

Insulin Resistance Syndrome in Type - 2 Diabetes Mellitus Patients

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Objective: To find out the presence or absence of insulin resistance syndrome (IRS) in type-2 diabetes mellitus patients.

Material & Methods: The study included 55 T2DM patients (34 male & 21 female), who were already taking oral anti diabetic drugs for the last 3 – 5 years. Obesity or weight gain in T2DM patients aggravates metabolic disturbances along with increased insulin resistance. The five variables in T2DM patients were studied as per recommendations of the United States National Cholesterol Education Program Adult Treatment Panel-III (ATP-III), to find out the presence or absence of insulin resistance syndrome (IRS) in T2DM patients. The T2DM patients who had shown the presence of three or more variables out of five were considered to have IRS.

Results: 32 (58.18%) T2DM patients (20 male & 12 female) had IRS. The T2DM patients with IRS had significant ($p < 0.001$) increase in mean blood glucose levels, waist circumference, triglyceride levels and in systolic and diastolic blood pressure. The mean HDL Cholesterol was significantly ($p < 0.001$) decreased in T2DM patients with IRS as compared to T2DM patients without IRS.

Conclusion: An increase in waist circumference in T2DM patients will increase the prevalence of insulin resistance syndrome.

Keywords: Type 2 diabetes mellitus (T2DM), Insulin Resistance Syndrome (IRS), Fasting Plasma Glucose (FPG), Blood Pressure (BP), Obesity.

Introduction

Obesity or weight gain in T2DM patients aggravates metabolic disturbances along with increased insulin resistance.¹ Insulin resistance is the decreased biological response of insulin, endogenous or exogenous to suppress hepatic glucose production and to enhance glucose clearance principally into skeletal muscles in T2DM patients.² The clustering of insulin resistance with hyperglycemia, dyslipidemia, hypertension and overall obesity is called Insulin Resistance Syndrome or Metabolic Syndrome.³ Insulin resistance is more common in overweight individuals and is associated with increased risk for T2DM and CVD.⁴

The United States National Cholesterol Education Program Adult Treatment Panel-III (ATP-III) report recommends the use of 5 variables for the clinical diagnosis of the insulin resistance syndrome which includes:⁵

1. Waist circumference
2. Fasting Plasma Glucose level
3. HDL-cholesterol level
4. Serum Triglyceride level
5. Blood Pressure

T2DM patients meeting 3 of the above 5 variables were classified as having insulin resistance syndrome.⁵

The peripheral resistance to the action of insulin is often very marked in obese T2DM patients and blood glucose control in these patients is achieved at the expense of severe hyperinsulinemia.⁶ The characteristic lipid disorders in subjects having insulin resistance were, elevated triglyceride levels, low HDL-Chol, while total & LDL-Chol were raised to a lesser extent.^{1,7} Increased physical activity & life style modification in T2DM patients with insulin resistance syndrome showed a marked improvement in glycaemic control and decreased risk for future development of CVD and other complications of T2DM.^{2,8}

Material and Methods

Fifty Five T2DM patients aged between 30-60 years from both sexes were included in the study to evaluate for 5 variables for the diagnosis of the insulin resistance syndrome.

A-Physical Measurements:

1. Waist circumference was the inclusion criteria for obese T2DM patients, measured in centimeters.⁹
2. Blood pressure was recorded with mercury column type BP apparatus in mmHg.

B-Biochemical Analysis:

After 10 to 12 hours overnight fast a 4ml sample of

venous blood was taken and analyzed for the following:

1. FPG by hexokinase method^{6,10}
2. Triglyceride levels were determined after enzymatic hydrolysis with lipases.^{6,11}
3. HDL-cholesterol was measured by treating the sample with phosphotungstic acid in the presence of magnesium ions, to precipitate the LDL, VLDL & chylomicrons and after centrifugation the cholesterol concentration in the HDL fraction was measured in supernatant.^{6,12}

The data was analyzed statistically by evaluating the mean, standard deviation, and using the student's t test.

Results

The study included 34 male and 21 female T2DM patients (n=55) and subjects meeting 3 or more out of 5 studied variables were said to have IRS, when evaluated as following.⁵

1. Waist circumference
 - > 80 cms (Female)
 - > 90 cms (Male)
2. Fasting plasma glucose level (FPG)
 - > 110 mg/dL (Male/Female)
3. HDL- Cholesterol Levels
 - < 50 mg/dL(1.3 mmol/L) Female
 - < 39 mg/dL(1.0 mmol/L) Male
4. Blood Pressure levels

> 130/85 mmHg (Male/Female)

5. Serum Triglyceride levels

> 150 mg/dL (1.7 mmol/L) (Male/Female)

Thirty two (58.18%) T2DM patients (20 male and 12 female) were having three or more variables positive and hence showed that they had IRS. 23 (41.82%) T2DM patients (14 male and 9 female) had either one or two variables positive and hence showed no IRS (**Table-1**).

Table-1: The number of T2DM patients with/ or without Insulin Resistance Syndrome.

Number of Patients	T2DM with IRS	T2DM without IRS
Male (n=34)	20	14
Female (n=21)	12	09
Total (n=55)	32	23

The T2DM patients with IRS had significantly ($p < 0.001$) higher waist circumference, FPG, Triglycerides, systolic & diastolic BP levels as compared to T2DM patients without IRS (Table-2). The HDL-Chol levels in T2DM patients with IRS were significantly ($p < 0.001$) low as compared to T2DM patients without IRS (**Table-2**).

It was seen that 11 T2DM patients (7 male & 4 female) with IRS had all the five variables present (34.37%) whereas 21 T2DM patients (13 male & 8 female) with IRS had three variables present (65.63%).

Table-2: Different variables in T2DM patients with and without IRS (Mean \pm SD is given).

Sr. No.	Variables in T2DM (n=35)	T2DM with IRS (n=32)	T2DM without IRS (n=32)
1	Waist Circumference (cm)	97.94 \pm 9.65	73.29 \pm 5.52
2	Fasting plasma glucose (mg/dl)	133.43 \pm 12.54	97.86 \pm 9.39
3	HDL-Chol (mg/dl)	37.75 \pm 5.19	47.08 \pm .24
4	Triglycerides (mg/dl)	190.09 \pm 30.92	139.21 \pm 6.92
5	BP (mmHg)	Systolic	138.59 \pm 7.85
		Diastolic	92.96 \pm 3.78
			120.65 \pm 9.20
			76.52 \pm 6.29

Discussion

If T2DM patients are obese or are over weight, the chances of insulin resistance and metabolic disturbances are much increased.¹³ The peripheral resistance to the action of insulin is often very marked in obese T2DM patients.⁶ Weight gain in T2DM patients above normal causes aggravation of metabolic disturbances, like insulin resistance, dyslipidemia and hypertension.³ The prevalence of IRS is more in obese T2DM patients as compared to non-obese T2DM patients.¹⁴ When diabetes, hypertension or family history of these diseases is present, treatment will be more beneficial when a

lesser degree of obesity is present in these patients.¹⁵

It has been noted that obesity in T2DM patients will have more cardiovascular risk factors with high blood pressure, dyslipidemia (increased triglycerides & decreased HDL-Chol) and hyperglycemia.^{1,15,16}

Prevalence of IRS in male T2DM patients was higher i.e. 62.50% as compared to IRS in female T2DM patients i.e. 37.50% and similar findings have been observed in earlier studies carried out by various workers.^{5,17,18}

It has also been reported that the prevalence of IRS increases with increasing age of T2DM patients.^{5,18,19} Insulin sensitivity has been reported to be improved with weight loss in obese

T2DM patients and a better glycaemic control is achieved with a routine treatment for the disease and less incidence of future complications in these patients.^{2,13,19}

Conclusion

Increasing waist circumference in T2DM patients will increase the prevalence of insulin resistance

syndrome/metabolic syndrome and is more common in men.

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References

1. Davidson MB. Clinical implication of insulin resistance syndromes. *Am J Med* 1995; 99: 420-6.
2. Walker M. Obesity, insulin resistance and its link to non-insulin dependent diabetes mellitus. *Metabolism* 1995; 44(9) suppl3: 18-20.
3. Ali N, Afzal N, Ahmad MZ, Shahjahan S, Shaikh AS. Obesity Indices and lipid levels in healthy relatives of Type 2 Diabetes Mellitus patients. *Pak Post graduate Med J* 2003; 14(4): 189-93.
4. Edelman SV. Type II diabetes mellitus. *Adv Intern Med* 1998; 43: 449-500.
5. Tam CE, Ma S, Wai D, Chen SK, Tai ES. Can we apply the National Cholesterol Education Program Adult Treatment Panel definition of the metabolic syndrome to Asians? *Diabetes Care* 2004; 27(5):1182-86.
6. Ali N, Afzal N, Shahjahan S, Ahmad MZ, Baseer A. A study of insulin resistance in obese and non-obese healthy FDRs of T2DM patients. *Pak Post graduate Med J* 2004; 15(2): 81-92.
7. Modan M, Halkin H, Lusky A, Segal P, Fuchs Z, Chetrit A. Hyperinsulinemia is characterized by jointly disturbed plasma VLDL, LDL and HDL levels. *Arteriosclerosis* 1988; 8: 227-36.
8. Sowers JR. Obesity and cardiovascular disease. *Clin Chem* 1998; 44 (8): 1821-5.
9. Lapidus L, Bengtsson C, Larsson B, Pennert K, Rybo E, Sjostrom L. Distribution of adipose tissue and risk of cardiovascular disease and death: a 12 year follow up of participants in the population study of women in Gothenberg Sweden. *Br Med J* 1984; 289: 1257-61.
10. Meilling GE. A kinetic method for glucose that is insensitive to variations in temperature and enzyme activity. *Clin Chem* 1979; 22:1581.
11. Fossati P, Prencipe L. Serum triglycerides determined calorimetrically with an enzyme that produces hydrogen peroxide. *Clin Chem* 1982; 28: 2077-80.
12. Burstein M, Scholnick HR, Morfin R. Rapid method for the isolation of lipoproteins from human serum by precipitation with polyanions. *J Lipid Res* 1970; 11: 583-95.
13. Masud F, Hasan M, Abaidullah S, Alam I. Assessment of metabolic profile and body mass index (BMI) in type II diabetics treated with metformin and insulin. *Pak J Med Sci* 1992; 9 (1): 29-34.
14. Maegawa H, Kashiwagi A, Shigeta Y. Obesity as a risk factor for developing non-insulin dependent diabetes mellitus. Obesity and insulin resistance. *Nippon Naibumpi Gakkai Zasshi* 1995; 71 (2): 97-104.
15. Caro JF. Insulin resistance in obese and non-obese men. *J Clin End Met* 1991; 73 (4): 691-95.
16. Ferrannini E. Insulin resistance versus insulin deficiency in non-insulin dependent diabetes mellitus: problems and prospects. *Endocr Rev* 1998; 19 (4): 477-90.
17. Ezenwaka CE, Nwagbara E, Seales D, Okali F, Hussaini S, Raja B et al. A comparative study of the prevalence of the metabolic syndrome and its components in type 2 diabetic patients in two Caribbean islands using the new International Diabetes Federation definition. *Arch Physiol Biochem* 2007; 113: 1-9.
18. Funahashi T, Matsuzawa Y. Metabolic syndrome: clinical concepts and molecular basis. *Ann Med* 2007; Jul 20: 1-13.
19. Haffner SM, Stern MP, Hazuda HP, Pugh JA, Patterson JK. Hyperinsulinemia in a population at high risk for non-insulin dependent diabetes mellitus. *N Eng J Med* 1986; 315: 202-4.