

ORIGINAL ARTICLE

Study of Insulin Resistance in Male and Female Diabetics

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ABSTRACT

Objectives: To determine the insulin resistance in diabetic type 2 males and females in the fasting state in the population of Lahore, Pakistan.

Methods: The study group comprised of 122 individuals (49 males and 73 females), who were > 30 years old. Parameters, serum glucose and serum insulin levels were estimated in fasting state and based on those, the insulin resistance indices (IRI) was calculated by HOMA-IR 1 in the total sample population, in males and in females separately.

Results: The study group had increased average levels of serum glucose (10.008 ± 0.326 mmol/L) and insulin resistance indices (5.370 ± 0.396) when compared with the normal adult population. There was no difference based on gender. IRI was significantly different based on groups of W/ht in males. On the other hand, the correlations of all the clinical parameters with their respective serum glucose, serum insulin and IRI were strongly positive ($r > 0.8$) and highly significant (p value < 0.001) irrespective of gender status and parameter type.

Conclusion: The results for anova could mean that the fat distribution only in males is responsible for metabolic derangements; though the results for correlation show no discrimination based on gender.

Key words , hyperglycemia, hyperinsulinemia. insulin resistance ,diabetic type 2

INTRODUCTION

Insulin resistance is the core metabolic abnormality in type 2 diabetes. Its high prevalence and its association with dyslipidemia, hypertension, hyperinsulinemia, and high coronary and cerebrovascular mortality put it in the forefront as the target for intervention. Insulin resistance is a state in which physiologic concentrations of insulin produce a subnormal biologic response.¹ It underlies abnormalities of glucose, lipid, and blood pressure homeostasis.² This cluster of metabolic abnormalities is referred to as the insulin resistance.

Insulin resistance implies that the body's cells lose sensitivity to insulin, . At the molecular level, a cell senses insulin through insulin receptors, with the signal propagating through a cascade of molecules collectively known as signalling pathway. Recent studies suggested that the pathway may operate as a switch under physiologic conditions for certain types of cells, and insulin response may well be a threshold phenomenon.³

When the levels of glucose increase too much, there is enhanced release of insulin because of which, the glucose starts reducing towards its usual levels. On the contrary, reduction of blood

glucose triggers the release of glucagons which acts in a converse manner to raise the glucose towards usual levels. In majority of situations, feedback regulation provided by insulin is more significant than that of glucagons, but when there is food deprivation or one is performing exercise or if there is stress to the body due to various reasons, causing more than normal usage of glucose, the later mechanism is also shown to be beneficial.⁴

Insulin triggers production of glycogen, protein and triglycerides and it inhibits synthesis of glucose by the body and triggering removal of glucose from blood. Also, insulin's operation is peculiar to the tissue, because it is dependent on uniting with its receptor present on the surface of cell. The receptor for insulin consists of two beta chains (which exist throughout the thickness of membrane and two alpha chains (which exist outside the cell). This receptor has innate tyrosine kinase action and when insulin binds to the receptor, a series of reactions in initiated which involve phosphorylation episodes and outcomes related to complete set of DNA within a single cell⁵

Resistance to insulin is an indication of caution that it is difficult for the body to process glucose and it is a feature of a condition in which the blood

sugar is higher than normal but not high enough to cause diabetes. Individuals having resistance to insulin at an early stage or which is at an average level do not complain of anything; though, if no notice is taken, there is likelihood that the conditions such as diabetes mellitus type 2, high blood pressure, increased levels of lipids and cardiac illness develop in them many years later. Hazards for resistance to insulin comprise of gross overweight, in particular in abdomen; close relatives suffering from diabetes mellitus or resistance to insulin, diabetes during pregnancy; condition comprising of menstrual cycles which are not regular, more than normal amount of hair on face or remaining body and egg producing glands which contain multiple cysts⁶

The review of different studies illustrates that how the glucose, insulin and insulin resistance are related to each other and especially how the later develops early in the course of diabetes and what is the value of assessing diabetic patients early (since with increasing duration, the disease progresses) from the point of view of their obesity status as well as other factor such as age, so that the treatment or preventive measures can be targeted at those who are more at risk. More than that, the healthy subjects should be screened keeping in view the risk factors for developing diabetes, so that the condition can be arrested at the stage of prediabetes (which is a metabolic derangement but still cannot be classified as diabetes) for as long as possible. In this regard, other factors which could not be evaluated (such as dietary habits and activity levels of the individuals in addition to compliance with the medication) cannot be overlooked though.^{7,8,9,10}

The current investigation was commenced to determine serum glucose and serum insulin levels during fasting and insulin resistance indices in male and female diabetic subjects in a population of Lahore, Pakistan.

MATERIALS AND METHODS

Study Setting

The individuals from the Lahore city and its suburbs were examined in order to select a representative part of a population for the purpose of determining parameters or characteristics of the whole population. For the matter, JAIDE (Jinnah Hospital and Allama Iqbal Diabetic Education Centre) of Jinnah Hospital Lahore was selected as a place of study. The patients attending the outpatient clinic (JAIDE) were all diabetics (both

males and females) with age above 30 years. They were assessed on the whole (without being categorized into subgroups) for serum glucose levels in mmol/L and serum insulin levels in mIU/L (both during fasting) and insulin resistance index (IRI); later is determined by a HOMA-IR (Homeostasis model assessment for insulin resistance) formula in which the product of serum glucose and serum insulin (levels during fasting) is divided by 22.5 and thus gives the estimated value.

Blood Sample Handling

5 ml quantity of blood was obtained with sterile disposable syringes and was then allowed to clot. The serum was separated from blood after being centrifuged. The clear serum was collected in a 1.5 ml vial and stored in a freezer at -20 degree centigrade to be analysed later for serum insulin; though, the estimation of glucose was done right after.

RESULTS

Fasting Glycemia, Insulin and Insulin resistance indices (IRI) had been studied in a sample population of Type 2 DM. It included 122 subjects, out of which 49 were males and 73 were females. Fasting Glycemia, Fasting Insulin concentration in serum and IRI were analyzed in all subjects (overall) and then for different parameters like gender (male and females separately) as well as groups of other parameters like Age, Duration of Diabetes.

The average values for serum glucose (fasting), serum insulin (fasting) and insulin resistance indices (IRI) in the whole sample population (122 subjects) were 10.008 ± 0.326 mmol/L, 12.120 ± 0.694 μ IU/ml, and 5.370 ± 0.396 respectively.

The average values for serum glucose (fasting), serum insulin (fasting) and insulin resistance indices (IRI) in male subjects (49 in total) were found to be 10.546 ± 0.546 mmol/L, 11.18 ± 1.20 μ IU.mL and 5.414 ± 0.748 respectively. Independent t test was run to see whether there are any significant differences or not in the average values of serum glucose (fasting) levels, serum insulin (fasting) levels and insulin resistance indices (IRI) based on gender; it was found out that there were no significant differences in the average values of any of these parameters (P-Value = 0.286), (P-Value = 0.186) and (P-Value = 0.933) respectively.

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The average values for serum glucose (fasting), serum insulin (fasting), and insulin resistance indices (IRI) in males according to the status of their age were 9.694 ± 0.678 mmol/L, 5.616 ± 0.733 μ IU/mL and 2.424 ± 0.406 respectively for the first group of age; respective values for the second group were 11.554 ± 0.934 mmol/L, 12.49 ± 2.33 μ IU/mL and 6.46 ± 1.37 and

lastly, the third group had average values of 10.174 ± 0.842 mmol/L, 12.13 ± 1.70 μ IU/mL and 5.70 ± 1.13 respectively.

In all the age groups, the average values in males were not significantly different from each other for the serum glucose (fasting), serum insulin (fasting) and insulin resistance indices (IRI); p values were 0.418, 0.119 and 0.192 respectively.

Table 1: Serum glucose levels, serum insulin levels and insulin resistance indices (IRI) in the fasting subjects (males) with type 2 diabetes mellitus.

Age groups (ranges in years in males)	Number of subjects	Parameters values (means \pm S.E.M)		
		Serum glucose levels mmol/L	Serum insulin levels μ IU/mL	Insulin resistance indices (IRI)
1 st (34 to 50)	8	9.694 ± 0.678	5.616 ± 0.733	2.424 ± 0.406
2 nd (51 to 59)	16	11.554 ± 0.934	12.49 ± 2.33	6.46 ± 1.37
3 rd (61 to 79)	25	10.174 ± 0.842	12.13 ± 1.70	5.70 ± 1.13
P value		0.418	0.119	0.192

The average values for serum glucose (fasting), serum insulin (fasting) and insulin resistance indices (IRI) in females according to the status of their age were 9.85 ± 1.03 mmol/L, 12.68 ± 1.65 μ IU/mL and 5.41 ± 1.04 for the first group of age; for these parameters, the second group of age had average values as 9.432 ± 0.52 mmol/L, 14.16 ± 1.28 μ IU/mL and 5.924 ± 0.643

respectively; in the third group. Average values were 9.880 ± 0.815 mmol/L, 10.42 ± 1.31 μ IU/mL and 4.316 ± 0.682 respectively.

In all the age groups, the average values were not significantly different from each other for the serum glucose (fasting), serum insulin (fasting) and insulin resistance indices (IRI); (P values were 0.868, 0.151 and 0.279).

Table 2: Serum glucose levels, serum insulin levels and insulin resistance indices (IRI) in (females with type 2 diabetes mellitus)

Age groups (ranges in years in females)	Number of subjects	Parameters values (means \pm S.E.M)		
		Serum glucose levels mmol/L	Serum insulin levels μ IU/mL	Insulin resistance indices (IRI)
1 st (35 to 45)	14	9.85 ± 1.03	12.68 ± 1.65	5.410 ± 1.04
2 nd (46 to 59)	37	9.432 ± 0.520	14.16 ± 1.28	5.924 ± 0.643
3 rd (60 to 74)	22	9.880 ± 0.815	10.42 ± 1.31	4.316 ± 0.682
P value		0.868	0.151	0.279

The average values for serum glucose (fasting). Serum insulin (fasting) and insulin resistance indices (IRI) in males according to the duration of diabetes were 9.931 ± 0.640 mmol/L, 7.99 ± 1.61 μ IU/mL and 3.288 ± 0.667 for the first group; average values were 10.099 ± 0.917 mmol/L, 11.32 ± 1.64 μ IU/mL and 4.990 ± 0.818 for the second group. Lastly, for the third group, the average values were 11.61 ± 1.07 mmol/L, 13.61 ± 2.67 μ IU/mL and 7.67 ± 1.8 respectively.

serum insulin (fasting) and IRI (the p values were 0.200, 0.398 and 0.070 respectively).

The average values for serum glucose (fasting), serum insulin (fasting) and insulin resistance indices (IRI) in females according to the duration of diabetes were 9.965 ± 0.692 mmol/L, 11.23 ± 1.07 μ IU/mL and 4.883 ± 0.669 respectively for the first group; average values for the second group were 9.717 ± 0.667 mmol/L, 15.33 ± 1.53 μ IU/mL and 6.377 ± 0.774 respectively; lastly, for the third group, the average values were 9.179 ± 0.780 mmol/L, 11.25 ± 1.58 μ IU/mL and 4.553 ± 0.791 respectively.

In all the duration of diabetes groups in males, the average values were not significantly different from each other for the serum glucose (fasting),

In all the duration of diabetes groups in females, the average values were not significantly different from each other for the serum glucose

(fasting), serum insulin (fasting) and IRI (p Values were 0.744, 0.059 and 0.183 respectively)

Table 3: Serum glucose levels, serum insulin levels and insulin resistance indices (IRI) in (males) with type 2 diabetes mellitus.

Duration groups (ranges in years since diabetes was diagnosed in males)	Number of subjects	Parameters values (means ± S.E.M)		
		Serum glucose levels mmol/L	Serum insulin levels μ IU/mL	Insulin resistance indices (IRI)
1 st (1 to 9)	13	9.931 ± 0.640	7.99 ± 1.61	3.288 ± 0.667
2 nd (10 to 15)	20	10.099 ± 0.917	11.32 ± 1.64	4.990 ± 0.818
3 rd (16 to 35)	16	11.61 ± 1.07	13.61 ± 2.67	7.67 ± 1.88
P value		0.200	0.398	0.070

Table 4: Serum glucose levels, serum insulin levels and insulin resistance indices (IRI) in the (females) with type 2 diabetes mellitus.

Duration groups (ranges in years since diabetes was diagnosed in females)	Number of subjects	Parameters values (means ± S.E.M)		
		Serum glucose levels mmol/L	Serum insulin levels μ IU/mL	Insulin resistance indices (IRI)
1 st (0.16 to 9)	25	9.965 ± 0.692	11.23 ± 1.07	4.883 ± 0.669
2 nd (10 to 18)	27	9.717 ± 0.667	15.33 ± 1.53	6.377 ± 0.774
3 rd (19 to 32)	21	9.179 ± 0.780	11.25 ± 1.58	4.553 ± 0.791
P value		0.744	0.059	0.183

The average values for serum glucose (fasting), serum insulin (fasting) and insulin resistance indices (IRI) in males according to body mass indices (BMI) were 12.13 ± 1.50 mmol/L, 13.81 ± 3.60 μ IU/mL and 8.15 ± 2.56 respectively for the first group; for the second group, the average values were 10.715 ± 0.669 mmol/L, 9.20 ± 1.15 μ IU/mL and 4.373 ± 0.635 respectively; lastly for the third group, the average values were 8.849 ± 0.909 mmol/L, 13.45 ± 2.81 μ IU/mL and 5.47 ± 1.60 respectively.

In all the BMI groups in males, the average values were not significantly different from each other for the serum glucose (fasting), serum insulin (fasting) and IRI (p values were 0.120, 0.187 and 0.150 respectively).

DISCUSSION

This study could not find any significant differences of means between males and females for overall IRI (insulin resistance index). In other words, the insulin resistance is of the same level in both the sexes. But the thing is that, there is an appreciable difference in the number of males and females and if we had few more males in our study having relatively more insulin resistance indices, and

whose values after being added to the remaining sample might have made

The mean IRI significantly more than their female counterparts, and that way we would have supported the results of other studies which concluded that males are more insulin resistant than females. In fact, due to the deficiency of estrogens in males, they are possibly more insulin resistant than females though as we see later (while comparing our results with those of other studies) that we have to take into account the effect of other factors like age of the subjects, their hormonal status (males and females already have different hormones in different proportions and the differences in insulin resistance due to different gender can be attributed to that; though, the insulin resistance can vary depending on the extent to which these levels change in different conditions), and not only this, the distribution of fat stores is different in both sexes. The quantity of fat in abdominal viscera and liver is more in males^{11 12}

The normal range of serum fasting glucose in type 2 diabetics is 4 to 7 mmol/L (and same range is the target range as well for diabetics); this should be contrasted from value of 7 mmol/L and above which is required for the diagnosis of diabetes to be established; whereas, in our already diagnosed study population (overall, comprising of

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122 males and females altogether), the average values were found to be 10.008 ± 0.326 mmol/L, which is much higher than it should be for the normal adult population. It could be due to various reasons such as over consumption of food, especially carbohydrates, non compliance with the medication (people sometimes tend to skip their medication because of non availability, especially of insulin (most of the patient attending the diabetic clinic in Jinnah Hospital, Lahore belonged to poor socioeconomic background and they could not get the regular supply of medications); even if the medications are available, they do not take the medications in proper dosage or on proper time. They are either unable to check their blood sugar levels or they have to skip their meals either because the food is not available or they are suffering from nausea or vomiting, lack of activity (a lot of patients usually have been diagnosed with diabetes for a number of years; so complications like hypertension, ischemic heart disease and chronic kidney disease etc develop in these patients and sometimes one or more of these complications are at an advanced stage, therefore the individuals suffering from those are either too ill to pursue an active lifestyle, they are unemployed, are doing sedentary jobs or make it a habit because of lack of awareness about the lifestyle modifications expected of them during their illness).¹³ The IRI (insulin resistance index) cut off was ≥ 2 (though it varies from population to population); in our study population, it was found to be 5.370 ± 0.396 ; in males separately, it was 5.414 ± 0.748 and in females, it was 5.341 ± 0.436 . These results show that our population is more insulin resistant than the reference value for IRI (≥ 2) As mentioned before, one reason could be increased levels of serum glucose in our population (since IRI depends on the serum glucose as well as serum insulin levels); though other factors need to be considered as well as we see later in the discussion. Another factor responsible for different results may be the different metabolic trait of our population (which along with other factors elsewhere could be responsible¹⁴

In the study, the results for differences in serum insulin and serum glucose based on gender were not significant as well. In another investigation done previously, a total of 516 individuals were finally included in the study and their samples were collected for fasting blood glucose, total cholesterol, and triglycerides.

Different age groups had dissimilar means. The dissimilarities in the average values for fasting serum glucose between different age groups were seen to increase from 21-30 years age group [5.01 (95%CI:4.77-5.23)mmol/L] to higher values [6.25 (95%CI: 5.63-6.87)mmol/L] in subjects who were between 50 and 60 years old; although in later years, the average levels of fasting serum glucose were found to be relatively less [$P < 0.001$]. Being a male or female could not make any significant difference to serum glucose levels among the different groups. The correlation between age and fasting blood glucose was weak positive⁷

CONCLUSION

The results for anova (for W/H and W/ht) could mean that the fat distribution only in males is responsible for metabolic derangements; though the results for correlation show no discrimination based on gender as well as the parameter being tested

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