

## ORIGINAL RESEARCH

# Metabolic Status of Lean, Overweight, and Obese Type 2 Diabetes Mellitus Patients

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## ABSTRACT

**Aims:** To compare metabolic status of lean vs overweight/obese type 2 diabetes mellitus (T2DM) patients and correlate biochemical parameters with anthropometric measures.

**Materials and methods:** A total of 100 T2DM patients were categorized as lean and overweight/obese according to body mass index (BMI); 50 age- and sex-matched healthy controls were selected. Anthropometric measures of BMI, waist circumference (WC), and waist:hip (W:H) were recorded. Fasting blood samples were assayed for fasting plasma glucose (FPG), serum total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), and nonesterified free fatty acids (NEFA). Low-density lipoprotein (LDL) was calculated by Friedewald's formula and TG: HDL was measured as measure of insulin resistance (IR).

**Results:** Anthropometric measures of overall (BMI  $31.65 \pm 5.49$ ,  $20.34 \pm 2.45$  vs  $22.29 \pm 3.21$ ) and visceral adiposity (WC  $91.98 \pm 6.8$ ,  $75.45 \pm 4.34$  vs  $74.19 \pm 3.98$  and W:H  $0.99 \pm 0.12$ ,  $0.78 \pm 0.21$  vs  $0.76 \pm 0.32$ ) were significantly higher in overweight/obese ( $p < 0.05$ ) compared with lean T2DM and controls. Total cholesterol, TG, LDL, and NEFA were significantly raised and HDL decreased in T2DM compared with those of controls. But much higher values were observed in overweight/obese than in lean group. Triglycerides: HDL was significantly higher in obese than in lean patients ( $4.66 \pm 1.89$  vs  $7.91 \pm 3.01$ ), confirming significantly decreased insulin sensitivity among obese than non-obese diabetics. Positive correlation was observed between BMI, WC, W:H and TC, TG, LDL, NEFA, and TG:HDL, while negative correlation was observed with HDL in obese group. Lean individuals with normal BMI, WC had deranged lipids with IR.

**Conclusion:** Lean and obese T2DM have dyslipidemia and IR. Poor metabolic profile is associated with overall and visceral adiposity in obese and not in lean T2DM individuals.

**Keywords:** Lean, Lipid profile, Nonesterified free fatty acids, Obese, Type 2 diabetes mellitus.

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## INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder due to absolute or relative deficiency of insulin. The global transition of lifestyle, unhealthy habits of consumption of high-energy foods, physical inactivity, and stress are driving the epidemic of T2DM worldwide at a rapid pace. Wave of urbanization, sedentary lifestyle, and gene-environment interactions are the main causes for obesity, which is a strong determinant of T2DM. Among Asian Indians, paradox of occurrence of T2DM in lean or normal weight person and healthy metabolic status in overweight/obese individuals is seen frequently.<sup>1</sup>

Epidemiological data have shown varied patterns of clinical profile of T2DM patients worldwide. Indian studies reported 1.6 to 26% prevalence of low or normal body weight/lean T2DM individuals. On the contrary, in Western countries majority of T2DM individuals are overweight or obese.<sup>2</sup> One of the studies from South India reported prevalence of 3.5% lean, 63.5% ideal body weight, and 32.9% obese patients among 9,873 total diabetics.<sup>3</sup> Type 2 diabetes mellitus and obesity are strong independent risk factors for cardiovascular diseases.

Type 2 diabetes mellitus is a major health disaster globally. Body mass index (BMI) can vary widely among T2DM individuals, stratifying them into lean or normal weight and overweight/obese types. Body mass index correlates strongly with insulin resistance (IR) and T2DM. Its link with lipoprotein metabolism, vascular health, and visceral adiposity has been well established. Increased concentration of nonesterified free fatty acids (NEFA) from adipose tissue leads to IR and pancreatic

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$\beta$ -cell dysfunction, which are key pathogenic factors for the development of T2DM. Hence, obesity aggravates IR in T2DM patients.<sup>4,5</sup> Also obesity is a major complication of T2DM. Among Asian population, IR is more prevalent which is associated with high concentrations of NEFA in plasma even in lean persons. But these features are aggravated in obese persons leading to various complications. Nonesterified free fatty acid is the chief fuel for skeletal muscles and its concentration is proportional to body fat stores. Its positive correlation with obesity and T2DM and as a predictor of T2DM is documented by previous studies.<sup>6,7</sup> Lean and obese T2DM patients have different clinical course, complications, and metabolic profile.

With this background, we designed the present study to compare anthropometric and metabolic profile of lean *vs* overweight/obese T2DM patients and correlate biochemical parameters with anthropometric measures.

## MATERIALS AND METHODS

Institutional Ethical Committee approved the present case control study. A total of 100 diagnosed cases of T2DM were recruited from the Diabetes clinic. Out of 100 cases, lean group (group I) included 50 T2DM patients having BMI less than 25 kg/m<sup>2</sup> and 50 were overweight and obese (group II) with BMI above 25 kg/m<sup>2</sup>. A total of 50 age- and sex-matched healthy controls were selected as controls (group III). Patients with major illness like malignancy, renal failure, critical illness, severe infections, chronic obstructive pulmonary disease, and endocrinological disorders were excluded from the study.

Informed written consents were obtained from all participants. Demographic records of age, sex, personal habits about smoking, and alcoholism were obtained by administering questionnaire. History of duration of diabetes, medication, complications, associated comorbidities, past and family medical history were obtained in detail. Anthropometric measures were recorded. Body mass index was calculated as weight (kg)/height (m<sup>2</sup>). Waist circumference (cm) and hip circumference (cm) were measured. After thorough clinical evaluation, all subjects were invited to give blood samples after 12 hours fast and were asked to abstain from smoking, alcohol consumption for 24 hours before investigations.

About 3 mL blood samples was collected in plain and 2 mL in fluoride bulbs. After clot formation, serum was separated and assayed for biochemical parameters. All investigations were carried out on fully automated chemistry analyzer XL640 from Transasia using commercial ERBA kits. Blood glucose was estimated by glucose oxidase-peroxidase method. Total cholesterol (TC) was measured by cholesterol oxidase-peroxidase, triglycerides (TG)

by lipase/glycerokinase/glycerophosphate oxidase method, and high-density lipoprotein (HDL) by precipitation methods. Nonesterified free fatty acid concentration was estimated by colorimetric method using commercial kit from Randox diagnostics. Acyl CoA synthase converts NEFA to acyl CoA, which gets acted by oxidase and peroxidase enzymes to give purple-colored adduct. Its color intensity is directly proportional to the concentration of NEFA. Low-density lipoprotein (LDL) was calculated by Friedewald's formula as LDL (mg/mL) = TC - (HDL + very LDL).

Ratio of TG:HDL was calculated and used as a measure of IR.

## Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) 11.0 statistical software. Continuous variables were calculated by descriptive statistics and reported as mean  $\pm$  standard deviation (SD). Continuous variables were compared across three groups by one-way analysis of variance (ANOVA). Pearson's correlation analysis was used to study correlation of biochemical parameters with anthropometric variables.

## RESULTS

Present study included 50 lean and 50 overweight and obese T2DM patients. In the lean group, 32 were males and 18 females, while in the overweight/obese group, 24 were males and 26 females. Mean age of group I was 43.6  $\pm$  5.45 years while of group II was 53.89  $\pm$  7.9 years. Demographic and anthropometric profile of the three groups is shown in Table 1. Metabolic profile of the studied participants in terms of biochemical characteristics are represented in Table 2.

Correlation of anthropometric and biochemical parameters in overweight/obese group was studied by Pearson's coefficient (*r* values) calculation. Table 3 shows correlation between metabolic health indicators (biochemical parameters) and anthropometric measures of overall and visceral adiposity among overweight/obese T2DM individuals.

## DISCUSSION

Our study investigated demographic, anthropometric, and metabolic profile of lean T2DM *vs* overweight and obese T2DM patients. On the basis of BMI, 100 diabetics were stratified into two groups – lean and overweight/obese. A total of 50 healthy age- and sex-matched controls were selected randomly. Anthropometric measures of overall (BMI) and visceral adiposity (waist circumference (WC), and waist:hip (W:H) were

**Table 1:** Demographic and anthropometric characteristics of studied population

Variables	Group I (lean T2DM BMI < 25 kg/m <sup>2</sup> ) n = 50 mean ± SD	Group II (overweight/obese T2DM BMI > 25 kg/m <sup>2</sup> ) n = 50 mean ± SD	Controls n = 50 mean ± SD
Age (years)	43.6 ± 5.45	53.89 ± 7.9*	46.57 ± 6.45
Sex Male:female	32:18	24:26	28:22
BMI (kg/m <sup>2</sup> )	20.34 ± 2.45	31.65 ± 5.49**	22.29 ± 3.21
WC (cm)	75.45 ± 4.34	91.98 ± 6.8**	74.19 ± 3.98
Waist:hip	0.78 ± 0.21	0.99 ± 0.12*	0.76 ± 0.32
Duration of diabetes	6.54 ± 4.24	9.2 ± 3.49*	Nil
Family history of T2DM	28 (56%)	24 (48%)	18 (36%)

Simultaneous comparison of three groups using ANOVA analysis p value vs control group (\*Significant at the 0.05 level; \*\*Highly significant at the 0.001 level)

**Table 2:** Metabolic profile of the studied participants

Biochemical variable	Group I (lean) mean ± SD	Group II (overweight/obese) mean ± SD	Controls mean ± SD
Fasting blood glucose, mg%	143.23 ± 18.24	153.46 ± 21.65	89.23 ± 12/98
TC, mg%	213.97 ± 23.54*	245.83 ± 32.87**	132.76 ± 21.45
TG, mg%	195.43 ± 42.64*	256.76 ± 45.67**	98.34 ± 21.43
LDL, mg%	132.64 ± 21.43*	164.32 ± 31.3*	73.23 ± 17.3
HDL, mg%	41.9 ± 6.3*	32.45 ± 5.65**	51.43 ± 7.89
TG/HDL	4.66 ± 1.89*	7.91 ± 3.01**	1.91 ± 0.65
NEFA	1.34 ± 0.83*	2.4 ± 1.32**	0.54 ± 0.11

Simultaneous comparison of three groups using ANOVA analysis p value vs control group (\*Significant at the 0.05 level; \*\*Highly significant at the 0.001 level)

**Table 3:** Correlation between anthropometric and biochemical variables in overweight/obese T2DM group

Variables	TC (mg%)	LDL (mg%)	HDL (mg%)	TG (mg%)	NEFA (mmol/l)	TG:HDL
BMI (kg/m <sup>2</sup> )	0.48	0.51	-0.32	0.3	0.41	0.23
WC (cm)	0.44	0.32	-0.28	0.38	0.39	0.28

significantly high in overweight/obese compared with lean T2DM and controls. Lipid parameters TC, TG, LDL and NEFA were significantly raised in both groups compared with controls. But much higher values were observed in overweight/obese than in the lean group. We calculated TG:HDL as an indirect measure of IR that was significantly higher in obese than in lean patients. This confirms significantly decreased sensitivity of insulin among obese compared with nonobese diabetics.

Many researchers carried out comparative evaluations among normal weight and obese T2DM patients. Barma et al<sup>8</sup> reported no significant deranged lipid profile in 100 lean T2DM patients. Similar types of observations of normal lipid profile are documented by previous studies.<sup>2,9,10</sup> Baynes et al<sup>11</sup> postulated high HDL levels due to excess hepatic lipase activity. Sinharoy et al<sup>12</sup> found raised TG and LDL in lean T2DM compared with normal weight and obese T2DM patients.

Coleman et al<sup>13</sup> reported 13% of T2DM with ideal weight among cohort of 18,000 patients in a Chicago study. Lean group had male preponderance with environmental insults by smoking and alcohol and pancreatitis with worst glycemic control compared with

obese counterparts. Lukich et al<sup>14</sup> studied impact of overall and abdominal adiposity among normal weight and obese diabetics. They reported significantly deranged levels of LDL, HDL, and TG among obese individuals defined by both BMI and WC measurements.

Il'yasova et al<sup>15</sup> studied prospective association between fasting NEFA T2DM in Insulin Resistance Atherosclerosis Study cohort of 902 subjects and 145 incident cases. Their results indicated positive association of fasting NEFA with diabetes risk (odds ratio 1.37: 0.87–2.15) per unit on log scale. Postload 2-hour glucose values were key confounding factor in this association. Fasting NEFA was associated positively with BMI, WC, and 2-hour glucose while it was negatively with insulin sensitivity.

In overweight and obese T2DM patients, insulin sensitivity is impaired, resulting in excess of lipolysis with raised concentration of NEFA and TG in circulation. Uptake of glucose by muscle tissue also gets reduced.<sup>16</sup> Adipose tissues affect metabolism by releasing hormones, proinflammatory substances, glycerol, and NEFA. Non-esterified free fatty acids and visceral fat are key factors to diminish sensitivity of insulin and develop IR.<sup>17,18</sup>

When NEFA levels are raised in plasma, transport of glucose toward muscles is diminished and breakdown of fat accelerated. This stimulates hepatic gluconeogenesis, causing dysglycemia leading to macrovascular and microvascular complications of T2DM.<sup>4</sup>

Nonesterified free fatty acids play important role in release of insulin in circulation. Among obese individuals, continuous exposure to NEFA diminishes synthesis of insulin by affecting glucose-stimulated insulin secretion pathway. Among T2DM patients, NEFA is the main link between  $\beta$ -cell dysfunction and IR. Hyperglycemia and raised NEFA in combination causes harmful effects of glucolipototoxicity.<sup>19</sup>

Comparison of lean and obese T2DM is important as high prevalence of microvascular complications among lean and macrovascular complications in obese T2DM patients has been reported in previous studies.<sup>3,8</sup> Clinical presentations, complications associated with T2DM, and metabolic profile differ among lean and obese patients. Lean T2DM is a distinct clinical entity characterized by onset at young age, male preponderance, abuse of smoking, and alcoholism and early failure to oral hypoglycemic agents influencing natural history of T2DM.<sup>20</sup> It is an independent variant of classical T2DM with inherent peculiarities in insulin kinetics in liver and altered profile of carbohydrate metabolism.<sup>21</sup> Insulin-stimulated utilization of glucose and sensitivity to insulin are significantly decreased in obese T2DM, while lean T2DM patients have defects in insulin secretion.<sup>22</sup>

Prevalence of T2DM is escalating significantly globally, imposing an economic burden on the health care system. Our studied population of T2DM, overweight/obese group, appear to be associated with significantly less favorable lipid profile. This emphasizes strict monitoring of metabolic health and need for weight reduction. Lean group also is associated with deranged cardiometabolic risk. So tight glycemic control and regular surveillance to prevent complications of T2DM remain the mainstay in the management.

## LIMITATIONS OF THE STUDY

Main limitation of the present study is the small sample size. We did not estimate actual IR, functioning of  $\beta$  cells, and total and visceral body fat.

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