RESEARCH PAPER

Metabolic Profile of Lean, Overweight and Obese Patients with Type 2 Diabetes Mellitus: A Comparative Study from Uttarakhand

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ABSTRACT

Background: Type 2 Diabetes Mellitus (T2DM) is a common metabolic disorder that can occur in individuals with different body mass index (BMI) categories. Although obesity is a well-known risk factor for diabetes, many people develop T2DM despite having a normal BMI. This study was conducted to compare metabolic characteristics, serum C-peptide levels and insulin resistance among lean, overweight and obese patients with T2DM. A hospital-based comparative cross-sectional study was carried out on 300 patients with T2DM and 200 healthy controls. Diabetic patients were categorized into lean, overweight and obese groups according to Asian Indian BMI criteria. Anthropometric measurements, fasting blood glucose, HbA1c, fasting insulin, serum C-peptide and lipid profile were assessed. Insulin resistance was estimated using HOMA-IR. Significant differences were observed in anthropometric and biochemical parameters among the three diabetic groups ($p<0.05$). HOMA-IR, fasting insulin, serum C-peptide, total cholesterol and triglyceride levels were highest in obese patients and lowest in lean patients. HDL cholesterol showed a decreasing trend with increasing BMI. Obese patients had the greatest metabolic abnormalities. However, lean diabetic patients also showed significant metabolic disturbances when compared with healthy controls. The study demonstrated distinct metabolic differences among lean, overweight and obese patients with T2DM. While obesity was associated with greater metabolic abnormalities, lean diabetic patients also showed significant metabolic alterations, highlighting the importance of BMI-based metabolic assessment in the management of T2DM.

Keywords: Type 2 Diabetes Mellitus, Lean T2DM, C-peptide, Insulin Resistance, BMI
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Introduction-

Type 2 Diabetes Mellitus (T2DM) is a heterogeneous metabolic disorder marked by persistent hyperglycemia due to impairments in insulin secretion, insulin action, or a combination of both. While obesity is recognized as a significant risk factor for T2DM, the clinical manifestations of the disease can differ greatly among individuals. In India, a considerable number of patients develop T2DM even with a normal body mass index, highlighting the variety of diabetic phenotypes and the need for phenotype-specific evaluation (1,2,7). Body mass index (BMI) is commonly used to categorize individuals into lean, overweight, and obese. Previous research has indicated that body composition affects glucose metabolism, insulin

sensitivity, and cardiovascular risk factors. Lean patients with type 2 diabetes mellitus often exhibit impaired β-cell function, while those who are overweight or obese are more prone to exhibit insulin resistance and related metabolic disorders (3). The Indian population is known to possess unique metabolic characteristics, often referred to as the "Asian Indian phenotype," which includes increased abdominal adiposity, insulin resistance and a higher susceptibility to diabetes and cardiovascular disease at relatively lower BMI levels. As a result, metabolic disturbances may differ significantly across various BMI categories of patients with T2DM (4). The population of India is recognized for its distinct metabolic characteristics, commonly termed the "Asian Indian phenotype." This phenotype is characterized by increased abdominal fat, insulin resistance and an increased v susceptibility to diabetes and cardiovascular diseases, even at comparatively lower BMI levels. As a result, metabolic disturbances may vary considerably among different BMI categories of individuals with T2DM (4). Insulin resistance plays a crucial role in determining glycemic control and the progression of T2DM. The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) is a well-recognized surrogate marker for evaluating insulin resistance and has been widely utilized in both epidemiological and clinical research. Furthermore, serum C-peptide acts as a measure of endogenous insulin secretion and the activity of pancreatic β-cells. When combined with lipid profile parameters, these markers offer significant insights into the metabolic condition of patients with diabetes (5,6). Identifying the variations in metabolic characteristics among lean, overweight and obese patients with T2DM may improve understanding of disease heterogeneity and help in developing individualized management strategies. However, data comparing these metabolic phenotypes in the Uttarakhand population remain limited. Therefore, the present study was undertaken to compare the metabolic profile, serum C-peptide levels and insulin resistance among lean, overweight and obese patients with T2DM attending a tertiary care center in Uttarakhand.

Aim – To compare the metabolic profile of lean, overweight and obese patients with Type 2 Diabetes Mellitus in Uttarakhand.

Objective-1. To compare demographic and anthropometric characteristics among lean, overweight and obese T2DM patients.

2. To compare serum C-peptide & HOMA-IR levels among lean, overweight and obese T2DM patients.

3. To compare diabetic groups with healthy controls

Material & methods-

The current research was a hospital-based comparative cross-sectional observational study carried out in the Department of Biochemistry at S.G.R.R. Medical College, associated with Shri Mahant Indiresh Hospital in Dehradun, Uttarakhand. After obtained Institutional Ethical Committee approval from S.G.R.R ethical committee (IEC No. SGRR/IEC/07/23), this study aimed to assess and compare the anthropometric and metabolic characteristics of lean, overweight, and obese patients diagnosed with T2DM. A total of 400 individuals with T2DM were screened throughout the duration of the study. After following the inclusion and exclusion criteria, a total of 300 eligible diabetic patients were included into the final analysis with 200 healthy controls. Informed written consent was obtained from both the cases and controls. The study included patients aged between 18 and 60 years who had confirmed cases of type 2 diabetes. Patients with the following conditions were excluded: Type 1 diabetes, Gestational diabetes, Secondary diabetes, chronic kidney disease (CKD), Chronic liver disease (CLD), and Diabetic emergencies. A comprehensive history of each patient, including the duration of diabetes and medication, was collected. Anthropometric measurements, such as height, weight, waist circumference, hip circumference and blood pressure, were recorded in accordance with standard procedures. The Body Mass Index (BMI) is determined by dividing weight in kilograms by the square of height in meters (kg/m^2). Patients diagnosed with Type 2 Diabetes Mellitus were classified into lean, overweight and obese categories based on the revised Asian Indian guidelines (3). Individuals with a BMI <23 kg/m^2 were considered lean, those with a BMI ranging from 23 to 24.9 kg/m^2 were overweight and those with BMI ≥25 kg/m^2 were classified as obese. Central obesity is characterized by a waist circumference exceeding 90 cm in males and 80 cm in

females **(8)**.5 ml blood sample was taken from each subject after a period of overnight fasting of 8 hours & fasting blood glucose, HbA1c, fasting insulin, serum C-peptide and lipid profile parameters including total cholesterol, triglycerides and HDL-cholesterol were analyzed. Serum lipid parameters were estimated by spectrophotometric methods. Fasting plasma glucose was measured using the hexokinase method. HbA1c estimation was performed by high-performance liquid chromatography (HPLC). Serum insulin and C-peptide levels were measured using a chemiluminescent immunoassay (CLIA) technique. Insulin resistance was assessed using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) formula: HOMA-IR = [Fasting Blood Glucose (mg/dL) × Fasting Insulin (μIU/mL)] / 405 **(9).** Higher HOMA-IR values indicate greater insulin resistance. Based on the study by Gayoso-Diz et al., a HOMA-IR cut-off value of ≥2.77 was used to express insulin resistance in the current study **(10).** Statistical analysis was performed using SPSS (version 23.0). Continuous variables values were expressed as mean + standard deviation. Comparison of the continuous variable were perform using ANOVA. P- value < 0.05 considered as statistically significant while <0.001 considered as highly significant.

Results-

A total of 300 patients diagnosed with T2DM were included in the study, comprising 150 individuals classified as lean, 75 categorized as overweight, and 75 identified as obese, in addition to 200 healthy control subjects. The baseline demographic, anthropometric and biochemical analyses of the study population were conducted.

Table-1

Baseline Demographic and Anthropometric Characteristic of the study participants

Characteristic	**Lean T2DM (150)**	**Overweight T2DM (75)**	**Obese T2DM (75)**	**p-value**
Age (Years)	46.2 ± 9.1	50.1±8.9	52 ± 7.4	0.03*
Sex- Male Female	92 58	33 42	26 49	
Weight (kg)	55.4 ± 6.2	74.6 ± 9.2	90.6 ± 12.3	<0.001**
Height (cm)	165.1 ± 6.8	163.9 ± 6.9	164.1 ± 5.2	0.42 (N.S)
BMI (Kg/m^2)	20.3 ± 1.6	23.9± 0.8	32.7 ± 5.1	<0.001**
Waist Circumference (cm)	79.6 ± 6.8	94.7 ± 8.1	101.2 ± 9.7	<0.001**
Hip Circumference (cm)	86.2 ± 8.9	96.2. ± 9.4	103 ± 9.4	<0.001**
Systolic B.P (mmHg)	125 ±15	140 ± 20	150 ± 20	<0.001**
Diastolic B.P (mmHg)	80 ± 10	90 ± 10	90 ± 15	<0.05*
Duration of Diabetes(years)	5.1 ± 3.2	7.2 ± 4.1	9.1 ± 4.7	<0.05*

p < 0.05 considered as statistically significant (*).
p <0.001 considered as statistically highly significant (**).
N. S=Not significant

Demographic characteristic & anthropometric measurement of lean, overweight & obese T2DM patients were shown in table-1. There was statistically significant difference (p value <0.05) shown in age, BMI, Systolic & Diastolic blood pressure, duration of diabetes, hip & waist circumference between all three groups. In the case of gender distribution, male female ratio in lean, overweight & obese T2DM were 92/58, 33/42 & 26/49 respectively.

Table-2

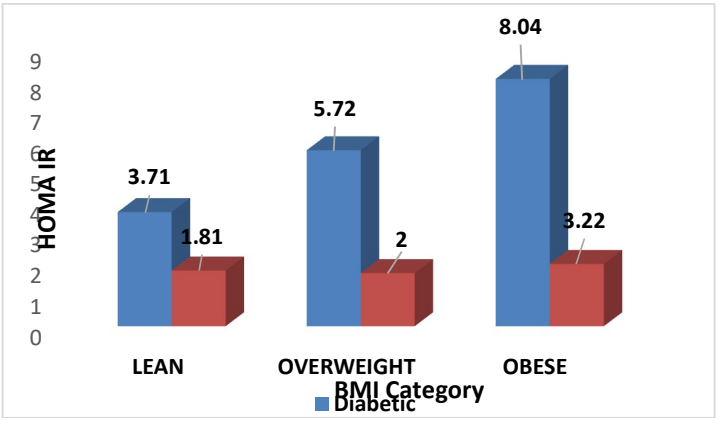
Biochemical characteristic Lean, Overweight and Obese T2DM patients

Parameter	**Lean T2DM (150)**	**Non lean (Overwe**
Fasting Blood Glucose	200.2 ± 45.19	165.01 ±
Fasting Insulin	9.2 ± 3.5	14.07 ± 4

Fasting C-Peptide	1.52 ± 0.53	2.7±0.64
HOMA-IR	3.71 ± 0.74	5.72 ± 2.07
HbA1C	8.20 ± 1.64	7.54 ± 1.0
Cholesterol	182.94 ± 43.63	200.15 ± 39.6
Triglyceride	177.03 ± 50.40	206.15 ± 63.1
HDL	40.98 ± 6.12	39.08 ± 6.74

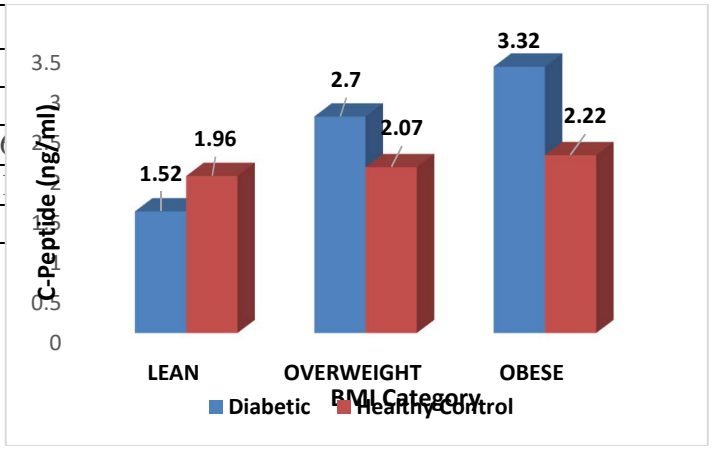
$p < 0.05$ considered as statistically significant (*).
$p < 0.001$ considered as statistically highly significant (**).
N. S=Not significant

Biochemical profile of lean, overweight & obese T2DM patients were shown in table no. 2. Fasting blood sugar, Cholesterol, Triglycerides, HDL, HbA1c, C peptide, insulin & HOMA IR value were shown statistically significant difference (p value <0.05) between all three groups.



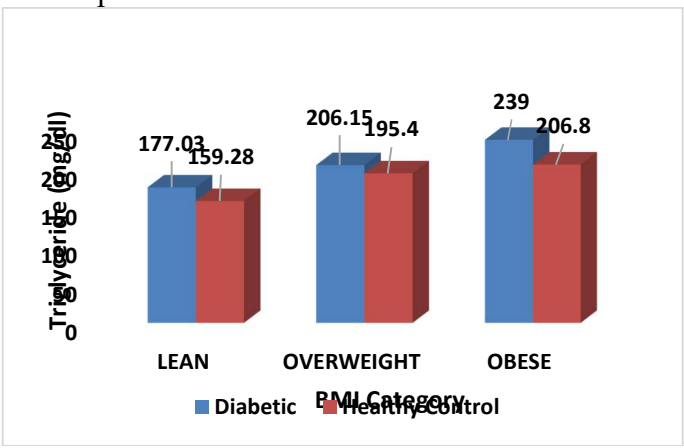
Bar graph-1: Comparison of HOMA IR among Lean, overweight & obese T2DM patients with Healthy controls

Bar graph 1 shows the comparison of HOMA-IR among Lean, Overweight and Obese T2DM patients with healthy controls. HOMA-IR levels were higher in diabetic patients as compared to healthy controls in all three groups. The highest HOMA-IR values were observed in obese T2DM patients, followed by overweight and lean T2DM groups.



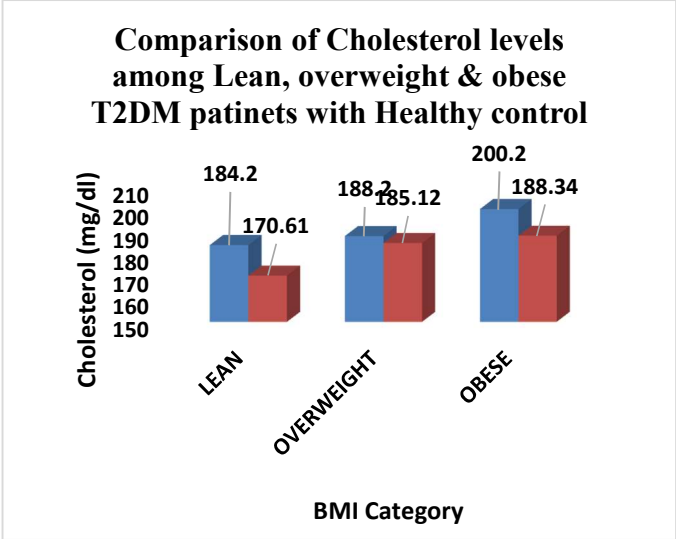
Bar graph-2: Comparison of C-peptide levels among Lean, overweight & obese T2DM patients with Healthy controls

Bar graph 2 shows the comparison of C-peptide levels among Lean, Overweight and Obese T2DM patients with healthy controls. C-peptide levels were higher in overweight and obese T2DM patients as compared to healthy controls, while lean T2DM patients showed lower C-peptide levels than healthy controls. The highest C-peptide levels were observed in obese T2DM patients.



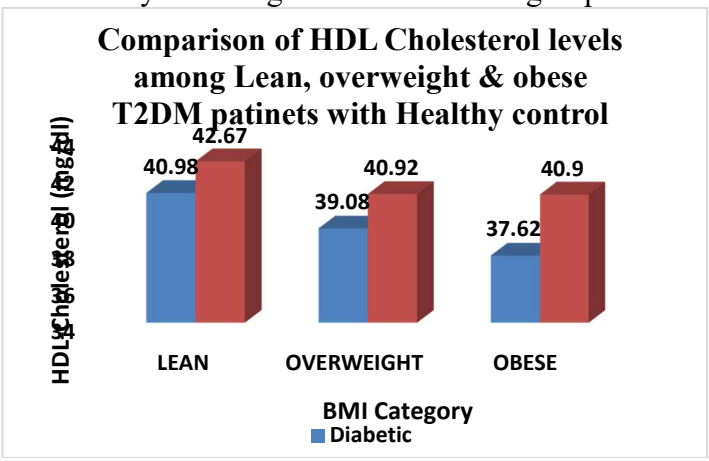
Bar graph-3: Comparison of Triglyceride levels among Lean, overweight & obese T2DM patients with Healthy controls

Bar graph 3 shows the comparison of triglyceride levels among Lean, Overweight and Obese T2DM patients with healthy controls. Triglyceride levels were higher in T2DM patients as compared to healthy controls in all three groups. The highest triglyceride levels were observed in obese T2DM patients, followed by overweight and lean T2DM groups.



Bar graph-4: Comparison of Cholesterol levels among Lean, overweight & obese T2DM patients with Healthy controls

Bar graph 4 shows the comparison of cholesterol levels among Lean, Overweight and Obese T2DM patients with healthy controls. Cholesterol levels were higher in T2DM patients as compared to healthy controls in all three groups. The highest cholesterol levels were observed in obese T2DM patients, followed by overweight and lean T2DM groups.



Bar graph-5: Comparison of HDL Cholesterol levels among Lean, overweight & obese T2DM patients with Healthy controls

Bar graph 5 shows the comparison of HDL cholesterol levels among Lean, Overweight and Obese T2DM patients with healthy controls. HDL cholesterol levels were lower in T2DM patients as compared to healthy controls in all three groups. The lowest HDL cholesterol levels were observed in obese T2DM patients, followed by overweight and lean T2DM groups.

DISCUSSION

The present study was conducted at Shri Mahant Indiresh Hospital, Dehradun, to evaluate metabolic differences among lean, overweight, and obese patients with Type 2 Diabetes Mellitus (T2DM). In the current study, body weight, BMI, waist circumference, and hip circumference showed a significant increase from lean to overweight and obese diabetic patients. These findings are consistent with the observations of Misra et al. (3), who reported that increasing adiposity among Asian Indians is associated with a higher metabolic risk and greater insulin resistance. Similar observations were reported by Asegaonkar SB et al. (11), who demonstrated significantly higher BMI, waist circumference, hip circumference, and visceral adiposity in overweight and obese T2DM patients compared with lean diabetic subjects and healthy controls. These findings support the role of excess adiposity in worsening metabolic health among individuals with T2DM.In the present study, fasting insulin levels increased progressively with increasing BMI, with the highest values observed in obese diabetic patients. Comparable findings were reported by Mohan et al. (12), who observed significantly higher fasting insulin concentrations among obese diabetic individuals compared with lean diabetic subjects. Singh et al. (6) also suggested that obesity is associated with compensatory hyperinsulinemia resulting from increasing insulin resistance.One of the important findings of the present study was the progressive rise in HOMA-IR values from lean to overweight and obese diabetic patients. Obese diabetic patients exhibited the highest degree of insulin resistance. These findings are in agreement with those reported by Singh et al. (6), who observed significantly elevated HOMA-IR values among obese Indian patients with T2DM. Similar results were reported by Gayoso-Diz et al. (10), who identified obesity as an important predictor of insulin resistance and demonstrated the usefulness of HOMA-IR as a reliable

marker of insulin sensitivity. Bautista FP et al. (13) reported that obese individuals had a greater possibility of developing insulin resistance and a lower probability of preserving normal β-cell function when compared with lean individuals. The findings of the present study are consistent with these observations and further emphasize the adverse metabolic impact of increasing BMI in patients with T2DM. Serum C-peptide levels showed a progressive increase from lean to overweight and obese diabetic patients in the present study. The highest C-peptide concentrations were observed among obese diabetic subjects, suggesting increased endogenous insulin secretion in response to insulin resistance. Similar findings were reported by S. Gadre et al. (14), who documented a positive association between BMI and serum C-peptide levels. Anoop et al. (15) also reported significantly higher C-peptide concentrations among overweight and obese individuals with T2DM, indicating compensatory β-cell activity associated with increasing insulin resistance. Comparable observations were reported by Hardeep Singh Deep et al. (16), who found significantly higher C-peptide levels in obese diabetic patients compared with non-obese diabetic subjects. The authors suggested that elevated C-peptide levels accompanied by increased fasting blood glucose may reflect underlying insulin resistance. The findings of the present study are in agreement with these observations and further support the relationship between obesity, hyperinsulinemia and insulin resistance. The present study also demonstrated significant alterations in lipid profile parameters across different BMI categories. Total cholesterol and triglyceride levels increased progressively from lean to obese diabetic patients and remained consistently higher than those observed in healthy controls. In contrast, HDL-cholesterol levels showed a gradual decline with increasing BMI, with obese diabetic patients exhibiting the lowest HDL concentrations. Similar findings were reported by Asegaonkar SB et al. (11), who observed higher total cholesterol and triglyceride levels along with lower HDL concentrations among obese T2DM patients compared with lean diabetic subjects and healthy controls. Mooradian (17) also described elevated triglyceride levels as a characteristic feature of diabetic dyslipidemia. Similarly, Sandhya Shukla et al. (18) reported significantly higher triglyceride and cholesterol levels together with reduced HDL cholesterol in obese diabetic individuals. Although fasting blood glucose and HbA1c levels were elevated in all diabetic groups, obese patients demonstrated a more adverse metabolic profile characterized by greater insulin resistance, higher serum C-peptide concentrations and more pronounced dyslipidemia. However, it is important to note that lean diabetic patients also showed significant metabolic abnormalities when compared with healthy controls. These findings indicate that BMI has a substantial influence on the metabolic phenotype of patients with Type 2 Diabetes Mellitus and highlight that lean T2DM represents a distinct clinical entity requiring careful metabolic assessment and management.

Conclusion-

The current study showed significant metabolic differences in lean, overweight and obese patients with Type 2 Diabetes Mellitus. While obese diabetic patients exhibited the highest insulin resistance, serum C-peptide levels and lipid abnormalities, lean diabetic patients also showed considerable metabolic disturbances when compared with healthy controls. These findings indicated that Type 2 Diabetes Mellitus in lean individuals represents a unique metabolic phenotype and should not be considered a metabolically benign condition. Consequently, evaluating insulin resistance, serum C-peptide, and lipid profiles may prove beneficial in identifying high-risk individuals and enhancing the clinical management of patients across various BMI categories.

Limitations:

The research was carried out at one tertiary care hospital therefore the results may not be applicable to all populations. Furthermore, lifestyle factors and treatment-related variables that could affect metabolic parameters were not thoroughly evaluated.

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