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Study of Insulin Resistance in Nondiabetic First Degree Relatives of Patients with Type II Diabetes Mellitus.

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ABSTRACT

First-degree relatives (FDRs) of patients with type II diabetes mellitus (T2DM) are genetically predisposed to develop insulin resistance, a precursor to diabetes. Early identification of insulin resistance in this group may facilitate preventive interventions. To assess the degree of insulin resistance in nondiabetic FDRs of T2DM patients and compare it to individuals without a family history of diabetes. This cross-sectional study included 50 nondiabetic FDRs and 50 age- and sex-matched controls. Fasting plasma glucose and serum insulin levels were measured, and insulin resistance was estimated using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR). Anthropometric data were recorded. Statistical analysis was performed to compare groups. FDRs exhibited significantly higher BMI, waist-hip ratio, fasting glucose, fasting insulin, and HOMA-IR values compared to controls ($p<0.05$). Insulin resistance (HOMA-IR >2.5) was present in 62% of FDRs versus 28% of controls. Higher BMI strongly correlated with increased insulin resistance. Nondiabetic FDRs of T2DM patients demonstrate a higher prevalence of insulin resistance. Early screening and lifestyle interventions in this high-risk group may delay or prevent diabetes onset.

Keywords: Insulin resistance, first-degree relatives, type II diabetes mellitus.

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INTRODUCTION

Type II Diabetes Mellitus (T2DM) is a chronic metabolic disorder marked by insulin resistance and impaired insulin secretion [1]. The disease has a strong genetic predisposition, with first-degree relatives (FDRs) of T2DM patients being at significantly higher risk of developing the disease. Studies suggest that insulin resistance may manifest in these individuals even before overt hyperglycemia appears, making it a valuable marker for early risk stratification and preventive interventions. Given the rising global and national burden of T2DM, especially in genetically predisposed populations such as Indians, it becomes imperative to identify and manage high-risk groups. Early detection of insulin resistance among FDRs can help implement lifestyle modifications to delay or prevent the onset of diabetes [2-4]. Despite the known familial association, data on insulin resistance among nondiabetic FDRs in Indian settings remain limited. This study aims to bridge this gap by assessing the degree of insulin resistance in nondiabetic FDRs of T2DM patients and comparing it to individuals without such familial predisposition [5].

METHODOLOGY

This was a cross-sectional observational study conducted at a tertiary care teaching hospital over a one-year period. Ethical clearance was obtained, and informed consent was collected from all participants prior to enrollment. The study population consisted of nondiabetic first-degree relatives (parents, siblings, or offspring) of patients with diagnosed T2DM. A control group comprising age- and sex-matched individuals without any family history of T2DM was also included for comparative analysis.

Participants were screened to exclude individuals with pre-existing diabetes, known metabolic or endocrine disorders, chronic illnesses, or on medications affecting glucose metabolism. Fasting plasma glucose levels were measured to ensure inclusion of only nondiabetic individuals, based on WHO guidelines. Demographic data, anthropometric measurements (height, weight, BMI, waist-hip ratio), and blood pressure readings were recorded.

Venous blood samples were collected after an overnight fast for estimation of fasting blood glucose and fasting serum insulin levels. The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was calculated using the formula: HOMA-IR = (Fasting Insulin μU/mL × Fasting Glucose mg/dL) / 405. Participants were categorized into insulin-resistant and non-insulin-resistant groups based on HOMA-IR values.

Data were statistically analyzed using SPSS software. Continuous variables were expressed as mean ± standard deviation. Categorical variables were presented as percentages. Independent t-tests were employed to compare mean values between groups, and chi-square tests were used for categorical variables. A p-value of <0.05 was considered statistically significant.

RESULTS

Table 1: Demographic Characteristics of Study Population

Parameter	FDR Group (n = 50)	Control Group (n = 50)	p-value
Age (years)	39.4 ± 8.2	38.9 ± 7.6	0.62
Male:Female ratio	28:22	27:23	0.81
BMI (kg/m^2)	26.2 ± 3.1	24.5 ± 2.9	0.004 **
Waist-Hip Ratio	0.91 ± 0.04	0.87 ± 0.05	0.001 **

Table 2: Fasting Glucose and Insulin Levels

Parameter	FDR Group (n = 50)	Control Group (n = 50)	p-value
Fasting Plasma Glucose (mg/dL)	94.6 ± 8.5	90.1 ± 7.9	0.02 *
Fasting Serum Insulin (μU/mL)	14.2 ± 5.6	9.8 ± 4.1	0.001 **

Table 3: HOMA-IR Values

Parameter	FDR Group (n = 50)	Control Group (n = 50)	p-value
HOMA-IR (mean ± SD)	3.32 ± 1.25	2.18 ± 0.97	<0.001 **
% Insulin Resistance (HOMA-IR > 2.5)	62%	28%	<0.001 **

Table 4: Correlation of BMI with HOMA-IR

BMI Category (kg/m^2)	% Insulin Resistant in FDR Group	% Insulin Resistant in Control Group
< 23	18%	5%
23 - 25	40%	15%
> 25	85%	45%

DISCUSSION

The present study demonstrates a significantly higher prevalence of insulin resistance in nondiabetic first-degree relatives (FDRs) of T2DM patients compared to controls without a family history. This finding aligns with the hypothesis that genetic predisposition and shared environmental factors contribute to the early development of insulin resistance even before overt glucose abnormalities manifest [6, 7].

The demographic characteristics were comparable between the two groups, eliminating potential confounding effects of age and sex. However, BMI and waist-hip ratio were significantly higher in FDRs, suggesting that central obesity may partly mediate the observed insulin resistance. Prior studies have similarly highlighted abdominal adiposity as a key driver of insulin resistance [8].

Fasting plasma glucose levels, although within normal limits in both groups, were modestly but significantly higher among FDRs. This subtle elevation may reflect an early impairment of glucose homeostasis, consistent with prior reports indicating that FDRs exhibit higher postprandial glucose excursions and impaired beta-cell compensation.

Serum insulin levels and HOMA-IR values were significantly elevated in the FDR group. The proportion of insulin-resistant individuals (HOMA-IR >2.5) was 62% among FDRs, more than double that observed in controls. These findings underscore the utility of HOMA-IR as a practical and sensitive tool for identifying at-risk individuals in the prediabetic stage [9-11].

Interestingly, the correlation between BMI and HOMA-IR reinforces the role of adiposity in modulating insulin sensitivity. Among FDRs, those with BMI >25 kg/m^2 exhibited alarmingly high rates of insulin resistance (85%), highlighting the synergistic effect of genetic susceptibility and modifiable lifestyle factors. This emphasizes the need for targeted interventions, particularly weight management and physical activity, in high-risk individuals.

Our study contributes to the growing body of evidence supporting proactive screening of FDRs of T2DM patients. Routine measurement of fasting glucose and HOMA-IR, along with anthropometric assessment, can aid in early identification of those at heightened risk. Early lifestyle interventions in this group could delay or prevent the onset of T2DM, offering substantial public health benefits.

CONCLUSION

Nondiabetic FDRs of T2DM patients demonstrate a higher prevalence of insulin resistance. Early screening and lifestyle interventions in this high-risk group may delay or prevent diabetes onset.

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