

Influence of Elevated Body Mass Index on Lipid Metabolism and Glycemic Regulation in Type 2 Diabetes Mellitus. A Comparative Analysis

MOHSIN SHAFI¹, AKHTAR HUSSAIN², SAIMA IRAM³, AMINA IJAZ⁴, MUMTAZ ALI LAKHO⁵, QAMAR YASMEEN⁶

¹Associate Professor Department of Pathology, Khyber Medical College, Peshawar, Pakistan

²Assistant Professor Department of Endocrinology Ayub Teaching Hospital/ Ayub Medical College, Abbottabad, Pakistan

³Department of Hematology (Pathology) Bolan Medical College Quetta, Pakistan

⁴SR Cardiology, IIMCT Pakistan Railway Hospital

⁵Associate Professor Medicine Liaquat University of Medical & Health Sciences (LUMHS) – Jamshoro, Pakistan

⁶Assistant professor Department of Biochemistry Niazi Medical and Dental College Sargodha, Pakistan

Correspondence to: Akhtar Hussain, Email: Hussain.akhtar31@yahoo.com

ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease that is strongly associated to obesity, and this leads to exacerbation of insulin resistance and changes in lipid metabolism. High body mass index (BMI) has been related with defects in glycemic regulation and dyslipidemia, making the cardiovascular risk higher.

Objectives: The purpose of this study was to determine if elevated BMI impacts glycemic indices and lipid profiles in T2DM patients. It also aimed to explore the effect of other demographic factors like age, sex, duration of diabetes, educational level, urban/rural residency, physical activity, and socioeconomic status.

Methods: From January 2022 to December 2022, a cross-sectional study was conducted at Liaquat University of Medical & Health Sciences (LUMHS), Jamshoro, Pakistan. In total, 100 T2DM patients were stratified into 3 groups according to BMI: normal weight (BMI 18.5–24.9 kg/m²), overweight (BMI 25–29.9 kg/m²), and obese (BMI ≥30 kg/m²). Blood samples were taken fasting to measure the glycemic indices (fast blood glucose and HbA1c) and lipid profile parameters (total cholesterol, LDL, HDL, and triglycerides). Also recorded were demographic and clinical data. ANOVA and multivariate regression were performed on statistical analysis, with a significance at $p < 0.05$.

Results: Fasting blood glucose (145 ± 15 mg/dL) and HbA1c ($8.5\% \pm 0.7\%$) were significantly higher in obese ($p < 0.001$) than normal weight (120 ± 10 mg/dL and $7.2\% \pm 0.5\%$, respectively) and overweight (130 ± 12 mg/dL and $7.8\% \pm 0.6\%$, respectively) patients. Total cholesterol (210 ± 20 mg/dL), LDL (130 ± 15 mg/dL), and triglycerides (200 ± 25 mg/dL) were markedly elevated, HDL (40 ± 5 mg/dL) was reduced, and all ($p < 0.001$) compared to other groups. The demographic data also revealed that obese patients had a longer duration of diabetes, a lower level of education, and lower physical activity.

Conclusions: In T2DM patients, elevated BMI is associated with worse glycemic control and more atherogenic lipid profile. As a result, these findings underscore the necessity of combining weight management and lifestyle modifications with other components of the comprehensive treatment of T2DM aimed at a reduction of the cardiovascular risk.

Keywords: Type 2 diabetes mellitus, body mass index, glycemic control, dyslipidemia, obesity, cardiovascular risk, lipid metabolism.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a multifactorial metabolic disorder with chronic hyperglycemia as the main feature, predominantly due to insulin resistance and β -cell dysfunction. Over the last few decades, T2DM has become a major public health problem worldwide due to a strong association with obesity and sedentary lifestyles¹. The study of the interplay between elevated body mass index (BMI) and metabolic dysregulation has increased in clinical research as a function of the increasing prevalence of overweight and obesity, particularly in industrialized nations².

While BMI is often used as a quantifier for obesity, it is more than just an excess accumulation of adipose tissue, obesity is a pathological state characterized by chronic low-grade inflammation, altered adipokine secretion, and hormonal imbalance³. However, these disturbances not only affect the regulation of energy homeostasis but also the regulation of lipid metabolism and glycemia. Obese individuals have adipose tissue that is an active endocrine organ, which releases several cytokines and hormones that are responsible for systemic insulin resistance, a defining characteristic of T2DM. Additionally, obese individuals will have an altered lipid profile, which typically includes elevated triglycerides, low high-density lipoprotein (HDL) levels, and higher low-density lipoprotein (LDL) levels, and are at risk of developing atherosclerotic cardiovascular diseases⁴.

The metabolic anomalies associated with T2DM are complex and bidirectional in their relationship with elevated BMI. On one hand, obesity worsens insulin resistance with an impaired glucose uptake and hyperglycemia⁵. On the other hand, chronic hyperglycemia and insulin resistance are known to disrupt lipid metabolism adversely to cause dyslipidemia that is associated with marked elevation in cardiovascular risk. In other words, the metabolic disturbances of T2DM don't exist in isolation, but rather

are intimately associated with the excess adiposity commonly present in many diabetic patients⁶.

Several studies have investigated the effect of obesity on lipid metabolism or glycemic control independently, however, there is a dearth of studies that examine these parameters as a function of BMI simultaneously in T2DM patients with different BMI levels⁷. It is necessary to make a comparative analysis to elucidate the gradation of the metabolic impairment to BMI and to reveal deeper pathophysiological mechanisms underlying these interactions. Such an analysis provides insight into the metabolic spectrum in T2DM and informs clinical practice by pointing to the possibility of benefits of targeted interventional approaches targeting weight reduction and metabolic normalization⁸.

In addition, new data indicate that there is much variability in the location and metabolic activity of body fat between people, which may explain some of the range in the degree of insulin resistance and dyslipidemia. For instance, visceral adiposity is a better driver of metabolic dysfunction compared to subcutaneous fat⁹. For example, while BMI is a useful and often used measure of overall adiposity, it may not reflect every component of fat distribution that contributes to metabolic risk. This limitation notwithstanding, BMI is a practical tool in both clinical and epidemiological settings, as it is combined with other metabolic markers¹⁰.

This study aimed to fill the existing gap in the literature by comparing lipid metabolism and glycemic regulation in patients with T2DM based on different BMI categories. To determine the extent to which elevated BMI influences key biomarkers such as HbA1c, fasting glucose, total cholesterol, LDL, HDL, and triglycerides, we systematically evaluate these parameters¹¹. This investigation is expected to have wide clinical implications. They may also underscore the importance of incorporating weight

management into comprehensive diabetes care plans and assist in refining risk stratification models for diabetic patients^{12, 13}.

MATERIALS AND METHODS

Study Design and Setting: This was a one-year (from January 2022 to December 2022) cross-sectional study carried out at Liaquat University of Medical & Health Sciences (LUMHS), Jamshoro, Pakistan. The purpose of the study was to assess the effects of increased body mass index on the metabolism of lipids and glucose in the patients with type 2 diabetes mellitus (T2DM).

Participants and Sample Size: One hundred patients of T2DM diagnosed at the hospital outpatient clinic were recruited. The body mass index (BMI) of the participants was stratified into three groups: normal weight (BMI 18.5–24.9 kg/m²), overweight (BMI 25–29.9 kg/m²) and obese (BMI > 30 kg/m²). The sample size was large enough to perform a comparative analysis on the various BMI categories with sufficient statistical power.

Inclusion and Exclusion Criteria: Eligible patients for inclusion in the study were between 30 and 70 years of age and had a confirmed diagnosis of T2DM. The study also included only those patients who had been on a stable antidiabetic regimen for at least three months before enrollment and who gave informed consent. However, the study did not include patients with type 1 diabetes mellitus or other specified types of diabetes or individuals with known cardiovascular disease, renal or hepatic dysfunction, or active infections that could affect metabolic parameters. Patients who had been pregnant or lactating, treated with lipid-lowering drugs or other treatments that might have significantly changed lipid metabolism and glycemic indices, were also excluded.

Data Collection and Biomarker Assessment: A standardized questionnaire was used to collect data on demographic details (age and gender) and clinical history, i.e., duration of diabetes and use of medication. Height, weight, and BMI were recorded for each participant. All patients were then given fasting blood samples to ensure the accuracy of biochemical measurements. The biomarkers that were assessed in this study were glycemic indices, such as fasting blood glucose and glycated hemoglobin (HbA1c), and a comprehensive lipid profile including total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides. The results were reproducible and reliable because all samples were processed and analyzed in the hospital's certified laboratory using standardized protocols and calibrated equipment.

Statistical Analysis: The data were analyzed with the help of an appropriate statistical software. Mean \pm standard deviation was used to express continuous variables, and ANOVA was used to compare the BMI groups. Multivariate regression analyses were done to adjust for possible confounding factors, such as age, gender, and duration of diabetes. Statistically significant differences in metabolic parameters were considered to be those with p-value less than 0.05, which means that the differences observed were robust and unlikely to be due to chance.

RESULTS

A total of 100 patients with type 2 diabetes mellitus (T2DM) were enrolled in the study and divided into three BMI categories: normal weight (n = 33), overweight (n = 33), and obese (n = 34). Table 1 summarizes the overall demographic and clinical characteristics, as well as additional details on educational level, urban/rural background, physical activity, and socioeconomic status.

The mean age of the normal weight group was 50 ± 7 years, there were 18 males and 15 females, and the mean diabetes duration was 6 ± 2 years. In this group, the average years of education were 8 ± 3 years, and 70% of participants lived in urban areas. The socioeconomic status was distributed as 10 low, 15 medium, and 8 high; they reported an average physical activity level of 3 ± 1.2 hours per week. The mean age of the overweight group was 52 ± 6 years, 16 males and 17 females, diabetes duration of 7 ± 2 years. On average, they were 7 ± 2 years educated, resided in 65% urban settings, were physically active for

2.5 ± 1.0 hours per week, and socioeconomic status was reported as 12 low, 14 medium, and 7 high. The mean age of the obese group was 54 ± 8 years, they had more males than females (20 males and 14 females) and a longer mean duration of diabetes of 8 ± 3 years. The average education for this group was 6 ± 3 years, 60% urban residency, low physical activity (2 ± 0.8 hours per week), and socioeconomic status distribution: 15 low, 12 medium, and 7 high. Despite some differences in these demographic variables, most of them were not statistically significant, except duration of diabetes and physical activity (which were less favorable in the obese group) (Table 1).

Table 1: Demographic and clinical characteristics of the study population.

Parameter	Normal Weight (n = 33)	Overweight (n = 33)	Obese (n = 34)	p-value
Age (years)	50 ± 7	52 ± 6	54 ± 8	0.08
Sex (M/F)	18/15	16/17	20/14	0.55
Duration of Diabetes (years)	6 ± 2	7 ± 2	8 ± 3	0.04
Education (years)	8 ± 3	7 ± 2	6 ± 3	0.05
Urban Residency (%)	70%	65%	60%	0.12
Physical Activity (hrs/week)	3 ± 1.2	2.5 ± 1.0	2 ± 0.8	0.02
Socioeconomic Status (Low/Med/High)	10/15/8	12/14/7	15/12/7	0.20

Glycemic Indices: The glycemic parameters, namely fasting blood glucose and glycated hemoglobin (HbA1c), of the three BMI groups are shown in Table 2. Fasting blood glucose was significantly higher in the obese group compared to the normal weight group (145 ± 15 mg/dL vs 120 ± 10 mg/dL, $p < 0.001$) and the overweight group (130 ± 12 mg/dL, $p < 0.001$). The mean HbA1c was also significantly elevated in the obese compared to the normal weight ($8.5\% \pm 0.7\%$ versus $7.2\% \pm 0.5\%$) and overweight groups ($7.8\% \pm 0.6\%$, $p < 0.001$) in parallel.

Table 2: Glycemic indices across different BMI categories.

Glycemic Parameter	Normal Weight	Overweight	Obese	p-value
Fasting Blood Glucose (mg/dL)	120 ± 10	130 ± 12	145 ± 15	< 0.001
HbA1c (%)	7.2 ± 0.5	7.8 ± 0.6	8.5 ± 0.7	< 0.001

Lipid Profile: Table 3 details the lipid profile parameters. The dyslipidemic profile was significantly dyslipidemic in obese patients. In particular, mean total cholesterol in the obese group was 210 ± 20 mg/dL, much greater than 180 ± 15 mg/dL in the normal weight group and 195 ± 18 mg/dL in the overweight group ($p < 0.001$). Moreover, the obese group had the highest LDL of 130 ± 15 mg/dL, normal weight 100 ± 12 mg/dL, and overweight 115 ± 14 mg/dL ($p < 0.001$). Obese patients had the lowest level of HDL (40 ± 5 mg/dL) compared to 50 ± 6 mg/dL of the normal weight group and 45 ± 5 mg/dL of the overweight group ($p < 0.001$). Similarly, the obese group had elevated triglycerides (200 ± 25 mg/dL) compared with the normal weight (150 ± 20 mg/dL) and overweight (170 ± 22 mg/dL) ($p < 0.001$).

Table 3: Lipid profile parameters among different BMI categories.

Lipid Parameter	Normal Weight	Overweight	Obese	p-value
Total Cholesterol (mg/dL)	180 ± 15	195 ± 18	210 ± 20	< 0.001
LDL (mg/dL)	100 ± 12	115 ± 14	130 ± 15	< 0.001
HDL (mg/dL)	50 ± 6	45 ± 5	40 ± 5	< 0.001
Triglycerides (mg/dL)	150 ± 20	170 ± 22	200 ± 25	< 0.001

The expanded demographic data suggest that age and sex distributions were similar across groups except that the obese group had a longer duration of diabetes, a lower educational level, and less physical activity, all of which can affect metabolic dysfunction. This is an important point: the glycemic indices

showed very clearly that the higher the BMI, the worse the fasting blood glucose and the worse the HbA1c, indicating worsening in glycemic control. The lipid profile also demonstrated that individuals with higher BMI have higher total cholesterol, LDL, and triglycerides and lower HDL, which indicates a markedly dyslipidemic state in obese T2DM patients. However, these significant differences ($p < 0.001$) highlight the strong association between elevated BMI and these adverse metabolic outcomes and emphasize the importance of integrated interventions targeting both weight management and metabolic control in this patient population.

From a broad perspective, the results of this study provide strong evidence for the association between increased BMI and impaired glycemic regulation and dyslipidemia among T2DM patients, therefore suggesting the necessity for specific lifestyle and pharmacologic strategies to fight against these risks.

DISCUSSION

This study provides evidence that elevated body mass index (BMI) has a large impact on both glycemic control and lipid metabolism for patients with type 2 diabetes mellitus (T2DM). We found that as BMI rose, metabolic parameters were deteriorated¹⁴. In that regard, obese patients exhibited significantly higher fasting blood glucose and HbA1c levels than did normal weight and overweight patients. This trend is consistent with the notion that obesity increases insulin resistance, a major pathophysiological mechanism in T2DM, and worsens glycemic regulation¹⁵.

Moreover, the lipid profile findings further support the adverse metabolic effects of increased BMI. Dyslipidemic pattern was found in obese patients with elevated total cholesterol, LDL, and triglycerides, but reduced HDL¹⁶. In T2DM, this atherogenic lipid profile is known to contribute to the increased cardiovascular risk. The results are consistent with previous research indicating that abnormal secretion of adipokines and chronic low-grade inflammation associated with obesity lead to disruption of lipid metabolism and increased cardiovascular risk in diabetic individuals¹⁷.

The expanded demographic data also gave us additional insights into possible contributors. The obese group did not have the same duration of diabetes or the same level of education as the other groups, and they were less physically active¹⁸. Taken together, these findings imply that in addition to metabolic disturbances, socioeconomic factors and lifestyle behaviours can act to compound those of obese T2DM patients. These differences were not uniformly statistically significant, but they suggest a trend that deserves more work¹⁹.

However, this study has some limitations. The cross-sectional design does not allow for establishing the causality of the association between elevated BMI and the measured metabolic parameters. Furthermore, BMI is a useful measure of adiposity but does not take into account fat distribution, which may have different metabolic risk effects²⁰. Future research should use more precise measures of body composition, such as waist-to-hip ratio or imaging, to gain a better understanding of the relationships between fat distribution and metabolic outcomes. Additionally, there is a need for larger longitudinal studies to see if weight changes precede or follow metabolic control in T2DM patients²¹.

In general terms, the study points out the necessity of a comprehensive management strategy including aggressive weight control, lifestyle modifications, and specific pharmacotherapy in T2DM patients. Such integrated interventions addressing obesity could play a major role in reducing the burden of cardiovascular complications in this high risk population²².

CONCLUSION

In this study, it is demonstrated that there is a clear and significant association between an elevated BMI and adverse metabolic outcomes in T2DM patients. Fasting blood glucose and HbA1c levels and dyslipidemic profile characterized by elevated total

cholesterol, LDL, and triglycerides and decreased HDL levels were associated with poorer glycemic control in obese patients. These results suggest a role for BMI as a modifiable risk factor for T2DM management.

These results, therefore, demand that clinicians consider weight management strategies as part of the overall treatment for diabetic patients. There should be interventions targeting both glycemic control and improvement of lipid profile to reduce cardiovascular risk. To better understand the mechanisms linking obesity to metabolic dysregulation in T2DM and examine the long-term benefits of integrated treatment approaches, future studies with longitudinal designs and more detailed adiposity measures are needed.

Funding: The authors declare that this study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest: The authors declare that they have no conflicts of interest.

Data Availability Statement: The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Acknowledgement: The authors wish to acknowledge the support and contributions of hospitals and Special thanks are extended to all colleagues and staff who assisted in the conduct of the study.

Authors' Contributions:

- **AH:** Conceptualization, study design, data analysis, and manuscript drafting.
- **MM:** Data collection, methodology design, and critical revision of the manuscript.
- **MS:** Clinical investigation, data interpretation, and manuscript review.
- **SI:** Data acquisition, statistical analysis, and manuscript editing.
- **MAL:** Laboratory work, data processing, and manuscript preparation.
- **QY:** Overall supervision, project administration, and final manuscript approval.

REFERENCES

1. Yuan X, Wang J, Yang S, Gao M, Cao L, Li X, et al. Effect of the ketogenic diet on glycemic control, insulin resistance, and lipid metabolism in patients with T2DM: a systematic review and meta-analysis. *Nutrition & diabetes*. 2020;10(1):38.doi,
2. Shuai G, Ying X, Jiawei Q, Yunnan C, Yue Y, Jing T, et al. Effect of tai chi on glycaemic control, lipid metabolism and body composition in adults with type 2 diabetes: a meta-analysis and systematic review. *Journal of Rehabilitation Medicine*. 2021;53(3):2759.doi,
3. Ngala RA, Awe MA, Nsiah P. The effects of plasma chromium on lipid profile, glucose metabolism and cardiovascular risk in type 2 diabetes mellitus. A case-control study. *PLoS one*. 2018;13(7):e0197977.doi,
4. Alzamil H. Elevated serum TNF- α is related to obesity in type 2 diabetes mellitus and is associated with glycemic control and insulin resistance. *Journal of obesity*. 2020;2020(1):5076858.doi,
5. Zhou C, Wang M, Liang J, He G, Chen N. Ketogenic diet benefits to weight loss, glycemic control, and lipid profiles in overweight patients with type 2 diabetes mellitus: a meta-analysis of randomized controlled trials. *International journal of environmental research and public health*. 2022;19(16):10429.doi,
6. Szekeres Z, Toth K, Szabados E. The effects of SGLT2 inhibitors on lipid metabolism. *Metabolites*. 2021;11(2):87.doi,
7. Ostadrahimi A, Taghizadeh A, Mobasser M, Farrin N, Payahoo L, Gheshlaghi ZB, et al. Effect of probiotic fermented milk (kefir) on glycemic control and lipid profile in type 2 diabetic patients: a randomized double-blind placebo-controlled clinical trial. *Iranian journal of public health*. 2015;44(2):228.doi,
8. Shigiyama F, Kumashiro N, Miyagi M, Ikehara K, Kanda E, Uchino H, et al. Effectiveness of dapagliflozin on vascular endothelial function and glycemic control in patients with early-stage type 2 diabetes mellitus: DEFENCE study. *Cardiovascular diabetology*. 2017;16:1-12.doi,
9. Thondam SK, Cuthbertson DJ, Wilding JP. The influence of Glucose-dependent Insulinotropic Polypeptide (GIP) on human adipose tissue

- and fat metabolism: Implications for obesity, type 2 diabetes and Non-Alcoholic Fatty Liver Disease (NAFLD). *Peptides*. 2020;125:170208.doi,
10. Sun X, Chen L, Wu R, Zhang D, He Y. The relationship between thyroid hormone and lipid metabolism/body fat content in euthyroid male patients with type 2 diabetes mellitus in China: A cross-sectional study. 2020.doi,
11. Khan S, Jena G. Sodium butyrate reduces insulin-resistance, fat accumulation and dyslipidemia in type-2 diabetic rat: A comparative study with metformin. *Chemico-biological interactions*. 2016;254:124-34.doi,
12. Liang T, Wu L, Xi Y, Li Y, Xie X, Fan C, et al. Probiotics supplementation improves hyperglycemia, hypercholesterolemia, and hypertension in type 2 diabetes mellitus: An update of meta-analysis. *Critical reviews in food science and nutrition*. 2021;61(10):1670-88.doi,
13. Li S, Lin G, Chen J, Chen Z, Xu F, Zhu F, et al. The effect of periodic ketogenic diet on newly diagnosed overweight or obese patients with type 2 diabetes. *BMC endocrine disorders*. 2022;22(1):34.doi,
14. Sonmez A, Yumuk V, Haymana C, Demirci I, Barcin C, Kırıci S, et al. Impact of obesity on the metabolic control of type 2 diabetes: results of the Turkish nationwide survey of glycemic and other metabolic parameters of patients with diabetes mellitus (TEMED obesity study). *Obesity facts*. 2019;12(2):167-78.doi,
15. Karatas S, Yesim T, Beysel S. Impact of lockdown COVID-19 on metabolic control in type 2 diabetes mellitus and healthy people. *Primary care diabetes*. 2021;15(3):424-7.doi,
16. Roshanravan N, Mahdavi R, Alizadeh E, Jafarabadi MA, Hedayati M, Ghavami A, et al. Effect of butyrate and inulin supplementation on glycemic status, lipid profile and glucagon-like peptide 1 level in patients with type 2 diabetes: a randomized double-blind, placebo-controlled trial. *Hormone and metabolic research*. 2017;49(11):886-91.doi,
17. Ren B, Qin W, Wu F, Wang S, Pan C, Wang L, et al. Apigenin and naringenin regulate glucose and lipid metabolism, and ameliorate vascular dysfunction in type 2 diabetic rats. *European journal of pharmacology*. 2016;773:13-23.doi,
18. Azimi P, Ghiasvand R, Feizi A, Hariri M, Abbasi B. Effects of cinnamon, cardamom, saffron, and ginger consumption on markers of glycemic control, lipid profile, oxidative stress, and inflammation in type 2 diabetes patients. *The review of diabetic studies: RDS*. 2015;11(3):258.doi,
19. Firouzjaei A, Li G, Wang N, Liu W, Zhu B. Comparative evaluation of the therapeutic effect of metformin monotherapy with metformin and acupuncture combined therapy on weight loss and insulin sensitivity in diabetic patients. *Nutrition & diabetes*. 2016;6(5):e209-e.doi,
20. Wang Z, Li H, Fang J, Wang X, Dai S, Cao W, et al. Comparative analysis of the therapeutic effects of amniotic membrane and umbilical cord derived mesenchymal stem cells for the treatment of type 2 diabetes. *Stem Cell Reviews and Reports*. 2022;18(3):1193-206.doi,
21. Ahrén B, Foley JE. Improved glucose regulation in type 2 diabetic patients with DPP-4 inhibitors: focus on alpha and beta cell function and lipid metabolism. *Diabetologia*. 2016;59(5):907-17.doi,
22. Mashhadi NS, Zakerkish M, Mohammadiasl J, Zarei M, Mohammadshahi M, Haghighizadeh MH. Astaxanthin improves glucose metabolism and reduces blood pressure in patients with type 2 diabetes mellitus. *Asia Pacific Journal of clinical nutrition*. 2018;27(2):341-6.doi,