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PRESCRIBING PATTERNS, SAFETY, AND CLINICAL PERSPECTIVES ON EMPAGLIFLOZIN-LINAGLIPTIN COMBINATION AMONG INDIAN HEALTHCARE PROFESSIONALS AND PATIENTS WITH T2DM

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ABSTRACT

Background: The rising burden of type 2 diabetes mellitus (T2DM) leads to disability and complications, highlighting the need for effective and well-tolerated therapies. The current study aims to evaluate the reasons for initiating and switching therapies, the safety and tolerability profile, and patient perceptions of prescribed therapy.

Methods: This questionnaire-based online survey was conducted among health care professionals (HCPs) across India. A structured 17-item questionnaire was used to explore HCP preferences and prescribing patterns for empagliflozin-linagliptin combination with metformin, focusing specifically on their last 10 patients with T2DM, emphasising on the reasons for initiating, switching, tolerability, side effects, discontinuation due to adverse effects, quality of life and practices related to patient education.

Results: A total of 377 HCPs were included in this study. Inadequate glycemic control was reported by 54.64% of HCPs as the primary reason for initiating, and by 44.30% of HCPs as the main reason for switching to, the empagliflozin-linagliptin combination as an add-on to metformin. A significant proportion (41.38%) of HCPs reported that this combination was very well-tolerated. The most common side effects observed were genital or urinary tract infections (26.79%) and gastrointestinal discomfort (14.06%), while 54.91% of them rarely observed this side effects in patients with empagliflozin-linagliptin combination. More than half (65.52%) of HCPs found that none of the patients discontinued the treatment due to adverse effects. Approximately 31% of HCPs reported that 3-10 patients treated with the empagliflozin-linagliptin combination showed an improved quality of life. The majority of HCPs (61.01%) preferred a combination of verbal and written education when counselling patients about potential side effects.

Conclusion: HCP responses indicate that the empagliflozin-linagliptin combination is effective, well-tolerated, and rarely discontinued, with associated improvements in patient quality of life, supporting its value in routine T2DM management.

Keywords: Fixed-dose combination, Adherence, Side effects, Tolerability, T2DM

1 INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease characterized by insulin resistance and progressive dysfunction and loss of insulin-secreting pancreatic β -cell [1]. According to the International Diabetes Federation (IDF), approximately 89.8 million people currently live with diabetes, a number projected to increase to 156.7 million by 2050 [2]. In India, the rising prevalence of diabetes contributes to significant disability and serious complications, thereby increasing the overall financial burden [3].

Alongside pharmacological therapy, lifestyle interventions including dietary changes, regular physical activity, and stress management are essential for optimal disease control. While metformin remains the first-line treatment for T2DM [4], metformin monotherapy often fails to achieve adequate glycaemic control [5]. Consequently, metformin is commonly combined with other oral antidiabetic agents, such as sulfonylureas (SUs), thiazolidinediones, dipeptidyl peptidase-4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, and glucagon-like peptide-1 (GLP-1) receptor agonists, to achieve improved clinical outcomes [6].

An SGLT2 inhibitor such as empagliflozin lowers blood glucose by blocking renal glucose reabsorption and promoting urinary glucose excretion, independent of insulin [7]. Linagliptin, a DPP-4 inhibitor, enhances incretin activity, thereby promoting glucose-dependent insulin secretion and reducing glucagon levels, resulting in improved glycaemic control with a low risk of hypoglycaemia [8]. Clinical studies have demonstrated that the fixed-dose combination of empagliflozin and linagliptin is effective and well-tolerated. Randomised trials and long-term evaluations have shown greater reductions in glycated haemoglobin (HbA1c) and fasting plasma glucose (FPG) with the combination than with either drug used alone [9]. Furthermore, empagliflozin-linagliptin as an add-on to metformin provides a potent, well-tolerated, oral treatment option with a favourable safety profile and potential adherence benefits due to reduced pill burden [7].

The present study aimed to assess clinical preferences, perceptions, and utilization of the empagliflozin-linagliptin combination as an add-on to metformin in Indian patients with T2DM, focusing on treatment initiation and switching patterns, safety and tolerability, prescribing frequency, perceived barriers, and patient education practices.

2 METHOD

2.1 Study design

This questionnaire-based online survey was conducted among Indian healthcare professionals (HCPs). Participation in the study was entirely voluntary, and both the study procedures and data analysis were designed to maintain the confidentiality and anonymity of all participating HCPs.

2.2 Study questionnaire

The study questionnaire was developed based on existing literature, clinical guidelines, and expert opinion. It comprised a total of 35 questions, of which 17 specifically focused on HCPs' experiences with empagliflozin-linagliptin combination as an add-on therapy to metformin in patients with T2DM. These questions addressed reasons for treatment initiation, switching, and prescribing; prescribing frequency and placement within treatment algorithms; sources of information; use in specific patient populations; tolerability, side effects, and dose adjustments; patient perceptions and quality of life; treatment discontinuation due to adverse effects; and barriers and practices related to patient education.

2.2.1 Study procedure

Healthcare practitioners received a brief explanation of the study along with instructions for completing the questionnaire. The study protocol, informed consent form, and digital questionnaire were provided to HCPs through a secure online platform. Participation in the study was entirely voluntary, and no patient-identifying information was collected. All completed questionnaires were checked for completeness and internal consistency prior to inclusion in the final analysis. Written informed consent was obtained from all participating HCPs before completion of the survey. The study protocol was approved by an independent ethics (IEC No: CIEC/2025/056).

2.2.2 Data analysis

Responses of HCPs were entered into Microsoft Excel, and descriptive statistics, such as frequencies and percentages, were used to present the data.

3 RESULTS

A total of 377 HCPs were included in this study. The majority (54.64%) of HCPs reported that inadequate glycemic control was the primary reason for initiating empagliflozin-linagliptin combination as an add-on therapy to metformin. Similarly, a significant proportion of HCPs (43.50%) reported poor glycemic control with previous therapy as the reason for switching to combination therapy. With respect to the primary reason for prescribing the combination, effective HbA1c reduction was reported by 44.30% of HCPs, followed by cardiovascular risk reduction (26.26%). In the treatment algorithm for T2DM, 44.83% of HCPs preferred empagliflozin-linagliptin combination as second-line therapy, while 31.03% considered it for high-risk patients. Medical literature and guidelines were the primary sources of information for nearly half of the HCPs (45.98%) when prescribing the empagliflozin-linagliptin combination as an add-on therapy to metformin. A substantial proportion of HCPs (44.03%) reported that this combination has a role as an early intervention in patients with newly diagnosed diabetes, whereas 24.14% considered its use primarily in high-risk patients. The majority of HCPs (88.06%) recommended empagliflozin-linagliptin combination as the preferred management approach for T2DM patients (Table 1).

Table 1: Prescribing preference and pattern for the empagliflozin-linagliptin combination

Parameter	Response of HCPs (N=377)
Primary reason for initiating empagliflozin-linagliptin add-on to metformin	
Inadequate glycemic control with previous therapy	206 (54.64)
Presence of cardiovascular risk factors	77 (20.42)
Weight management benefits	57 (15.12)
Patient preference	37 (9.81)
Reason for switching to the combinational therapy	
Poor glycemic control on previous regimen	164 (43.50)
Need for cardiovascular protection	91 (24.14)
Better patient adherence	66 (17.51)
Reduced risk of hypoglycemia	56 (14.85)
Primary reason for prescribing combination therapy	
Effective HbA1c reduction	167 (44.30)
Cardiovascular risk reduction	99 (26.26)
Weight management benefits	60 (15.92)
Lower risk of hypoglycemia	51 (13.53)
Preference for earlier use in the T2D treatment algorithm	
Yes, as first-line therapy	50 (13.26)
No, as second-line therapy	169 (44.83)
Only in high-risk patients	117 (31.03)
Not sure	41 (10.88)
Primary source of information on this combination therapy	
Medical literature and guidelines	173 (45.89)
Peer discussions	83 (22.02)
Clinical experience	76 (20.16)
Pharmaceutical representatives	45 (11.94)
Role of this therapy in patients with newly diagnosed diabetes	
Yes, as an early intervention	166 (44.03)

Only in high-risk patients	91 (24.14)
No, only in later stages	59 (15.65)
Not sure	61 (16.18)
Recommendation of this therapy as the preferred management option for T2D	
Yes, strongly recommend	160 (42.44)
Yes, with some reservations	172 (45.62)
No, prefer other options	29 (7.69)
Not sure	16 (4.24)
Data represented as n (%). HbA1c, glycated haemoglobin; HCPs, healthcare professionals; T2D, type 2 diabetes.	

Genital or urinary tract infection (UTI) (26.79%) and gastrointestinal discomfort (14.06%) were the most commonly reported side effects associated with the empagliflozin-linagliptin combination, while 46.68% of HCPs reported no significant side effects. According to 41.38% of HCPs, the empagliflozin-linagliptin combination with metformin was very well tolerated, and a similar proportion (41.38%) reported the presence of manageable tolerability issues. Side effects such as genital or UTIs were reported as a rare by 54.91% of HCPs and occasional by 29.71%. Additionally, 31.30% of HCPs reported that 3-10 of their last 10 patients treated with the empagliflozin-linagliptin combination as an add-on to metformin experienced improvements in quality of life (Table 2).

Table 2: Tolerability, side effects and safety of the empagliflozin-linagliptin combination

Parameter	Response of HCPs (N=377)
Most common side effect observed	
Genital or urinary tract infections	101 (26.79)
Gastrointestinal discomfort	53 (14.06)
Hypoglycaemia	47 (12.47)
No significant side effects	176 (46.68)
Tolerability of the combination as add-on therapy to Metformin	
Very well tolerated	156 (41.38)
Some tolerability issues but manageable	156 (41.38)
Poorly tolerated	22 (5.84)
Not sure	43 (11.41)
Frequency of genital or urinary tract infections	
Always	8 (2.12)
Frequently	50 (13.26)
Occasionally	112 (29.71)
Rarely	207 (54.91)
Improvement in overall quality of life	
1-2 patients	92 (24.40)
3-5 patients	118 (31.30)
6-10 patients	118 (31.30)
None	49 (13.00)
Data represented as n (%). HCPs, healthcare professionals.	

HCPs shared their clinical experience based on their most recent 10 patients regarding the use of and challenges associated with prescribing the empagliflozin-linagliptin combination. Approximately 38.46% of HCPs identified cost as the most common barrier to prescribing this combination in patients with T2DM, while 31.30% reported insurance coverage as an additional barrier. The majority of the HCPs (61.01%) preferred a combination of verbal and written education to inform patients about potential side effects (Table 3).

Table 3: Healthcare utilization and barriers while prescribing empagliflozin-linagliptin combination

Parameter	Response of HCPs (N=377)
Most common barrier to prescribing this therapy in T2D	
Cost	145 (38.46)
Insurance coverage	118 (31.30)
Patient adherence	87 (23.08)
Availability	27 (7.16)
Methods of educating patients about potential side effects	
Verbal explanation	55 (14.59)
Written materials	56 (14.85)
Both verbal and written education	230 (61.01)
No specific patient education	36 (9.55)
Data represented as n (%). HCPs, healthcare professionals; T2D, type 2 diabetes.	

More than half of the HCPs (65.52%) reported that none of their patients discontinued the empagliflozin-linagliptin combination due to adverse effects, whereas 26.53% noted discontinuation in 1-3 patients. Dose adjustment was not required for any patient according to 55.17% of HCPs, while 28.12% reported dose adjustment in 1-3 patients in their clinical practice (Figure 1). The empagliflozin-linagliptin combination was often prescribed by 45.36% of HCPs, and occasionally by 36.07%. As an add-on to metformin, this combination was used occasionally in patients with diabetic nephropathy by 47.48% and often by 29.44% (Figure 2).

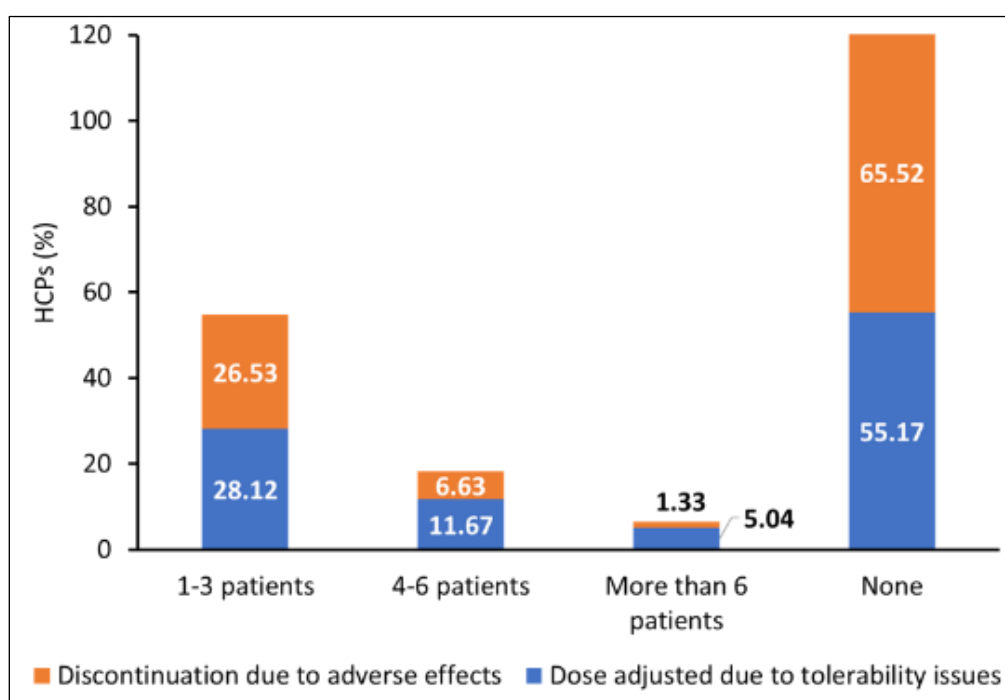


Figure 1: Distribution of empagliflozin-linagliptin combination discontinuation and dose adjustments

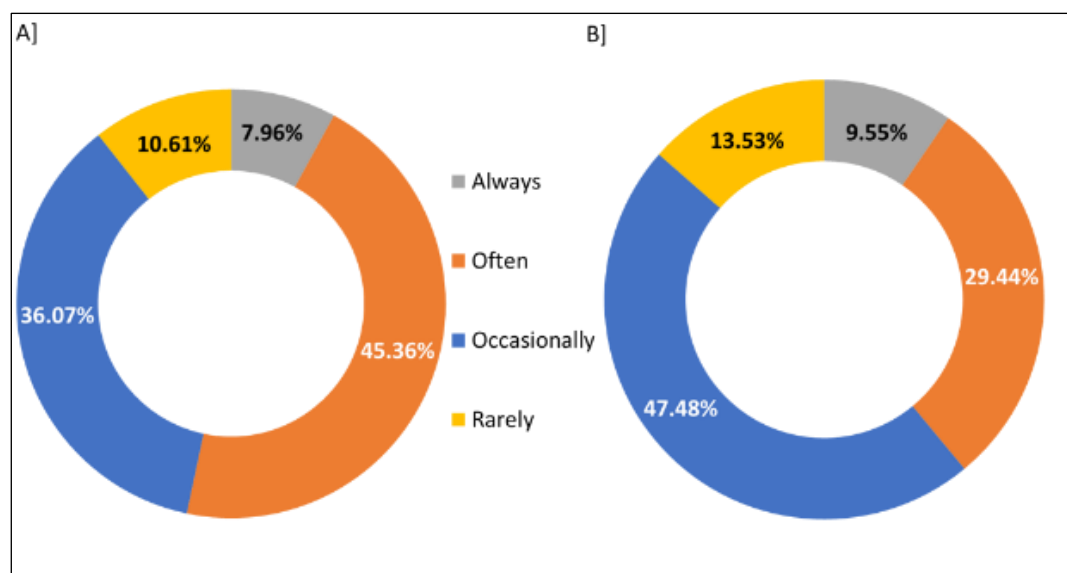


Figure 2: Frequency of prescribing empagliflozin-linagliptin combination and its use in diabetic nephropathy

A) Frequency of prescribing combination therapy B) Use of combination therapy in diabetic nephropathy

4 DISCUSSION

The present study provides clinical preferences, perceptions, and utilization of empagliflozin-linagliptin combination as an add-on therapy to metformin in Indian patients with T2DM, focusing on factors influencing treatment initiation and switching, the safety and tolerability profile, prescribing patterns, barriers to use, and approaches to patient education.

Of the 377 HCPs, nearly half (54.64%) reported that inadequate glycemic control was the primary reason for initiating empagliflozin-linagliptin combination as an add-on therapy to metformin. Similarly, 43.50% of them found poor glycemic control for switching to the combination therapy. This observation was supported by two 52-week Phase III studies that showed that adding empagliflozin and linagliptin to metformin reduced HbA1c more effectively than either agent alone, with a rapid glucose-lowering effect consistent with HCP-reported improvements by around three months [7]. The empagliflozin-linagliptin combination was preferred as second-line therapy by nearly half of HCPs.

The American Diabetes Association recommends using SGLT2 inhibitors, DPP-4 inhibitors, along with metformin, in patients who require additional glucose-lowering medications [6]. Regarding the source of information for prescribing the empagliflozin-linagliptin combination as an add-on therapy to metformin, nearly half (45.98%) of HCPs reported relying on medical literature and clinical guidelines. This trend is consistent with guideline-driven decision-making reported in real-world diabetes management studies [6]. According to 44.03% of HCPs, the empagliflozin-linagliptin combination had a role as an early intervention in patients with newly diagnosed diabetes. The majority of HCPs (88.06%) believe that the empagliflozin-linagliptin combination is the preferred management approach for T2DM patients. Clinical evidence showed that the empagliflozin-linagliptin combination provides superior glycemic control, weight reduction, and a favourable safety/tolerability profile [10].

The common adverse effects observed with empagliflozin-linagliptin combination were genital or UTI and gastrointestinal discomfort, as reported by 26.79% and 14.06%, respectively, while 46.68% of them observed no significant side effects. More than half of the HCPs rarely observed genital infection or UTI. These findings align with the previous study wherein the empagliflozin-linagliptin combination increases the risk of genital infection or UTI [7]. A significant proportion of HCPs (41.38%) found that the empagliflozin-linagliptin combination, along with metformin, was very well tolerated. This finding is consistent with a study demonstrating that empagliflozin/linagliptin, when added to metformin for 52 weeks, was well tolerated [7]. In contrast to the findings of Nagayama A et al., which reported no significant improvement in overall quality of life, the present study suggests that the empagliflozin-linagliptin combination as an add-on to metformin may enhance patients' quality of life [11].

A study conducted by Yaseen A et al. revealed that barriers to prescribing GLP-1 receptor agonists and SGLT2 inhibitors, such as high cost, still exist [12]. These findings are consistent with the current study, in which a significant proportion of HCPs identified cost as the most common barrier to prescribing the empagliflozin-linagliptin combination. Furthermore, a previous study reported that educating patients using written or visual materials helps reinforce and enhance patients' knowledge regarding the benefits of treatment adherence [13]. This aligns with the findings of the

present study, wherein the majority of HCPs recommended verbal and written methods for educating patients about potential side effects.

In pooled analyses of clinical trials, the empagliflozin-linagliptin combination has demonstrated a favourable safety and tolerability profile, with a low rate of serious adverse events and minimal treatment discontinuations due to adverse effects [7]. In contrast, findings from the current study indicate that more than half of HCPs observed no treatment discontinuation due to adverse effects among their patients. Furthermore, more than half of HCPs (55.17%) reported that dose adjustment was not required for any patient receiving the empagliflozin-linagliptin combination, with only a small proportion (28.12%) adjusting the dose for 1-3 patients in routine clinical practice. This observation is consistent with clinical pharmacokinetic evidence indicating that the coadministration of empagliflozin and linagliptin does not necessitate dose modification [14]. A substantial proportion of HCPs in the present study reported prescribing the empagliflozin-linagliptin combination either often (45.36%) or occasionally (36.07%) in patients with T2DM. As an add-on therapy to metformin, the combination was prescribed occasionally in patients with diabetic nephropathy by 47.48% of HCPs, while 29.44% reported prescribing it often. These findings align with clinical evidence demonstrating that the empagliflozin-linagliptin combination results in significant reductions in HbA1c, FPG, body weight, and systolic blood pressure and also provides potential cardio-renal protective benefits [10].

Recent real-world evidence further supports the potential renal benefits of empagliflozin-linagliptin fixed-dose combination therapy in patients with T2DM. In a real-world case-control study, treatment with the empagliflozin-linagliptin combination was associated with favourable CKD-related outcomes, supporting its clinical utility in patients with diabetic kidney disease. These findings complement the present survey, in which HCPs reported occasional and frequent use of the combination in patients with diabetic nephropathy. Although renal-related adverse effects and treatment tolerability should be considered during therapy, the available real-world evidence supports the use of empagliflozin-containing combination therapy as an option in appropriate patients with T2DM and CKD [15].

4.1 Limitations

This study has several limitations, including a relatively small sample size and a physician population restricted to India, which may limit the generalizability of the findings and overlook regional differences in clinical practice patterns. Additionally, reliance on self-reported data introduces the potential for response bias, and the questionnaire may not have captured all relevant clinical considerations.

5 CONCLUSION

The responses from this questionnaire-based study indicate that, in routine clinical practice, the empagliflozin-linagliptin combination is perceived by HCPs as a reliable and well-tolerated add-on option for patients who continue to have suboptimal glycemic control on metformin alone. Many HCPs value its ability to meaningfully reduce HbA1c with minimal adverse effects, and frequently prescribe it in high-risk situations, including those with diabetic nephropathy. Despite ongoing challenges related to cost and insurance coverage, the low rate of treatment discontinuation reported by HCPs reflects overall confidence and a positive clinical experience with this therapy in the management of T2DM.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

Funding Source

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Disclosure of conflict of interest

All authors have no conflicts of interest to declare.

Statement of ethical approval

The study protocol was approved by an Independent Ethics Committee (IEC No: CIEC/2025/056).

Statement of informed consent

Informed written consent was obtained from all participants before enrollment in the study.

REFERENCES

- [1] Lu X, Xie Q, Pan X, Zhang R, Zhang X, Peng G, et al. Type 2 diabetes mellitus in adults: pathogenesis, prevention and therapy. *Signal Transduct Target Ther*. 2024;9(1):262.
- [2] India. Diabetes country report 2000-2050. International Diabetes Federation. 2025. Available at <https://diabetesatlas.org/data-by-location/country/india/>. Last accessed on 17 September 2026.
- [3] Sahay RK, Mittal V, Gopal GR, Kota S, Goyal G, Abhyankar M, et al. Glimepiride and Metformin Combinations in Diabetes Comorbidities and Complications: Real-World Evidence. *Cureus*. 2020;12(9):e10700.
- [4] Borse SP, Chhipa AS, Sharma V, Singh DP, Nivsarkar M. Management of Type 2 Diabetes: Current Strategies, Unfocussed Aspects, Challenges, and Alternatives. *Med Princ Pract*. 2021;30(2):109-121.
- [5] St Onge EL, Miller S, Clements E. Sitagliptin/Metformin (janumet) as combination therapy in the treatment of type-2 diabetes mellitus. *P T*. 2012;37(12):699-708.
- [6] American Diabetes Association Professional Practice Committee; 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2025. *Diabetes Care* 1 January 2025; 48 (Supplement_1): S181–S206. <https://doi.org/10.2337/dc25-S009>
- [7] DeFronzo RA, Lee C, Kohler S. Safety and Tolerability of Combinations of Empagliflozin and Linagliptin in Patients with Type 2 Diabetes: Pooled Data from Two Randomized Controlled Trials. *Adv Ther*. 2018;35(7):1009-1022.
- [8] Kasina SVSK, Baradhi KM. Dipeptidyl Peptidase IV (DPP IV) Inhibitors. [Updated 2023 May 22]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026.
- [9] Kaku K, Haneda M, Tanaka Y, Lee G, Shiki K, Miyamoto Y, et al. Linagliptin as add-on to empagliflozin in a fixed-dose combination in Japanese patients with type 2 diabetes: Glycaemic efficacy and safety profile in a two-part, randomized, placebo-controlled trial. *Diabetes Obes Metab*. 2019; 21: 136-145.
- [10] Kawamori R, Haneda M, Suzaki K, Cheng G, Shiki K, Miyamoto Y, et al. Empagliflozin as add-on to linagliptin in a fixed-dose combination in Japanese patients with type 2 diabetes: Glycaemic efficacy and safety profile in a 52-week, randomized, placebo-controlled trial. *Diabetes Obes Metab*. 2018;20(9):2200-2209.
- [11] Nagayama A, Inokuchi T, Ashida K, Inada C, Homma T, Miyazaki H, et al. Assessing the Metabolic and Physical Effects of Combined DPP4 and SGLT2 Inhibitor Therapy in Patients with Type-2 Diabetes Mellitus: An Observational Prospective Pilot Study. *JMA J*. 2024;7(3):387-400.
- [12] Yaseen A, Lahiri SW. Health Care Provider Prescribing Habits and Barriers to Use of New Type 2 Diabetes Medications: A Single-System Survey Study. *Clin Diabetes*. 2023;41(4):490-501.
- [13] Selvan C, Lathia T, Chawak S, Katdare P, Nayak R, Chittem M. The Weight of Words: Indian Physicians' Perspectives on Patient Communication to Promote Diabetes Adherence. *Indian J Endocrinol Metab*. 2021;25(5):395-401.
- [14] Friedrich C, Metzmann K, Rose P, Mattheus M, Pinnetti S, Woerle HJ. A randomized, open-label, crossover study to evaluate the pharmacokinetics of empagliflozin and linagliptin after coadministration in healthy male volunteers. *Clin Ther*. 2013;35(1):A33-42.
- [15] Sanyal D, RoyChaudhuri S. Effectiveness of Empagliflozin-Linagliptin Fixed-Dose Combination on Chronic Kidney Disease Outcomes in Patients With Type 2 Diabetes in a Real-World Setting. *Cureus*. 2025;17(12):e100108.