Insulin Resistance, a surrogate marker, in type 2 Diabetes Mellitus

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Abstract— Type 2 diabetes mellitus (T2DM) is an insulin resistant state associated with accelerated atherosclerosis, hypertension, dyslipidemia and abnormal vasomotor responses to insulin. One hundred and thirty nine T2DM patients were included in this study. Out of the total 139 patients, 120 (86.33%) had hyper-insulinemia. According to the NCEP-ATP III criteria, the prevalence of IRS was 103 (74.1%) among the total patients. But, among the hyper-insulinemic group alone, 79.15% had IRS. There is lesser prevalence of diabetes in the 7th decade and beyond. The results showed that WHR has better correlation with IRS than the BMI. The control of diabetes was poor among nearly 2/3rd of the patients. 1/5th of males and 1/3rd of females had CAD. 67.21% of males and 71.19% of females had hypertension. 50% had positive family history of diabetes among 1st degree relatives. The lipid abnormalities were of lesser classical nature. More number of patients had abnormal LDL levels than having TGL or HDL abnormalities. 52.1% of males and 55% females had statistically significant lower calcium levels, whereas the uric acid levels were normal in more than 90%. The study also showed that the fasting insulin level is higher (90.4μU/ml for males and 72.3 μU/ml for females) and that it correlates well with the degree of insulin resistance. It may therefore be necessary to measure insulin level along with blood glucose and lipids in type 2 diabetes mellitus.

Index Terms— Diabetes Mellitus, Insulin Resistance, Insulinemia, Insulin..

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1 INTRODUCTION

Type 2 diabetes mellitus (T2DM) is an insulin resistant state associated with accelerated atherosclerosis, hypertension, dyslipidemia and abnormal vasomotor responses to insulin.[1] Insulin resistance is a hallmark of type 2diabetes that precede and predict the disease for several years.[2],[3] About 80-90% of all type diabetes coexists with insulin resistance which usually also precedes the first symptoms of the disease.[4],[5] The prevalence of the insulin resistance syndrome has varied markedly between different studies, most likely because of the lack of accepted criteria for the definition of the syndrome.[6] There is abundant evidence that insulin resistance is a treatable precursor of type 2diabetes and perhaps of cardiovascular disease as well.[2],[7] Risk factors for Type 2 diabetes and atherosclerotic vascular disease such as insulin resistance, dyslipidemia, and hypertension cluster together in affected individuals.[8] Insulin resistance is a common pathologic state in which target cells fail to respond to ordinary levels of circulating insulin. It is frequently associated with a number of diseases, including chronic infection, human obesity, and type 2diabetes. Though insulin resistance could also be due to a defect in the binding of insulin to the receptor, it is mostly attributed to a post-binding defect in the hormone actions. In non-diabetic as well as diabetic subjects, insulin resistance is related to several cardiovascular risk factors, including hyperglycemia, dyslipidemia, hypertension, thrombophilia.[9],[10]

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2 MATERIALS AND METHODS

The patients for this study were drawn from the diabetic outpatient department at District Hospital, Manjeri, Malappuram, Kerala. They are screened for the presence of diabetes by checking the fasting and the post-prandial blood sugar levels according to the American Diabetes Association's new criteria for the diagnosis of diabetes mellitus.[11] Patients who were on insulin, other types of diabetes like Fibro-Calcific Pancreatic Diabetes (FCPD), Type-1DM (Insulin Dependent Diabetes Mellitus), Secondary Diabetes, Drug induced Diabetes, Gestational Diabetes Mellitus (GDM) and patients with fasting blood sugar >300mg/dl were excluded from the study. After a run-in period of 3 months and a further 2 months for screening for eligibility for inclusion in the study out of a total of 723 patients, 103 were selected for the final study. These patients who were not treated with insulin are further screened for the presence of hyper-insulinemia by measuring the blood level of fasting insulin concentration. Samples for the fasting blood Glucose, Lipids, Uric Acid, Calcium and fasting insulin levels were collected after at least 8 hours of overnight fasting. . Before enrolling the patients for this study a consent letter was signed by each patient after explaining the details of the study to them. The Ethics Committee of the institution approved this project.

The Insulin resistance syndrome was diagnosed according to the NCEP ATP III definition.[12] A participant was deemed to have the syndrome when three or more of the following criteria were satisfied (Table 1)

Table 1. Criteria for selection as insulin resistance syndrome

1) Waist circumference >102 cm in men and >88 cm in women
2) Triglyceride level >150mg/dL;
3) HDL cholesterol < 40mg/dL in men and < 50mg/dL in women
4) Blood pressure >130/85 mmHg or known treatment for hypertension
5) Fasting glucose level of > 110mg/dL or a known diabetic

HDL: High density lipoprotein

Since all participants in the study are already diagnosed as diabetics, only any two of the other 4 items (items 1 to 4) need to be positive to diagnose the presence of the syndrome.

Table 2. Mean values and Statistical significance of different parameters in diabetes with IR.

| Parameters	Male: N=61 Mean	Female: N=59 Mean	T TEST Significance P VALUE		
			Male v/s Female)	Male v/s Normal Value	Female v/s Normal Value
FBS	158.08	155.27	0.784	NV=<126, P=0.001‡	NV=<126. P= 0.001‡
PPBS	235.21	230.50	0.715	NV=<140, P=0.001‡	NV=<140, P=<0.001‡
F.Insulin	92.10	72.28	0.056	NV=<30, P=<0.001‡	NV=<30, P=<0.001‡
Chol	195.92	206.47	0.144	NV=<200, P=0.4581	NV=<200, P=0.1669
TGL	153.42	149.03	0.777	NV=<150, P= 0.741	NV=<150, P=0.933
HDL-C	47.95	53.34	0.044‡	NV=>40, P=<0.001‡	NV=>50, P=0.0889
LDL-C	117.49	126	0.180	NV=100, P=<0.001‡	NV=100, P=<0.001‡
UA	6.11	5.55	0.718	NR	
Ca	8.13	8.14	0.954	NV=8.5-10.5, P=< 0.001‡	NV=8.5-10.5, P= 0.005‡

FBS: Fasting Blood Glucose in mg/dL, PPBS: Post prandial Blood Glucose in mg/dL, F.Insulin: Fasting Insulin in mU/ml, Chol: Total Cholesterol in mg/dL, TGL: Triglycerides in mg/dL, HDL-C: High Density Lipoprotein Cholesterol in mg/dL, LDL-C: Low Density Lipoprotein Cholesterol in mg/dL, UA: Uric acid in mg/dL, Ca: Calcium in mg/dl NV: Normal Value, ‡ Significant

The results of the present study are given in the table 2. The mean serum fasting insulin levels are higher in this study population than many other groups, indicating that we suffer from more insulin resistance than others. This study population has both high prevalence of insulin resistance and higher levels of fasting insulin levels. The diabetic dyslipidemia in the study population is of a lesser classical nature with the serum triglyceride levels lower than many others. Likewise, HDL levels are also found to be abnormal in only around 50% of the diabetics studied, where as the LDL cholesterol abnormalities were observed in a greater proportion (¾ to ⁴/₅). It is observed that serum TGL was elevated and HDL cholesterol values were decreased. Low mean serum calcium levels among the diabetics, predominantly among male diabetics and especially in the poorly controlled group, was observed. Mean serum calcium levels among the diabetics, predominantly among male diabetics and especially in the poorly controlled group, was observed.

Several longitudinal studies of initially non diabetic individuals have also found fasting hyper insulinemia to be predictive of future cardiovascular events.[13] In the presnt study 86.33%, (120 of the total 139) patients had hyper insulinemia. Equating hyper insulinemia with insulin resistance as done in many other studies, gives us an estimate of insulin resistance among our T2DM patients, meaning that 86.33% of the total diabetics studied have insulin resistance which is similar to the findings of Steven et al.[14] The TGL value was significantly higher in the western studies, compared to to the present study. Few studies which reported such higher values are Sangeetha et al.,[15] and Nystrom et al.,[16] Low HDL cholesterol levels are often accompanied by elevated triglyceride levels and the combination has been strongly associated with an increased risk of CHD. Elevated TGL reported from other geographical areas.

Figure 1: Mean values of different parameters in diabetes with IR.
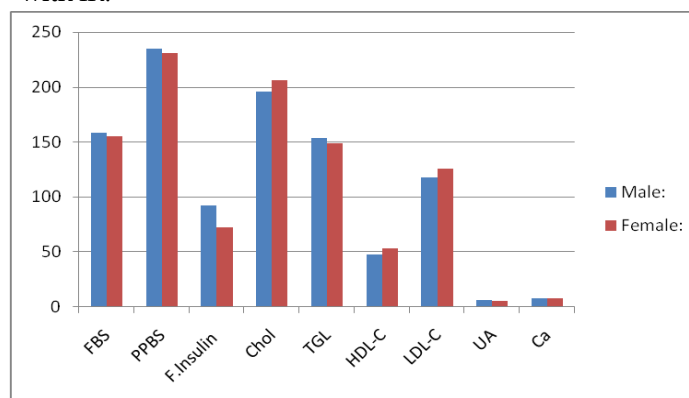
FBS: Fasting Blood Glucose in mg/dL, PPBS: Post prandial Blood Glucose in mg/dL, F.Insulin: Fasting Insulin in mU/ml, Chol: Total Cholesterol in mg/dL, TGL: Triglycerides in mg/dL, HDL-C: High Density Lipoprotein Cholesterol in mg/dL, LDL-C: Low Density Lipoprotein Cholesterol in mg/dL, UA: Uric acid in mg/dL, Ca: Calcium in mg/dl

The cause of hypocalcaemia detected in the present study, need further evaluation. It could either be due to intracellular deficiency of Mg2+[17] or probably due to the abnormal functioning of one of the least attended counter-regulatory hormones called PTH (parathormone) secondary to insulin resistance. From the study it can be concluded that IR is the cause of the biochemical alterations and the leading cause of secondary complications in T2DM.

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