E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/16.01.578

Research Article

Comparative Impact of Empagliflozin and Semaglutide on Lipid Profile in Patients with Type-2 Diabetes Mellitus: A Cross-Sectional Study

Zeemal Iqbal[1*], Muhammad Oneeb Mehboob[2], Sehrish Ijaz[3], Mazhar Murtaza[4], Sheikh Maria Qammar[5], Bushra Shaheen[6]

[1*]Senior Demonstrator, Pharmacology, Multan Medical & Dental College, Multan, Pakistan.
[2]Demonstrator, Pharmacology, Multan Medical & Dental College, Multan, Pakistan.
[3]Assistant Professor, Pharmacology, Multan Medical & Dental College, Multan, Pakistan.
[4]Assistant Professor, Forensic Medicine & Toxicology, Multan Medical & Dental College, Multan, Pakistan.
[5]Associate Professor, Pharmacology, Rashid Latif Medical College, Lahore, Pakistan.
[6]Associate Professor, Pharmacology, DG Khan Medical College, DG Khan, Pakistan.

Corresponding Author: Dr Zeemal Iqbal
Senior Demonstrator, Pharmacology, Multan Medical & Dental College, Multan, Pakistan.
Email: xeeiq181@gmail.com
Received: 14.03.2026, Revised: 08.06.2026, Accepted: 14.06.2026

ABSTRACT

Objective: To assess and compare the impact of empagliflozin and semaglutide on lipid profile indicators among patients with type 2 diabetes mellitus (T2DM).

Study design: A cross-sectional study.

Place and Duration: Ibn-e-Siena Hospital and Research Institute, Multan, from October 2025 to May 2026.

Methodology: A total of 80 patients with T2DM receiving either empagliflozin (n=40) or semaglutide (n=40) for at least six months were selected for the study through non-probability consecutive sampling. Baseline data was collected using a structured proforma. Blood samples in fasting condition were obtained for the assessment of lipid profile and glycaemic parameters in both study groups.

Results: Patients receiving semaglutide demonstrated significantly lower total cholesterol (178.6±26.9 vs. 192.4±28.7 mg/dL, p=0.030), LDL-C (104.3±20.5 vs. 118.5±22.1 mg/dL, p=0.004), triglycerides (165.2±31.8 vs. 186.7±34.5 mg/dL, p=0.005), and VLDL-C levels (33.1±6.3 vs. 37.3±6.9 mg/dL, p=0.006) in contrast to empagliflozin group. HDL-C levels were significantly higher among semaglutide users (46.8±8.1 vs. 41.2±7.6 mg/dL, p=0.002). Furthermore, semaglutide-treated patients exhibited lower HbA1c (7.4±0.9% vs. 7.9±1.0%, p=0.021) and fasting blood glucose levels (142.3±25.7 vs. 156.8±28.4 mg/dL, p=0.017).

Conclusion: Semaglutide was associated with a more favorable lipid profile and better glycaemic control compared with empagliflozin among T2DM diagnosed patients. These findings support role of semaglutide in providing additional cardiometabolic benefits in diabetic patients with concomitant dyslipidaemia.

Keywords: Type 2 Diabetes Mellitus, Semaglutide, Empagliflozin, Lipid Profile, Dyslipidaemia, LDL Cholesterol, HDL Cholesterol.

INTRODUCTION

Type 2 diabetes mellitus (T2DM), a chronic metabolic disorder, isdefined as progressive β-cell dysfunction leading to impaired insulin secretionand eventually insulin resistance[1, 2]. It has become a major global health concern due to its increasing prevalence and association with serious complications, particularly cardiovascular and renal diseases[2, 3]. Cardiovascular disease remains one of the major causes of morbidity and mortality among patients with T2DM, underscoring the importance of therapeutic approaches that go beyond blood glucose management[4].

Diabetic dyslipidaemia is a major contributor to cardiovascular complications in patients with T2DM. It is characterized by raised triglycerides levels, higher very-low-density lipoprotein (VLDL) and small dense low-density lipoprotein (sdLDL) particles aligned by reduced high-density lipoprotein cholesterol (HDL-C) levels[5]. Insulin resistance promotes increased free fatty acid release, hepatic lipid synthesis, and impaired lipoprotein

metabolism, resulting in an atherogenic lipid profile[6]. Therefore, improving lipid abnormalities represents an important therapeutic target in reducing cardiovascular risk among individuals with T2DM.

Recent advances in diabetes therapy have introduced glucose-lowering agents with additional cardiovascular and metabolic benefits, particularly sodium-glucose cotransporter-2 inhibitors (SGLT2 inhibitors) and glucagon-like peptide-1 receptor agonists (GLP-1 RAs)[7]. Empagliflozin, an SGLT2 inhibitor, reduces renal glucose reabsorption, leading to increased urinary glucose excretion and improved glycaemic control[8]. Large cardiovascular outcome trials have verified its cardioprotective and renoprotective effects in patients with T2DM[9, 10]. Additionally, empagliflozin has been reported to influence lipid metabolism through changes in body weight, energy metabolism, and lipoprotein profiles, although variations in LDL cholesterol responses have been observed among studies[11].

Semaglutide, a long-acting GLP-1 receptor agonist, enhances glucose metabolism by enhancing glucose-dependent insulin release, reducing glucagon secretion, slowing gastric emptying, and facilitating weight loss[12]. Clinical studies have substantiated its effectiveness in improving glycaemic control and reducing cardiovascular risk[13]. Moreover, GLP-1 receptor agonists have demonstrated favorable effects on lipid parameters, including reductions in total cholesterol, LDL cholesterol, triglycerides, and improvement in atherogenic lipid patterns[14].

Although both empagliflozin and semaglutide provide significant metabolic and cardiovascular benefits, their mechanisms of action differ and may result in distinct effects on lipid parameters. Previous studies have mainly evaluated their individual effects on glycaemic control, weight reduction, and cardiovascular outcomes, while direct comparative evidence regarding their impact on lipid profile remains limited. Therefore, this study was planned to compare the effects of empagliflozin and semaglutide on lipid profile parameters, including total cholesterol, triglycerides, LDL cholesterol, and HDL cholesterol, among patients with T2DM.

METHODOLOGY

Ourcross-sectional comparative study was held at Ibn-e-Siena Hospital and Research Institute, Multan over a period of 6 months to evaluate and compare the lipid profile parameters in patients with T2DM receiving either empagliflozin or semaglutide. The estimated sample size was 80 patients, calculated using a two-sample comparison of means formula based on expected differences in LDL-C levels reported in previous literature. The sample was equally distributed into two groups, with 40 patients receiving empagliflozin and 40 patients receiving semaglutide.

Adult patients aged 18 years and above with a confirmed diagnosis of T2DM and on stable treatment with either empagliflozin or semaglutide were considered for the study. Patients were enrolled from the outpatient department of medicine and endocrinology. Patients receiving combined therapy with both drugs, those with type 1 diabetes mellitus, pregnancy, chronic liver disease, severe renal impairment, active malignancy, recent acute cardiovascular events, or those with recent initiation or dose adjustment of lipid-lowering therapy were excluded to minimize confounding effects on lipid parameters.

Baseline Demographic and clinical information was collected from medical database and patient interviews, including age, gender, duration of diabetes, body mass index (BMI), and comorbid conditions such as hypertension and cardiovascular disease. Biochemical parameters were recorded at the time of data collection, including fasting blood glucose, glycated hemoglobin (HbA1c), and lipid profile. Lipid profile parameters included total cholesterol, triglycerides, LDL-C, and HDL-C, measured using standardized laboratory techniques of the hospital diagnostic laboratory.

The primary objective of the investigation was to compare lipid profile parameters between patients receiving empagliflozin and those receiving semaglutide. Secondary outcomes included comparison of glycaemic control and BMI between the two groups.

The collected data was analyzed using IBM SPSS Statistics version (version 12). Continuous variables were documented as mean ± standard deviation or median with interquartile range Whereas, categorical variables were recorded as frequencies along with percentages. Normality of the data was assessed using the Shapiro–Wilk test. Thereafter, independent sample t-test and Mann-Whitney wereapplied for comparison of normallydistributed and skewed variables, respectively. The chi-square test was used for categorical variables. The difference between

the analyzed variables was considered statistically significant upon achieving p-value of less than 0.05.

Ethical approval for the study was sought from the Ethical Review board of the hospital. Moreover, all participants were informed of the study objectives in detail followed by the documentation of their written consent. The confidentiality of participants' information was strictly conserved throughout the study.

RESULTS

The average age of patients in the empagliflozin group was 56.8 ± 9.4 years, whereas the semaglutide group had an average age of 55.2 ± 10.1 years. The participants of two study groups had comparable baseline characteristics (Table 1).

Comparison of lipid profile parameters between the two groups demonstrated statistically significant differences. Patients receiving semaglutide had significantly lower total cholesterol levels compared to those receiving empagliflozin (178.6 ± 26.9 mg/dL vs. 192.4 ± 28.7 mg/dL; p = 0.030). Similarly, LDL cholesterol values were significantly lower in the semaglutide group than in the empagliflozin group (104.3 ± 20.5 mg/dL vs. 118.5 ± 22.1 mg/dL; p = 0.004). HDL cholesterol levels were significantly higher among patients receiving semaglutide compared to those receiving empagliflozin (46.8 ± 8.1 mg/dL vs. 41.2 ± 7.6 mg/dL; p = 0.002). Moreover, triglyceride profile was also significantly improvedin the semaglutide group (165.2 ± 31.8 mg/dL) compared to the empagliflozin group (186.7 ± 34.5 mg/dL; p = 0.005). Lastly, VLDL levels wereanalyzed, and they were also significantly reduced among patients receiving semaglutide compared with those receiving empagliflozin (33.1 ± 6.3 mg/dL vs. 37.3 ± 6.9 mg/dL; p = 0.006) (Table 2).

Assessment of glycaemic and anthropometric parameters revealed that patients receiving semaglutide had significantly lower HbA1c levels than those receiving empagliflozin (7.4 ± 0.9% vs. 7.9 ± 1.0%; p = 0.021). The level of fasting blood glucose were also substantiallyreduced in the semaglutide group (142.3 ± 25.7 mg/dL) compared to the empagliflozin group (156.8 ± 28.4 mg/dL; p = 0.017). Although lower BMI and body weight values were observed among patients receiving semaglutide, these differences did not reach statistical significance (p > 0.05) (Table 3).

Table 1: Baseline Characteristics of Study Participants

Variable	Empagliflozin (n=40)	Semaglutide (n=40)	Test value	p-value
Age (years)	56.8 ± 9.4	55.2 ± 10.1	t = 0.74	0.46
Gender (M/F)	22 / 18	20 / 20	χ^2 = 0.20	0.65
Duration of T2DM (years)	8.1 ± 3.2	8.5 ± 3.6	t = 0.52	0.60
BMI (kg/m²)	30.6 ± 4.8	31.2 ± 5.1	t = 0.55	0.58
HbA1c (%)	8.4 ± 1.1	8.6 ± 1.0	t = 0.84	0.40
Hypertension (%)	62.5%	65%	χ^2 = 0.05	0.82

Table 2: Analysis of Lipid Profile in Two Study Groups

Lipid Parameter	Empagliflozin (n=40)	Semaglutide (n=40)	t-value	p-value
Total Cholesterol (mg/dL)	192.4 ± 28.7	178.6 ± 26.9	2.21	0.030
LDL-C (mg/dL)	118.5 ± 22.1	104.3 ± 20.5	3.00	0.004
HDL-C (mg/dL)	41.2 ± 7.6	46.8 ± 8.1	3.17	0.002
Triglycerides (mg/dL)	186.7 ± 34.5	165.2 ± 31.8	2.93	0.005
VLDL (mg/dL)	37.3 ± 6.9	33.1 ± 6.3	2.86	0.006

Table 3: Glycemic Control and Anthropometric Comparison

Parameter	Empagliflozin (n=40)	Semaglutide (n=40)	t-value	p-value
HbA1c (%)	7.9 ± 1.0	7.4 ± 0.9	2.35	0.021
Fasting Blood Glucose (mg/dL)	156.8 ± 28.4	142.3 ± 25.7	2.44	0.017
BMI (kg/m²)	30.6 ± 4.8	28.9 ± 4.5	1.65	0.102

Weight (kg)	82.4 ± 12.1	78.6 ± 11.5	1.42	0.159

DISCUSSION

T2DM is frequently accompanied by dyslipidaemia, characterized by elevated triglycerides, increased LDL-C, and reduced HDL-C, all of which contribute significantly to cardiovascular associated morbidity and mortality. Given the validated role of cardiovascular disease as cause of death among T2DM affected patients, the identification of antidiabetic therapies that provide favorable effects on lipid metabolism in addition to glycaemic control has become an important therapeutic objective.

The present study compared lipid profile parameters among patients with T2DM receiving either empagliflozin or semaglutide. The findings demonstrated that patients receiving semaglutide had significantly improved lipid profile, compared with those receiving empagliflozin. In addition, semaglutide-treated patients exhibited significantly lower HbA1c and fasting blood glucose levels, indicating better glycaemic control. These results suggest that semaglutide may offer greater benefits in improving cardiometabolic risk factors among patients with T2DM.

The superior glycaemic control observed in the semaglutide group is consistent with findings from previous clinical trials. Marso et al., in the SUSTAIN-6 trial, reported weekly administration of semaglutide helped in significant reduction of body weight, HbA1c levels, and adverse cardiovascular events[15]. Similarly, Wilding et al., in the STEP-2 trial, demonstrated that semaglutide produced substantial and sustained improvements in metabolic parameters among overweight and obese patients with T2DM[16]. Although the present study did not evaluate longitudinal changes in weight, the lower HbA1c and fasting glucose levels observed among semaglutide users are in agreement with these landmark trials.

The favorable lipid profile associated with semaglutide in the present study is also supported by previous literature. Tóth et al. reported significant reductions in LDL cholesterol and non-HDL cholesterol following long-term semaglutide therapy in patients with T2DM. Furthermore, semaglutide treatment was associated with favorable alterations in lipoprotein subfractions, suggesting a reduction in atherogenic lipid burden[17]. Similarly, Newsome et al. demonstrated that semaglutide improves several metabolic risk factors beyond glycaemic control, supporting its broader cardiometabolic benefits[18]. The lower LDL-C and triglyceride levels and higher HDL-C levels observed in our study are therefore consistent with the growing body of evidence supporting the lipid-modifying effects of GLP-1 receptor agonists.

Several biological mechanisms may explain these findings. Semaglutide plays a role in triggering insulin secretion,glucagon suppression, and delays gastric emptying, leading to decreased energy consumption and improved insulin sensitivity.Improved insulin sensitivity may reduce hepatic production of very-low-density lipoproteins and enhance lipid clearance, leading to reductions in circulating triglycerides and LDL-C. In addition, experimental work by Rakipovski et al. demonstrated that semaglutide may exert anti-atherosclerotic effects through mechanisms independent of weight reduction, including attenuation of vascular inflammation and reduction of atherosclerotic plaque development[19]. These effects may contribute to the cardiovascular protection observed with semaglutide therapy.

In contrast, patients receiving empagliflozin in the current study exhibited comparatively higher total cholesterol and LDL-C levels. These findings are consistent with observations reported by Rau et al., who demonstrated that empagliflozin treatment resulted in modest increases in LDL-C despite its favorable cardiovascular profile[20]. Several mechanisms have been proposed to explain this phenomenon, including alterations in lipid metabolism, increased lipolysis, and a metabolic shift from glucose utilization toward fatty acid oxidation. Although modest increases in LDL-C have been observed with SGLT2 inhibitors, these changes do not appear to negate their cardiovascular benefits.

Indeed, the cardiovascular benefits of empagliflozin have been well established. Zinman et al., in the EMPA-REG OUTCOME trial, reported significant reductions in cardiovascular mortality, heart failure associated hospitalization, and all-cause mortality among patients receiving empagliflozin[21]. Therefore, despite the comparatively less favorable lipid profile observed in our study, empagliflozin remains an important therapeutic option, particularly for patients at high cardiovascular or renal

risk. These findings emphasize that lipid profile changes should be clinically correlated with other prognostic factors in cardiovascular and renal protection.

The significantly lower HbA1c levels observed among semaglutide users in the present study are also supported by comparative studies. Rodbard et al. compared oral semaglutide with empagliflozin and found greater reductions in HbA1c among patients receiving semaglutide[22]. Improved glycaemic control may contribute indirectly to favorable lipid profile changes by reducing insulin resistance and improving hepatic lipid metabolism. This relationship may partly explain the more favorable lipid parameters observed among semaglutide-treated patients in the present study.

The clinical implications of these findings are noteworthy. Dyslipidaemia is a major modifiable cardiovascular risk factor in patients with T2DM, and the observed association between semaglutide therapy and a more favorable lipid profile suggests a potential advantage for patients with concomitant dyslipidaemia or obesity. However, treatment decisions should remain individualized, considering not only lipid profile and glycaemic control but also cardiovascular, renal, economic, and patient-specific factors.

This study has multiple short coming limitations. The cross-sectional study design does halts the determination of causal links between treatment exposure and lipid profile outcomes. Because measurements were obtained at a single point in time, it cannot be determined whether the observed differences were directly attributable to the medications or influenced by other factors. Moreover, it was a single center investigation with ratherlimited participants which limits the implications of the results on the generalized population. Lastly, potential confounding factors including dietary routine, physical activity, sideline medication, duration of treatment, and concurrent use of lipid-lowering agents were not fully controlled. It is suggested to conduct larger studies with heterogenous samplesto validate these findings and further establish the comparative effects of empagliflozin and semaglutide on lipid metabolism and cardiovascular risk.

CONCLUSION

Patients with T2DM receiving semaglutide exhibited significantly more favorable lipid profilescompared with patients receiving empagliflozin. Semaglutide was also associated with better glycaemic control. These findings suggest that semaglutide may provide additional cardiometabolic benefits beyond glucose lowering and may represent a valuable therapeutic option for patients with T2DM and concomitant dyslipidaemia.

REFERENCES

1. Chandrasekaran P, Weiskirchen R. The role of obesity in type 2 diabetes mellitus—An overview. International journal of molecular sciences. 2024;25(3):1882.doi:10.3390/ijms25031882
2. Młynarska E, Czarnik W, Dzieża N, Jędraszak W, Majchrowicz G, Prusinowski F, et al. Type 2 diabetes mellitus: new pathogenetic mechanisms, treatment and the most important complications. International journal of molecular sciences. 2025;26(3):1094.doi:10.3390/ijms26031094
3. Ciarambino T, Crispino P, Leto G, Mastrolorenzo E, Para O, Giordano M. Influence of gender in diabetes mellitus and its complication. International journal of molecular sciences. 2022;23(16):8850.doi:10.3390/ijms23168850
4. Ma C-X, Ma X-N, Guan C-H, Li Y-D, Mauricio D, Fu S-B. Cardiovascular disease in type 2 diabetes mellitus: progress toward personalized management. Cardiovascular diabetology. 2022;21(1):74.doi:10.1186/s12933-022-01516-6
5. Kalra S, Raizada N. Dyslipidemia in diabetes. Indian heart journal. 2024;76(Suppl 1):S80–S2.doi:10.1016/j.ihj.2023.11.002
6. Feingold KR, Grunfeld C. Diabetes and dyslipidemia. In: Feingold KR, Adler RA, Ahmed SF, Anawalt B, Blackman MR, Chrousos G, et al., editors. Diabetes and Cardiovascular Disease. South Dartmouth (MA): Springer; 2023. p. 425–72.
7. O'Hara DV, Janse RJ, Fu EL, Jardine MJ, Carrero J-J. Adherence and persistence to novel glucose-lowering medications in persons with type 2 diabetes mellitus undergoing routine care. Diabetes research and clinical practice. 2024;213:111745.doi:10.1016/j.diabres.2024.111745
8. El-Haggar SM, Hafez YM, El Sharkawy AM, Khalifa M. Effect of empagliflozin in

peripheral diabetic neuropathy of patients with type 2 diabetes mellitus. Medicina Clínica (English Edition). 2024;163(2):53–61.doi:10.1016/j.medcli.2024.01.027
9. Agarwal R, Green JB, Heerspink HJ, Mann JF, McGill JB, Mottl AK, et al. Finerenone with empagliflozin in chronic kidney disease and type 2 diabetes. New England Journal of Medicine. 2025;393(6):533–43.doi:
10. Gohari S, Reshadmanesh T, Khodabandehloo H, Karbalaee-Hasani A, Ahangar H, Arsang-Jang S, et al. The effect of EMPAgliflozin on markers of inflammation in patients with concomitant type 2 diabetes mellitus and Coronary ARtery Disease: the EMPA-CARD randomized controlled trial. Diabetology & Metabolic Syndrome. 2022;14(1):170.doi:10.1186/s13098-022-00951-5
11. Bauer KI, Baker D, Lerner R, Koeck T, Buch G, Fischer Z, et al. Effect of Empagliflozin on the plasma lipidome in patients with type 2 diabetes mellitus: results from the EmDia clinical trial. Cardiovascular Diabetology. 2025;24(1):359.doi:10.1186/s12933-025-02916-0
12. Li A, Su X, Hu S, Wang Y. Efficacy and safety of oral semaglutide in type 2 diabetes mellitus: a systematic review and meta-analysis. Diabetes Research and Clinical Practice. 2023;198:110605.doi:10.1016/j.diabres.2023.110605
13. Krüger N, Schneeweiss S, Desai RJ, Sreedhara SK, Kehoe AR, Fuse K, et al. Cardiovascular outcomes of semaglutide and tirzepatide for patients with type 2 diabetes in clinical practice. Nature medicine. 2026;32(1):342–52.doi:10.1038/s41591-025-04102-x
14. Miranda S, Choudhari J, Chauhan N, Parmar MS. Impact of semaglutide on lipid profiles in overweight and obese non-diabetic adults: a systematic review and meta-analysis of randomized controlled trials. European Journal of Pharmacology. 2025;1003:177953.doi:10.1016/j.ejphar.2025.177953
15. Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jódar E, Leiter LA, et al. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. New England Journal of Medicine. 2016;375(19):1834–44.doi:10.1056/NEJMoa1607141
16. Wilding JP, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, et al. Once-weekly semaglutide in adults with overweight or obesity. New England Journal of Medicine. 2021;384(11):989–1002.doi:
17. Tóth LI, Harsányi A, Csiha S, Molnár Á, Lőrincz H, Nagy AC, et al. Semaglutide improves lipid subfraction profiles in type 2 diabetes: insights from a one-year follow-up study. International Journal of Molecular Sciences. 2025;26(13):5951.doi:10.3390/ijms26135951
18. Newsome PN, Buchholtz K, Cusi K, Linder M, Okanoue T, Ratziu V, et al. A placebo-controlled trial of subcutaneous semaglutide in nonalcoholic steatohepatitis. New England Journal of Medicine. 2021;384(12):1113–24.doi:10.1056/NEJMoa2028395
19. Rakipovski G, Rolin B, Nøhr J, Klewe I, Frederiksen KS, Augustin R, et al. The GLP-1 analogs liraglutide and semaglutide reduce atherosclerosis in ApoE−/− and LDLr−/− mice by a mechanism that includes inflammatory pathways. JACC: Basic to Translational Science. 2018;3(6):844–57.doi:10.1016/j.jacbts.2018.09.004
20. Rau M, Thiele K, Hartmann N-UK, Moellmann J, Wied S, Boehm M, et al. Effects of empagliflozin on lipoprotein subfractions in patients with type 2 diabetes: data from a randomized, placebo-controlled study. Atherosclerosis. 2021;330:8–13.doi:10.1016/j.atherosclerosis.2021.06.915
21. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. New england journal of medicine. 2015;373(22):2117–28.doi:10.1056/NEJMoa1504720
22. Rodbard HW, Rosenstock J, Canani LH, Deerochanawong C, Gumprecht J, Lindberg SØ, et al. Oral semaglutide versus empagliflozin in patients with type 2 diabetes uncontrolled on metformin: the PIONEER 2 trial. Diabetes care. 2019;42(12):2272–81.doi:10.2337/dc19-0883