intolerance.[12]

We have found non-significant difference in fasting insulin between Group-III and Group-IV. These persons have difference in hereditary risk factor but both the groups are obese. This also suggests that only obesity is not responsible for increase in the fasting plasma insulin level. We have found significant difference in serum cholesterol, triglyceride, LDL and VLDL levels between non-obese (Group-I and Group-II) and obese groups (Group-III and Group-IV). Similar results are found by Khan M, Khaleel M as per their study when various parameters of blood lipid profile were compared it was observed that there was significant difference between obese in comparison to non-obese individuals.[13]

We have found non-significant difference in Insulin resistance between Group-I and Group-II. Persons in the Group I are control and persons in the Group II are non-obese and off-springs of type 2 diabetes mellitus so that insulin resistance is non-significant. In this respect our study does not correlate with Purnamasari D, Soegondo S, Oemardi M et al. who reported that individuals with a family history of diabetes have a higher insulin resistance than individuals without history of diabetes mellitus. They further added that influence of a history of type 2 diabetes mellitus in the father or mother or both at the incidence of insulin resistance cannot be viewed because it is not performed genetic analysis.[14]

We have found non-significant difference in insulin resistance between Group-I and Group-III. As persons in the Group I are control and persons in the Group III are obese, and off-springs of non-diabetic person so that insulin resistance is non-significant. Similar results are obtained by Lillioja S, Bogardus C. They suggest that at maximum plasma insulin concentration there is a significant, negative linear relationship between degree of obesity insulin resistance in males. The relationship between is much weaker at these higher insulin concentrations than at physiologic insulin concentrations.[8]

Ferrannini E, Natali A, Bell P et al found a nonlinear relationship between indices of insulin action and insulin secretion. They have shown that release of insulin secretion is simultaneously affected by insulin resistance and obesity.[15]

We have found significant difference in insulin resistance between Group-I and Group-IV Persons in the Group I are control means non obese as mentioned earlier and persons in the Group IV are obese and off-springs of type 2 diabetes mellitus so that fasting insulin resistance is significant which may be contributed by heredity factor as well as obesity. Thomas CB, Cohen BH. has also observed that obesity has genetic as well as environmental causes. It has a strong effect on the development of type 2 DM (Bjorntorp, 1992; Haffner et al., 1992) as it is found in Western countries (NDDG, 1979; Wilson et al., 1981) and some ethnic groups such as Pima Indians (Joffe et al., 1992; Knowler et al., 1993). Obesity is more than just a risk factor; it has a causal effect in the development of type 2 diabetes. The evolution from obesity to type diabetes mellitus results from a succession of pathophysiological events: (a) Augmentation of the adipose tissue mass, leading to increased lipid oxidation; (b) Insulin resistance noted early in obesity, revealed by euglycemic clamp, as a resistance to insulin mediated glucose storage and oxidation, blocking the function of the glycogen cycle. (c) Despite maintained insulin secretion, unused glycogen prevents further glucose storage leading to type 2 DM; (d) Complete b-c ell exhaustion appears later.[16]

We have found non-significant difference in insulin resistance between Group-II and Group-III. We have found significant difference in insulin resistance between Group-II and Group-IV. Our study results correlate with Lillioja S, Bogardus C. According to them genetic defect and obesity-induced changes in the biophysical properties of skeletal muscle combined knows insulin resistance. Because of this non-insulin-dependent diabetes mellitus develope.[8]

We have found non-significant difference in insulin resistance between Group-III and Group-IV. Guilherme A, Virbasius JV, Puri V suggests progression to type 2 diabetes mellitus occurs more frequently in obese humans compared with lean individuals, this association is highly dependent on genetic background.[17]

6. Conclusion

The purpose of our study was to identify insulin resistance individuals even before appearance of diabetes mellitus in the above groups by HOM-IR method. So that they can be targeted for aggressive lifestyle interventions and subsequent morbidity can be prevented. Serum insulin level and HOMA IR were strongly correlated with each other. Insulin levels were very significantly correlated with obesity and history of type 2 diabetes mellitus. This underlines strong influence of hyperinsulinemia/ insulin resistance on lipid metabolism. Insulin resistance is significantly high in the persons with heredity factors and obesity. Identification of insulin resistance in healthy off-springs of type- 2 diabetes mellitus and obese individuals becomes an important issue from clinical and public health perspective.

7. Source of Funding

None.

8. Conflict of Interest

None.

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