ORIGINAL ARTICLE

Comparison of Metabolic Profile of Lean and Obese Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Background: Obesity induced insulin resistance has long been used to explain the development of type 2 diabetes mellitus (T2DM). However, it cannot be used to explain the development of T2DM in lean individuals. Given the lifelong morbidity associated with T2DM and its sequelae, it is necessary to properly understand the disease process. Therefore, this study was designed to compare the physical and biochemical parameters in lean and obese patients of T2DM.

Materials and Methods: We included newly diagnosed patients of T2DM and categorized them as lean (BMI<18.5 kg/m^2) and obese (BMI >25 kg/m^2) individuals; 30 patients in each of the two groups. Routine biochemical parameters such as fasting blood glucose (FBG), 2-hour post-prandial blood glucose (PPBG) and lipid profile were estimated using autoanalyzer. Glycated hemoglobin ($HbA1_C$) levels were estimated in whole blood using BIO-RAD D-10 autoanalyzer. Serum insulin was measured by ELISA.

Results: Glycemic parameters (FBG, PPBG, and $HbA1_C$) were higher in the lean group compared to the obese group. Dyslipidemia was present in both groups but was worse in the obese group. Fasting serum insulin levels were higher in the obese group compared to the lean group. Atherogenic index of plasma was high in both groups.

Conclusion: Hyperglycemia was greater in lean compared to obese T2DM patients predisposing them to a greater risk of hyperglycemia induced cellular damage. Dyslipidemia was present in both the groups but was worse in the obese patients.

Keywords: Fat, Glycemic parameters, Lipid profile, Obesity, Thinness.

INTRODUCTION

Diabetes mellitus (DM) is defined as a group of metabolic diseases characterized by hyperglycemia, resulting from defects in insulin secretion and/or insulin action.[1] The incidence of DM continues to rise with the International Diabetes Federation (IDF) projecting a steep rise in the caseload of Type 2 Diabetes Mellitus (T2DM) by the year 2045.[2] The rise in cases of T2DM has been linked to the obesity pandemic in the developed world.[3,4]

Although majority of T2DM patients are obese (body mass index, BMI >25 kg/m^2), 10-20% of patients of T2DM are non-obese or lean (BMI <18.5 kg/m^2). The proportion of lean patients with T2DM is higher in developing countries compared to developed countries.[5] However, the exact etiopathogenesis of the disease in lean individuals is yet to be elucidated as the model of obesity induced insulin resistance does not hold true in these patients.

Most of the studies done till date solely focus on obese patients of T2DM. The very few studies done in lean T2DM patients have certain limitations namely difference in the methodology and analysis (for example, use of different BMI cut-offs for leanness, treatment status of the patients) which makes their comparison with studies done in the obese group difficult.[6,7]

A high prevalence of cardiovascular-related morbidity and mortality in T2DM and associated dyslipidemia, warrants early diagnosis and management in order to prevent these complications. Keeping this in mind the current study was designed to compare the physical and biochemical profile of newly diagnosed lean and obese patients with T2DM at diagnosis prior to initiation of pharmacotherapy.

MATERIALS AND METHODS

This descriptive study was designed and conducted in the Department of Biochemistry and Endocrinology of University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi. Prior approval of the Institutional Ethics Committee for Human Research (IEC-HR/2019/41/25) was obtained.

Newly diagnosed, age and sex matched patients of T2DM belonging to the age group of 20-65 years, who were not on any pharmacotherapy for T2DM, were recruited from the out-patient clinic of endocrinology department after obtaining a written informed consent. The diagnosis of T2DM was made as per WHO criteria.[8] The patients were divided into two groups – lean (BMI <18.5kg/m^2) and obese (BMI >25kg/m^2) based on Body Mass Index (BMI) as per WHO Asia-Pacific Guidelines.[9] Other causes of lean diabetes such as diabetes arising out of pancreatic insufficiency (secondary diabetes), and type 1 diabetes were excluded based on history, clinical examination and laboratory findings. Lean patients of T2DM were recruited first, followed by obese patients. Given the fixed duration of the study (18 months and the low frequency of lean patients (newly diagnosed) of T2DM, 30 patients were enrolled in each group. Patients with renal and hepatic disorders, severe co-morbid illnesses, thyroid disorders, chronic alcoholics, and pregnant and lactating women were excluded from the study.

A detailed history was taken from the patients recruited in the study, which was followed by a clinical examination and anthropometric measurements as per standard guidelines.[10] Fasting blood glucose (FBG), 2-hour post-prandial plasma blood (PPBG), and lipid profile were estimated using RANDOX RX Imola autoanalyzer, (RANDOX, UK) as per the instructions of the manu-facturer. $HbA1_C$ levels were estimated in whole blood using BIO-RAD D-10 autoanalyzer (BIO-RAD, USA) as per the instructions of the manufacturer. Fasting serum insulin level was estimated by sandwich ELISA (DRG International, USA) following the protocol provided by the manufacturer [sensitivity:1.76 µIU/mL; precision: intra-assay 2.8%, inter-assay 5.99%]. Atherogenic Index of Plasma (AIP) was calculated using the formula AIP = Log [Triglyceride/High Density Lipoprotein-Cholesterol].[11]

Statistical Analysis: Statistical analysis was carried out using SPSS version 26.0 (IBM Corporation, USA) software. Biochemical parameters such as fasting serum insulin, fasting plasma blood, 2-hour plasma blood, $HbA1_c$ and lipid profile were compared between the groups by the unpaired student t-test or Mann-Whitney U test. P value less than 0.05 was considered significant.

RESULTS

Out of the 30 patients in each group, 8 (26.7 %) were female and 22 (73.3%) were male in both groups. ***Table I*** shows the demographic characteristics of the study participants.

Out of the 30 patients in the lean group, there was positive family history of diabetes in a total of 7 (23.3%) patients. Out of these 7 patients, 2 had the presence of T2DM in both parents while 3 had only maternal history of T2DM and 2 had only paternal history of T2DM. In the obese group, out of 30 patients recruited, 12 (40%) reported a positive family history for T2DM. Out of these 12 patients, 3 had both parents suffering from T2DM, 5 had only maternal history and 4 had only paternal history of T2DM

TABLE I. Physical Parameters in Lean and Obese Patients of Type 2 Diabetes Mellitus

Variable	*Lean (n=30)*	*Obese (n=30)*
Age (years)*	52.1 (±10.7)	51.5 (±10.4)
Male sex#	22 (73.3%)	22 (73.3%)
BMI (kg/m^2)*	17.9 (±0.9)	27.2 (±2.7)
Percentage body fat (%)*	22.1 (±5.9)	36.0 (±5.8)

**Expressed as mean (± SD); # Expressed as n (%).*

Routine biochemical parameters were comparable between both groups. Glycemic parameters and lipid profile values are depicted in ***Table II***. As seen in ***Table II***, dysglycemia was worse in the lean group and dyslipidemia was worse in the obese group at diagnosis.

DISCUSSION

Diabetes is characterized by hyperglycemia and tends to be accompanied by dyslipidemia.[12] In this study we compared the glycemic parameters and lipid profile in newly diagnosed lean and obese patients of T2DM.

Glycemic status at diagnosis was worse in the lean group compared to the obese group. A significant difference was seen in the mean fasting blood glucose levels between the two groups. Post-prandial blood glucose level was also higher in lean patients of T2DM as compared to obese patients but the difference was not statistically significant. Glycated hemoglobin ($HbA1_c$) levels also followed the same trend as blood fasting glucose levels with a highly significant difference between the two groups. Conflicting reports exist on the glycemic para-meters in lean and obese patients of T2DM mainly due to the non-uniformity in BMI cut-offs used which makes comparison of these studies difficult. Coleman, *et al* reported a worse glycemic status in lean patients (BMI <25 kg/m^2) of T2DM compared to obese patients (BMI >30 kg/m^2).[13] Asegaonkar, *et al* reported a higher FBG level in obese patients (BMI >25 kg/m^2) of T2DM compared to lean patients (BMI <25 kg/m^2).[14] Bautista, *et al* reported higher values of glycemic parameters in obese patients (BMI >25 kg/m^2) of T2DM compared to lean patients (BMI <18.5 kg/m^2).[15]

TABLE II. Glycemic Parameters and Lipid Profile in Lean and Obese Patients of Type 2 Diabetes Mellitus

Parameter [mean (± SD)]	*Lean (n=30)*	*Obese (n=30)*	*P value*
Glycemic parameters			
Fasting blood glucose (mg/dL)	254.2 (± 63.1)	207.3 (± 73.8)	0.01
2-hour post prandial blood glucose (mg/dL)	361.2 (± 76.6)	329.2 (± 88.0)	0.13
$HbA1_c$ (%)	11.5 (± 2.6)	9.4 (± 2.1)	0.001
Lipid Profile			
Serum total cholesterol (mg/dL)	207.0 (± 35.2)	214.1 (± 35.4)	0.43
Serum triglyceride (mg/dL)	152.6 (± 66.4)	156.2 (± 53.7)	0.81
Serum low density lipoprotein (LDL) cholesterol (mg/dL)	124.3 (± 31.0)	137.5 (± 36.9)	0.13
Serum high density lipoprotein (HDL) cholesterol (mg/dL)	34.2 (± 11.1)	30.8 (± 7.5)	0.16
Miscellaneous Parameters			
Fasting serum insulin (μIU/mL)	16.1 (± 8.4)	27.1 (± 4.9)	0.001
LDL-C/HDL-C	4.0 (± 1.6)	4.8 (± 2.1)	0.09
Atherogenic index of plasma	0.61	0.77	0.006

Our findings suggest that lean individuals are exposed to higher levels of blood glucose compared to their obese counterparts. A possible explanation for higher blood glucose levels could be earlier β-cell failure in lean patients which is supported by our finding of lower fasting insulin levels in lean patients compared to obese patients,[13] or defects in insulin signalling pathways.[16]

Dyslipidemia although present in both groups was worse in the obese group. Although both groups had comparable high density lipoprotein (HDL) cholesterol and serum total cholesterol levels, serum triglycerides and low density lipoprotein (LDL) cholesterol levels were comparatively higher in obese patients which can be explained by the increased rate of lipolysis in their abundant fat reserves.[17] As with glycemic parameters conflicting data on lipid profile exists in lean and obese patients of T2DM. Bautista, *et al* reported no significant difference in lipid profile.[15] Barma, *et al* reported no significantly deranged lipid parameters while comparing lean (BMI <19 kg/m^2) vs obese patients (BMI >25 kg/m^2) of T2DM.[18] Some studies have reported normal serum lipid profile in lean patients of T2DM.[19,20] Our lipid profile findings are in line with the findings of Asegaonkar, *et al* the only difference being in the BMI cut-offs used.[14] In contrast to our study, Sinharoy, *et al* reported higher levels of serum triglyceride levels in lean patients (BMI <18.5 kg/m^2) of T2DM compared to obese patients (BMI >25 kg/m^2).[21]

Although dyslipidemia was worse in obese group, the lipid profile is also deranged in the lean group with a high LDL to HDL ratio predisposing them to the atherosclerosis and its sequalae. AIP is commonly used a predictor of cardiovascular risk with values higher than 0.24 be labelled as high risk.[11] In this study both lean patients and obese patients had an AIP value of more than 0.24 at diagnosis. Therefore, these patients can be considered to be at high risk of developing coronary sequelae, obese patients having a higher risk compared to their lean counterparts.

One of major limitations of this study is the small sample size. A study with a larger sample size and long-term follow up will enable a better understanding of the disease process especially in lean individuals.

CONCLUSIONS

Based on the available literature and our findings we can conclude that hyperglycemia tends to be more severe in lean patients compared to their obese counterparts. Lean T2DM patients are consequently exposed to the ill effects of deranged lipid metabolism *i.e.,* atherosclerosis and its sequelac as evidenced by a high LDL/HDL ratio and high AIP. Therefore, there is a need to control blood sugar levels more aggressively in lean T2DM patients to delay the chronic complications associated with the disease. Studies need to be planned to decipher the exact etiopathogenesis of hyperglycemia in lean individuals so that appropriate treatment protocols can be established.

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design, supervision, validation, analysis and interpretation of data, project administration, review of draft and critical inputs; DP: Visualization, supervision, validation, investigation and data analysis, project administration, review of draft and critical inputs. All authors approved the final manuscript and will be accountable for all aspects of the work.

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