Section: Physiology

Original Research Article

ASSESSMENT OF INSULIN RESISTANCE IN OFFSPRING OF DIABETIC AND NON DIABETIC PARENTS

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ABSTRACT

Background: Insulin resistance is syndrome resulting from reduced insulin activity and is a metabolic defect observed as an early event of genetic origin and it is a primary cause of the subsequent development of type 2 diabetes mellitus. To determine the levels of serum fasting glucose, serum fasting insulin in offspring of Single Diabetic Parent (SDP) group, Both Diabetic Parents (BDP) group and Non Diabetic Parents (NDP) group and to assess the insulin resistance by Homeostatic Model Assessment of Insulin resistance(HOMA-IR) in all participants in the group. **Materials and Methods:** This study was conducted among apparently healthy young adults aged between 18 and 21 years among both the sexes in the Department of Physiology at Madurai Medical College, Madurai and Department of Biochemistry, Madurai Medical College, Madurai for a period of one year. The study participants fulfilling the inclusion and the exclusion criteria were included. The final attained sample is 150. The study participants were divided three groups based on the parental history from medical students of Madurai Medical College, Madurai.After getting informed written consent from the subjects, detailed history was taken. General and Systemic examinations was done. Blood sample was collected. The demographic data were analysed. The data collected will be entered in the MS Excel and statistical analysis done through SPSS 23.P value <0.05 is considered as statistically significant. **Result:** Fasting glucose and fasting insulin level was found to be more in BDP group compared to SDP and NDP and found to be statistically significant. The mean HOMA IR value was found to be more in BDP group 2.62 followed by SDP 1.55 and mean difference was found to be statistically significant. **Conclusion:** The study concluded that insulin resistance is increased in young adults with both diabetic parents compared to offspring of single diabetic parent and offspring of non diabetic parent groups. Therefore it is recommended to assess the insulin resistance at an early stage of life.

INTRODUCTION

Diabetes mellitus is a major pressing public health concern in twenty first century associated with a rapidly growing socioeconomic burden.[1] It is one of the leading cause of mortality and morbidity which increases the overall disease burden.[2] Globally 80% of lower and middle income countries are suffering from it. 529 people were affected by Diabetes in the year 2021.[3]

Among this epidemic of diabetes the prevalence of type 2 diabetes mellitus or NIIDM (Non insulin dependent diabetes mellitus) due to insulin resistance accounts for over 85% of diabetes worldwide, and this incidence depends on different genetic variation, different environmental, dietary habits and various geographic factors in population that has allowed the problem to grow at frightening rate during the past few decades. Genetic factors remains the main cause of Diabetes mellitus throughout the world, sedentary lifestyle and obesity remains the other causes. Promoting physical activity and maintaining ideal body weight as per the WHO guidelines will prevent the progression of the Type 2 DM. This can also be achieved if insulin resistance was diagnosed earlier.[4]

Pathological and etiological factors for Diabetes mellitus have been extensively studied and it is now considered one amongst of the major diseases with multifactorial genetic as well as environmental pattern of inheritance based on familial clustering.

Family history is an important component of genetic background for development of diabetes mellitus. Transmission of genes to the offspring is a significant risk factor for diabetes in the future. A greater

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probability to acquire type 2 diabetes mellitus was seen among offspring of diabetic parents compared to those of non-diabetic parents in Indian population. Offspring of diabetic parents showed an increased risk of diabetes mellitus in western world with an age range of 35-45 year old.

People who develop type 2 diabetes mellitus usually passes through stages of insulin resistance initially, which is characterized by a reduced ability of insulin to stimulate glucose uptake in skeletal muscle, it is also part of a larger constellation of several symptoms called the metabolic syndrome. This stage of insulin resistance often go undiagnosed and unnoticed.

Insulin resistance is a pathological condition in which cells normally fail to respond to insulin hormone. Insulin resistance is syndrome resulting from reduced insulin activity and is a metabolic defect observed as an early event of genetic origin and it is a primary cause of the subsequent development of type 2 diabetes mellitus. Insulin resistance may be traced number of years before onset of diabetes mellitus. Fasting blood glucose and insulin levels during the last two decades have been used for calculating the insulin resistance or sensitivity.[5,6]

In 1985, Matthews et al,[7] First described under the name HOMA-IR (Homeostatic Model Assessment of Insulin Resistance) is a method used to quantify insulin resistance which is simpler, cheaper, less labor-intensive, less time consuming and more acceptable to young people and more practical method for application in large epidemiologic studies.[8]

HOMA-IR is an estimate of insulin resistance derived from fasting glucose and fasting insulin levels, with higher levels representing greater degrees of insulin resistance. Diabetes can cause most extensive damage if left untreated. Diabetes may cause damage to vital organs of the body such as heart, kidneys, eyes and brain. Recent studies have shown that type 2 diabetes can be prevented by changes in lifestyle modifications of high risk subjects. ELLIOT JOSLIN in 1920 identified exercise, along with dietary management had improved the insulin sensitivity.

Early screening for insulin resistance in young age, at least in offspring of diabetic parents becomes necessary so that prompt lifestyle modifications will help to delay the onset of Type 2 Diabetes mellitus. Hence we have undertaken a study to screen insulin resistance in offspring of diabetic parents by (HOMA-IR) Homeostatic Model Assessment Of Insulin Resistance.

Aims and Objectives

- To determine the levels of serum fasting glucose, serum fasting insulin in offspring of Single Diabetic Parent (SDP) group, Both Diabetic Parents (BDP) group and Non Diabetic Parents (NDP) group.
- To assess insulin resistance by Homeostatic Model Assessment of Insulin resistance(HOMA-IR) in all subjects of above mentioned groups. To compare and analyze Insulin resistance between these groups.

MATERIALS AND METHODS

Place of Study: Study was conducted in the Institute of Physiology, Madurai Medical College, Madurai and Department of Biochemistry, Madurai Medical College, Madurai for a period of six months.

Ethical Committee: Approval obtained from the ethical committee of Government Rajaji Hospital, Madurai.

Study Design: Observational case control study

Sample Size: Total subjects - 150(Study population - 100,Controls - 50)

Study Population: Apparently healthy young adults aged between 18 and 21 years, both male and female were included in this study

SDP Group: Offspring of single diabetic parent.

BDP Group: Offspring of both diabetic parents.

Control Group

NDP Group: Offspring of non diabetic parents.

Inclusion criteria:

1. Age between 18 – 21 years.
2. Fasting and postprandial blood sugar within normal limits.
   - Fasting blood sugar <126mg/dl
   - Post prandial blood sugar< 200 mg/dl

EXCLUSION CRITERIA:

1. Obesity (BMI > 25kg/ m2)
2. Polycystic ovarian syndrome,
3. On long term drugs like
   - Steroids,
   - Metformin.
4. H/o systemic diseases like
   - Diabetes mellitus,
   - Endocrinopathies like Cushing's syndrome etc.,
   - Liver disease,
   - Renal disease,
5. Nicotine dependence or alcohol use disorder.
6. Pancreatitis.

Materials Used for Study

1. Proforma – to record the anthropometric measurements and the clinical findings of the subjects.
2. Portable weighing machine – to record the body weight in kilograms.
3. Inch tape – to measure the standing height in centimeters and waist-hip circumference measurements in centimeters.
4. Standardized mercury sphygmomanometer – to record the Blood Pressure in mmHg.
5. Fasting venous blood sample – to estimate fasting blood sugar and fasting insulin levels.

Methodology

The study was initiated after obtaining permission from Dean, Madurai Medical College, Madurai.150 young healthy volunteers aged between 18- 21 years were selected according to the Inclusion and Exclusion Criteria and categorised into three groups

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based on the parental history from medical students of Madurai Medical College, Madurai.

After getting informed written consent from the subjects, detailed history was taken. General and Systemic examinations was done. Blood sample was collected following overnight fasting of 10 hours.

The fasting blood glucose was estimated using GOD-POD method (Glucose oxidase peroxidase method) specific for glucose. ADA guidelines used for blood glucose level. The fasting insulin level was measured through ELISA – Enzyme linked immunosorbent assay method.

Homeostatic Model Assessment of Insulin Resistance

In the late 1970s, Turner and coworkers constructed a mathematical model to predict the interaction of two potential determinants of glycemia in diabetic patients, namely, insulin deficiency and insulin resistance. It was termed the homeostatic model assessment(HOMA).

Homeostasis model assessment was first developed in 1985 by Matthews et al. It is a method used to quantify insulin resistance and beta-cell function from basal (fasting) glucose and insulin (or C-peptide) concentrations. HOMA-IR is a model of the relationship of glucose and insulin dynamics that predicts fasting steady-state glucose and insulin concentrations for a wide range of possible combinations of insulin resistance and β-cell function.

$$\text{HOMA – IR Index} = \frac{\text{Fasting Insulin(mU/ml) x Fasting Plasma glucose(mg/ dl)}}{405}$$

It is a simpler, cheaper, less labor-intensive, less time consuming and more acceptable to young people and more practical method for application in large epidemiologic studies. According to Resources for Gastroenterology and Hepatology Of India, HOMA-IR value,

Less than 2.60 - High insulin sensitivity,

2.60 – 3.80- Borderline,

More than 3.80 - Insulin resistance.

Statistics: Data was entered and analyzed using SPSS (Statistical Package for Social Sciences) software version 16, Mean was compared across all three groups using one way ANOVA (Analysis of Variance), after findings of significance of ANOVA, a multiple comparison between pair of means were made using the Scheffe method of multiple pair wise comparison, a p-value <0.05 was considered as significant as differences in means of two groups. Pearson correlation coefficient test was used to see the correlations among waist hip ratio and HOMA-IR, among all three groups independently, a correlation test p-value <0.05 considered as significant correlation between two parameters.

RESULTS

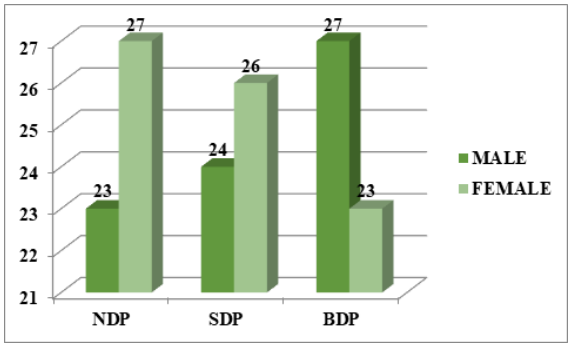

Figure 1: Sex distribution

74 male and 76 female were included in this study. Thus female preponderance was observed in NDP group, SDP group whereas males preponderance observed in BDP group.

Table 1: Fasting Blood sugar and Fasting insulin level

Mean± SD	NDP	SDP	BDP	P value
FBS	74.96±4.89	79.88±5.47	83.54±5.7	0.0001
FIL	5.84±1.56	8.02±1.66	11.81±3.32	0.0001

Fasting glucose was found to be more in BDP group compared to SDP and NDP. Fasting insulin level was more in BDP compared to SDP. Fasting blood sugar and Fasting insulin level was found to be statistically significant.

Table 2: HOMA IR among three groups

Mean± SD	NDP	SDP	BDP	P value
HOMA OR	1.02±0.31	1.55±0.34	2.62±0.82	0.0001

The mean HOMA IR value was found to be more in BDP group 2.62 followed by SDP 1.55 and mean difference was found to be statistically significant.

The Insulin resistance was found in BDP group. Borderline resistance was found more in BDP group 23(46%) followed by 12(24%).SDP Insulin sensitivity was found more in NDP group 48(96%).

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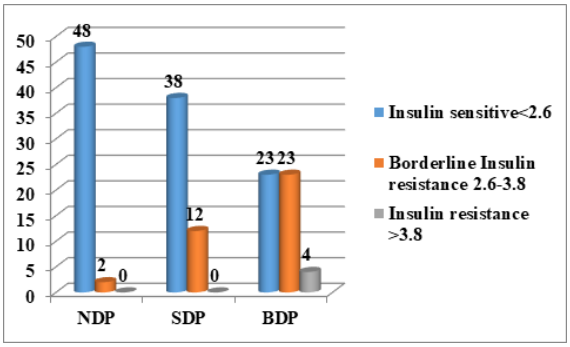

Figure 2: distribution of insulin resistance

Table 3: Anthropometric measurements

Mean± SD	NDP	SDP	BDP	P value
Body mass index	21.66±2.08	22.33±1.91	23.06±1.7	0.0012*
Waist hip ratio	0.86±0.09	0.93±0.14	1.10±0.23	0.0001*

The mean BMI was found to be 23.06 in BDP group which is more than other two group. Waist Hip ratio was also found to be more (1.10) in BDP group compared to other groups (SDP-0.93, NDP-0.86). Body mass index and Waist hip ratio was found to be statistically significant.

Table 4: correlation between waist HIP circumference ratio and homa – IR

Parameter	HOMA – IR	
	r – Value	p – Value
Waist hip circumference ratio	0.773	<0.00001

There was a strong positive linear correlation between Waist hip circumference ratio and Insulin resistance was statistically significant (r value of 0.773 and significant p value of < 0.00001.

Table 5: Sheffe multiple pair wise comparison of physical and biochemical parameters

Parameters	NDPVS SDP p-value	NDPVS BDP p-value	SDPVS BDP p-value
Body weight kg	0.06	0.006	0.65
BMI	0.5	0.005	0.015
Fasting blood glucose (mmol/l)	0.0004	0.0003	0.0017
Fasting Insulin (µU/ml)	0.0008	0.0002	0.0007
HOMA IR	0.0007	0.0001	0.0006
Waist hip circumference ratio	0.172	0.0009	0.0176

It shows that Insulin Resistance as assessed by HOMA-IR was statistically significant ($p<0.05$) in NDP versus BDP and SDP versus BDP. There was also a statistical significant difference values of Fasting blood glucose and Fasting insulin levels between NDP versus BDP and SDP versus BDP groups.

DISCUSSION

In our study NDP group the distribution of number of subjects with borderline insulin resistance were 2, the number of subjects with borderline insulin resistance in SDP group were 12, and in the BDP group the number of subjects with borderline insulin resistance were 23 and 4 subjects have insulin resistance in this group. This shows that insulin resistance is prevalent in BDP group compared to SDP as well as NDP group. The mean age group of this study were 18.06, 18.18 and 18.94 for NDP, SDP and BDP groups respectively. This study also shows a significant number of subjects with insulin resistance at an early age of their life.

Fasting blood sugar values were normal in all the three groups as the mean fasting blood glucose values were 75.6, 80.8 and 83.5 in NDP, SDP and BDP groups respectively. Even though when the fasting blood glucose values are within normal limits, it is higher in BDP group compared to SDP and NDP group and there was significant difference in fasting blood glucose levels in between NDP versus BDP and SDP versus BDP, and the p value is <0.05. The high normal rise in blood glucose levels in BDP and SDP group is probably due to significant increase in insulin resistance.

Mean Insulin resistance assessed by homeostatic model of insulin resistance method (HOMA-IR) for NDP, SDP and BDP groups were 1.05, 1.59 and 2.62 respectively. Even though when the insulin resistance values are within normal limits, it is higher in BDP group compared to SDP and NDP group and there was significant difference in insulin resistance levels in between NDP versus BDP and SDP versus BDP, and the p value is <0.05. The high level of insulin resistance in BDP group compared to SDP and NDP group shows that there is a strong genetic predisposition for occurrence of type 2 diabetes

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mellitus in offspring of both diabetic parents compared to offspring of single diabetic parent. And the offspring of single diabetic parent also has strong genetic predisposition for occurrence of type 2 diabetes mellitus compared to offspring of non diabetic parents.[8]

Similar results were also seen Shobha MV et al,[9] in the year 2013 the waist hip ratio was found more in BDP group compared to other two groups and the insulin resistance was also more in this BDP group compared to SDP and NDP groups. This waist hip ratio strongly correlates with the insulin resistance with r value of 0.77 with significant p value <0.05.

In Meraj Rahim et al,[10] study the mean Fasting insulin levels of NDP, SDP and BDP groups were 5.84, 8.02 and 11.8 respectively. Even though when the fasting insulin values are within normal limits, it is higher in BDP group, high normal in SDP group normal in NDP group and there was significant difference in fasting insulin levels in between NDP versus BDP and SDP versus BDP, and the p value is <0.05. This rise in fasting insulin levels in BDP group is due to increase in insulin resistance and there is an increase in blood glucose level, to compensate this rise in blood glucose level there is a compensatory rise in insulin levels. Thus BDP groups have more insulin levels compared to other two groups and this hyperinsulinemia factor governs insulin resistance.

Shahid et al,[11] found the study found that the offspring of single and both diabetic parents were increased prevalence of certain metabolic risk factors which may trigger or perpetuate the development of diabetes and cardiovascular disorders and also documented that offspring of diabetic parents are associated with increased predicting factors for developing diabetes. The incidence of diabetes mellitus for offspring of non diabetic parent is 10-11%, incidence of diabetes mellitus for offspring of single diabetic parent is 29-30% and incidence of diabetes mellitus for offspring of both diabetic parent is 55-60%.

CONCLUSION

It is found that insulin resistance is increased in young adults with both diabetic parents compared to offspring of single diabetic parent and offspring of non diabetic parent groups. It shows that the offspring of diabetic parents has insulin resistance at an early stage of life. So that the lifestyle modifications are accordingly advised to such individuals to postpone the occurrence of onset of type 2 diabetes mellitus and thereby further complications also prevented.

Therefore it is recommended to assess the insulin resistance at an early stage of life. It is suggested to do insulin resistance screening in person with diabetic parents as they are in high risk to develop diabetic mellitus. Screening can be done by Homeostatic model of assessment of insulin resistance (HOMA – IR) method as it is a simpler, cheaper, less labor-intensive, less time consuming and more acceptable to young people.

Understanding the pathogenesis of the disease will help to identify the better targets of treatment. Early screening for insulin resistance and prompt lifestyle modifications will help to delay the onset of diabetes mellitus. As most of the complications of diabetes mellitus depend on duration of hyperglycemia, early screening to identify insulin resistance and achieving pharmacological targets to reduce insulin resistance, thereby prevents the complication of Diabetes mellitus.

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