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ORIGINAL RESEARCH

A study of Metabolic Profiles in Lean, Overweight, and Obese Type 2 Diabetes Mellitus Patients

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ABSTRACT

Background: The most common kind of diabetes in the world is type 2 diabetes mellitus. Most instances in western nations include obesity. The situation can be different in several regions of India. A significant frequency of lean type 2 diabetes mellitus has been noted in studies with a body mass index under 19 kg/m2. To connect biochemical markers with anthropometric measurements and to assess the metabolic state of lean vs. overweight/obese type 2 diabetes mellitus (T2DM) patients.**Materials and Methods**: Body mass index (BMI) was used to classify 100 T2DM patients into lean and overweight/obese groups; 50 healthy controls with similar ages and sexes were chosen. BMI, waist circumference (WC), and waist:hip ratio (W:H) anthropometric measurements were taken. Fasting blood samples were analysed for high-density lipoprotein (HDL), nonesterified free fatty acids, serum total cholesterol, fasting plasma glucose, and triglycerides (NEFA). The Friedewald algorithm was used to compute low-density lipoprotein (LDL), and TG:HDL was evaluated to assess insulin resistance (IR).**Results:** Compared to lean T2DM and controls, overweight/obese individuals had substantially greater anthropometric parameters of total (BMI 33.22 ±5.9 , 20.35±2.22 *vs* 21.49±3.88) and visceral adiposity (WC 93.42 ±6.4, 76.45±4.14 *vs* 75.2 ±4.1 and W:H 0.98 ±0.14 , 0.8 ±0.22 *vs* 0.78±0.32). In comparison to controls, T2DM patients had significantly higher levels of total cholesterol, TG, LDL, and NEFA while having lower levels of HDL. However, the values in the overweight/obese group were substantially higher than those in the lean group. Triglycerides: HDL levels were substantially higher in obese individuals compared to lean patients (4.42 ± 1.6 vs 7.88 ± 3.22), indicating that obese diabetics had much worse insulin sensitivity than non-obese diabetics. BMI, WC, W:H, TG, LDL, NEFA, and TG:HDL showed positive correlations whereas HDL in the obese group showed negative correlations. Lean people with normal BMI, WC had abnormal lipids, and IR.

Conclusion: T2DM in obese and lean people has dyslipidemia and IR. Poor metabolic profile is not connected with lean T2DM patients' total and visceral obesity.

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

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INTRODUCTION

By diabetes type, different guidelines and warnings may apply to physical activity. Type 1 and type 2 diabetes are the two main varieties. The pancreatic -cells are destroyed by the immune system in type 1 diabetes (5–10% of cases), which causes an insulin shortage.[1] Although it can happen at any age, the pace of -cell destruction varies, usually happening more quickly in children than in adults. 90% to 95% of cases of type 2 diabetes are caused by a gradual reduction in insulin production, which is frequently accompanied by insulin resistance. In order to explain why certain type 2 diabetics who seem slender are actually "metabolically fat," researchers have discovered molecular proof. Obesity and being overweight are well-known risk factors for diabetes and heart disease. Diabetes rates do not closely correlate with obesity rates in Asia. India has modest obesity rates but significantly high type 2 diabetes rates.[1] Compared to Europeans, Asian populations have a greater chance of developing diabetes at lower BMIs. The "normal-weight metabolically obese" phenotype is thus one of the causes of the diabetes pandemic among Asians. Up until recently, nothing was known about the biochemical or molecular causes of "metabolic obesity."[2,3] The so-called metabolic syndrome (MetS), which includes hypertension, dyslipidemia, and hyperglycemia, is frequently encountered in association with excess fat mass. The obesity pandemic has been on the rise recently, and this has directly affected the prevalence of MetS.[3,4]

Numerous theories have been proposed to explain the pathophysiological pathways of obesity related metabolic disorders, including insulin resistance, systemic low-grade inflammation, abdominal and ectopic fat accumulation, and intestinal microbiota composition. These theories were sparked by comparisons of obese and lean subjects. Experimental data indicate that defective adipose tissue has a negative impact on metabolism and may be the root cause of various metabolic morbidities linked to obesity, including type 2 diabetes and insulin resistance. Additionally, dietary variables, low cardiovascular fitness, and inactivity may all play a role in MetS development.[5,6]

A chronic metabolic condition known as type 2 diabetes mellitus (T2DM) is caused by an absolute or relative insulin shortage. The global epidemic of T2DM is spreading quickly due to a variety of factors, including a change in lifestyle, bad eating habits, physical inactivity, and stress. The key factors contributing to obesity, which is a significant risk factor for T2DM, are a wave of urbanisation, a sedentary lifestyle, and gene-environment interactions. Asian Indians typically witness the paradoxical incidence of T2DM in lean or normal weight people and favourable metabolic condition in overweight/obese people. Epidemiological studies have revealed numerous variations in the clinical profiles of T2DM patients throughout the world. Studies conducted in India found a prevalence of low or normal body weight/lean T2DM patients ranging from 1.6 to 26%. Contrarily, the majority of T2DM patients in Western nations are fat or overweight. One study from South India found that out of 9,873 total diabetics, 3.5% were lean, 63.5% were at their optimal body weight, and 32.9% were obese. Obesity and type 2 diabetes mellitus are both significant independent risk factors for heart disease. Globally, type 2 diabetes mellitus is a serious health catastrophe. T2DM patients can be classified into lean or normal weight and overweight/obese kinds based on their body mass index (BMI), which can vary significantly between them. IR and T2DM have a high correlation with body mass index (BMI). It has a well-established relationship with vascular health, visceral obesity, and lipoprotein metabolism. IR and pancreatic -cell dysfunction are caused by an increase in nonesterified free fatty acids (NEFA) from adipose tissue. Therefore, obesity makes IR worse in those with T2DM. Another significant consequence of T2DM is obesity. Asians are more likely to have IR, which is linked to elevated plasma NEFA levels, even in slim individuals. However, these characteristics are amplified in fat people, which can cause a number of problems. The main source of fuel for skeletal muscles is unsaturated free fatty acid, and the concentration varies in direct

proportion to body fat levels. Previous investigations have shown a favourable link between it and T2DM as well as its potential predictive value. Clinical outcomes, complications, and metabolic profiles differ between T2DM patients who are lean and fat.[5,6]
To assess the anthropometric and metabolic profiles of lean vs. overweight/obese T2DM patients and connect biochemical markers with anthropometric measurements, we planned the current study with this background in mind.

MATERIALS & METHODS

The current case control research was authorized by the institutional ethical committee. The study was carried out at Mediciti Institute of Medical Sciences, Ghanpur Village, Telangana, India. 100 T2DM cases with confirmed diagnoses were gathered from the Diabetes clinic. Out of 100 cases, the lean group (group I) consisted of 50 T2DM patients with BMIs under 25 kg/m2, while the overweight and obese group (group II) consisted of 50 patients with BMIs over 25 kg/m2. A total of 50 healthy controls with similar age and sex were chosen as the controls (group III). The study excluded participants with serious illnesses such cancer, renal failure, critical sickness, severe infections, chronic obstructive pulmonary disease, and endocrinological abnormalities. All participants gave their written consent after being fully informed. A questionnaire was used to collect demographic data on age, sex, smoking and drinking habits, and sexual orientation. In-depth information was gathered on the duration of the diabetes, medication, complications, related comorbidities, prior medical history, and family medical history. Measurements of anthropometry were taken. Weight (kg)/height was used to compute body mass index (m2). Both the hip and waist circumferences were measured in centimetres. All individuals underwent complete clinical examination before being requested to provide blood samples following a 12-hour fast and a 24- hour period of no smoking or alcohol usage. The glucose oxidase-peroxidase technique was used to determine blood glucose. Triglycerides (TG) were determined using the lipase/glycerokinase/glycerophosphate oxidase technique, total cholesterol (TC) by cholesterol oxidase-peroxidase, and high-density lipoprotein (HDL) by precipitation methods. Using a commercial kit from Randox Diagnostics, the colorimetric approach was used to quantify the concentration of nonesterified free fatty acids. Acyl CoA synthase changes NEFA into acyl CoA, which is then oxidised and peroxidized by other enzymes to produce a purple adduct. The amount of NEFA present is directly inversely related to the intensity of its colour. According to Friedewald's method, low-density lipoprotein (LDL) was calculated as LDL (mg/mL) = TC - (HDL+ extremely LDL). The TG:HDL ratio was determined and utilised as a proxy for IR.

Statistical Analysis:

Statistical Package for the Social Sciences (SPSS) 11.0 was used to analyse the data. Descriptive statistics were used to calculate continuous variables, and the results were given as mean standard deviation (SD). Three sets of continuous variables were compared using a one-way analysis of variance (ANOVA). The relationship between anthropometric measures and biochemical markers was investigated using Pearson's correlation analysis.

RESULTS

The 50 lean and 50 overweight or obese T2DM patients were included in the current investigation. 30 men and 20 women made up the lean group, whereas 25 men and 25 women made up the overweight/obese group. Group I's mean age was 44.8 +/- 5.2 years whereas group II's was 56.89 +/- 7.1 years. Table 1 displays the demographic and anthropometric characteristics of the three groups. Table 2 illustrates the biochemical parameters of the subjects' metabolic profiles.

Table 1: Demographic and anthropometric characteristics ofstudied population

Variables	**Group I (lean T2DM BMI<25 kg/m^2)n=50 mean±SD**	**Group II (overweight/obese T2DM BMI>25 kg/m^2) n=50 mean±SD**	**Controls n= 50mean± SD**
Age (years)	44.8 ±5.2	56.89±7.1 *	45.55 ±6.25
Sex Male:female	30:20	25:25	27:23
BMI (kg/m^2)	20.35±2.22	33.22 ±5.9 **	21.49±3.88
WC (cm)	76.45±4.14	93.42 ±6.4 **	75.2 ±4.1
Waist:hip	0.8 ±0.22	0.98 ±0.14 *	0.78±0.32
Duration of diabetes	6.62±4.02	9.4±3.6*	Nil
Family history of T2DM	30 (60 %)	26 (52 %)	20 (40 %)

Simultaneous comparison of three groups using ANOVA analysis p value *vs* control group (*Significant at the 0.05 level; **Highlysignificant 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%	144.22±20.24	154.22±22.44	90.44 ±14.28
TC, mg%	216.88 ±22.62 *	246.83±32.82**	134.82 ±22.65
TG, mg%	196.23±40.44 *	258.62 ±48.24 **	99.24±20.28
LDL, mg%	130.64±21.24*	168.22 ±31.0*	73.6±18.6
HDL, mg%	41.22 ±6.4 *	32.88 ±5.24 **	51.38 ±7.42
TG/HDL	4.42±1.6*	7.88±3.22**	2.01±0.64
NEFA	1.82 ±0.36 *	2.8 ±1.12**	0.58 ±0.10

Simultaneous comparison of three groups using ANOVA analysis p value *vs* control group (*Significant at the level; **Highlysignificant 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:HD L**
BMI (kg/m^2)	0.49	0.52	–0.30	0.4	0.44	0.28
WC (cm)	0.42	0.36	–0.26	0.34	0.36	0.29

By calculating Pearson's coefficient (r values), the correlation between anthropometric and biochemical markers in the overweight/obese group was examined. Table 3 illustrates the relationship between anthropometric measurements of total and visceral adiposity in T2DM patients who are overweight or obese and metabolic health markers (biochemical parameters).

DISCUSSION

Our study compared the demographic, anthropometric, and metabolic profiles of lean T2DM patients to those who were overweight or obese. 100 diabetics were divided into two groups

based on BMI: lean and overweight/obese. 50 healthy controls that were matched for age and sex were chosen at random. When compared to lean T2DM and controls, overweight/obese individuals had substantially higher anthropometric measures of total (BMI) and visceral adiposity (waist circumference (WC) and waist: hip (W:H)). When compared to controls, both groups had considerably higher levels of the lipid markers TC, TG, LDL, and NEFA. However, the values in the overweight/obese group were substantially higher than those in the lean group. As a proxy for IR, we assessed TG: HDL, which was considerably greater in fat individuals than in lean patients. This demonstrates that insulin's sensitivity has drastically diminished. The average patient was 53 years old, and the average time they had had diabetes was 52 months. Our patients' mean ages are higher than those reported by Sinharoy et al.[7] and Das et al.,[8] who both reported mean ages of 47 years and 48 years, respectively. But Mukhyaprana et alanalysis .'s indicated a higher mean age of 60 years.[6] Previous studies by Banerji et al and Das et al,[8] had showed slight increase in TGL and HDL in lean diabetics. Numerous researches compared the outcomes of T2DM patients who were of normal weight and those who were obese. In 100 lean T2DM patients, Barma et al.[13] showed no signifcantly altered lipid profile. Previous research have provided documentation of similar sorts of observations of a normal lipid profile. High amounts of HDL may be caused by excessive hepatic lipase activity, according to Baynes et al. In comparison to patients with normal weight and obese T2DM, Sinharoy et al.[7] discovered elevated TG and LDL in lean T2DM patients. Lean diabetics who participated in earlier research by Banerji et al and Das et al,[8] experienced a small rise in TGL and HDL. In a cohort of 18,000 individuals, Coleman et al.[11] found 13 percent of T2DM with optimum weight in a Chicago research. When compared to their obese counterparts, the lean group had a higher percentage of males, worse glycemic control, pancreatitis, and environmental insults from alcohol and smoking. The effects of overall and abdominal adiposity in diabetics who are normal weight and obese were examined by Lukich et al.[12] They found that obese people as determined by both BMI and WC measures had considerably disordered levels of LDL, HDL, and TG. II'yasova et al.[10] investigated the prospective correlation between fasting NEFA T2DM and 145 incident cases in the Insulin Resistance Atherosclerosis Study cohort of 902 participants. Their findings showed a favourable correlation between fasting NEFA and the probability of developing diabetes (odds ratio 1.37: 0.87–2.15) per unit on a log scale. The main confounding factor in this connection was the post load 2-hour glucose readings. Fasting NEFA had a negative correlation with insulin sensitivity but a positive correlation with B MI, WC, and 2-hour glucose. The obvious lack of hyperlipidemia in these patients was revealed by Das et al.[8] Patients with diabetes who were slim had high HDL values. It has been suggested that high HDL is caused by too much hepatic lipase activity. Ikeda et al. found no significant differences in slim type 2 diabetics (BMI25kg/m2) regardless of their glycemic state. The patients of Mukhyaprana et al.[6] also had normal lipid profiles. In contrast, a research by Sinharoy et al [7]. found that lean type 2 diabetics had higher TG compared to those who were normal weight or obese. Even while it was lower than in the other two groups, LDL was still increased. Insulin sensitivity is decreased in T2DM patients who are overweight or obese, which leads to excessive lipolysis and an increase in the blood levels of NEFA and TG. Muscle tissue's ability to absorb glucose is similarly lowered. Adipose tissues release hormones, anti-inflammatory agents, glycerol, and NEFA that have an impact on metabolism. Visceral fat and non-esterified free fatty acids are important contributors to decreased insulin sensitivity and the development of IR. The transfer of glucose to muscles is reduced and fat breakdown is increased up when plasma NEFA levels are elevated. This promotes hepatic gluconeogenesis, resulting in dysglycemia and T2DM problems related to the macrovascular and microvascular systems. Free fatty acids that have not been esterified are crucial for the release of insulin into the bloodstream. Continuous exposure to NEFA reduces insulin synthesis in obese people via altering the glucose-stimulated insulin secretion route. The

primary connection between IR and -cell dysfunction in T2DM patients is NEFA. NEFA elevation and hyperglycemia work together to produce the damaging consequences of glucolipotoxicity. Comparison of lean and obese T2DM patients is crucial since prior research has indicated a high frequency of microvascular problems in lean T2DM patients and macrovascular issues in obese T2DM patients. Lean and obese individuals have different clinical manifestations, T2DM consequences, and metabolic profiles. Lean T2DM is a unique clinical condition marked by early start, male predominance, smoking and alcohol addiction, as well as early inability to respond to oral hypoglycemic agents. It is a distinct subtype of classic T2DM with unique hepatic insulin kinetics and a modified carbohydrate metabolism profile. Obese T2DM patients exhibit considerable reductions in insulin sensitivity and insulin-stimulated glucose utilization, whereas lean T2DM patients have abnormalities in insulin secretion. T2DM prevalence is rising sharply worldwide, placing a financial strain on the health care system. The overweight/obese group in our study population with T2DM appears to have a much less favourable lipid profile. This highlights the importance of thorough metabolic health monitoring and weight loss. Deranged cardio metabolic risk is also linked to lean body composition. As a result, maintaining strict glycemic control and routine observation to guard against T2DM complications remains the cornerstone of care.

CONCLUSION

Type 2 diabetes requires insulin resistance and -cell dysfunction. Anyone who is overweight or obese has insulin resistance, but diabetes only develops in those with insufficient insulin secretion. Lean type 2 diabetes is a clinical entity. Lean type 2 diabetics have distinct complications than fat or non-lean diabetics. T2DM patients showed greater total cholesterol, TG, LDL, and NEFA while having decreased HDL. Overweight/obese levels were much greater than lean ones. HDL values were much higher in obese persons compared to lean patients (4.42 1.6 vs 7.88 3.22), indicating that obese diabetics had much lower insulin sensitivity than non-obese diabetics. BMI, WC, W:H, TG, LDL, NEFA, and TG:HDL had positive associations, but HDL had negative correlations. Normal BMI, WC patients have abnormal lipids and IR. T2DM causes dyslipidemia and IR in obese and lean individuals. Therapists should advise diabetic patients on nutrition and exercise to manage weight.

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