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Linagliptin in Managing Type 2 Diabetes with Renal Impairment: Insights from Indian Nephrologists

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ABSTRACT

Type 2 Diabetes Mellitus (T2DM) is a significant contributor to chronic kidney disease (CKD) and end-stage kidney disease (ESKD). In the evolving landscape of diabetes management, nephrologists' perspectives are crucial for optimizing patient outcomes and planning future treatment strategies. This survey aims to evaluate the real-world in-clinic perspectives of nephrologists in managing T2DM patients with renal impairment, specially emphasising on the use of Linagliptin. The survey was conducted among 292 nephrologists across India. A structured questionnaire provided to assess the efficacy and safety of Linagliptin in managing T2DM patients with renal impairment. The survey revealed strong endorsement from nephrologists for the efficacy and safety of Linagliptin. Among the nephrologists surveyed, a significant majority indicated that Linagliptin is highly effective in controlling blood glucose levels in T2DM patients with renal impairment. Additionally, nephrologists highlighted the safety profile of Linagliptin, noting its minimal renal excretion and low risk of hypoglycemia, making it particularly suitable for patients with varying degrees of renal function. The survey also found that Linagliptin is preferred over other glucose-lowering agents due to its consistent efficacy and tolerability in patients with CKD and ESKD. Furthermore, nephrologists reported positive clinical outcomes, including improved glycemic control and stabilization of renal function, in patients treated with Linagliptin. The data underscores the broad consensus among nephrologists regarding Linagliptin as a first-line treatment option for managing T2DM in the context of renal impairment. Linagliptin is the primary choice among nephrologists for managing T2DM in patients with renal impairment, indicating its significant role as a preferred therapeutic option in this patient population. This insight underscores the need for continued focus on Linagliptin in clinical practice and future research.

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Key Words
Depression, SSRI, TCA, hamilton depression rating scale

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INTRODUCTION

Diabetes is a chronic disease characterized by the pancreas's inability to produce sufficient insulin or the body's inefficiency in utilizing the insulin produced. It is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation[1]. Type 2 Diabetes Mellitus (T2DM) is particularly notorious for its role in microvascular complications, being the leading cause of chronic kidney disease (CKD) and end-stage kidney disease (ESKD). The Indian Council of Medical Research India Diabetes (ICMR INDIAB) study, a cross-sectional population-based survey, reported that approximately 10.1 million people in India are affected by diabetes[2]. Globally, more than half a billion individuals live with diabetes, with projections indicating this number may rise to 1.3 billion by 2050[3]. Diabetic nephropathy, a chronic microvascular complication of T2DM, affects about 35% of diabetic patients and is the most common cause of ESKD and CKD. Chronic hyperglycemia in diabetes leads to impaired microvascular function, resulting in these complications[4]. In India, the prevalence of diabetic nephropathy varies widely, reported to range from 0.9-62.3%. CKD, a frequent consequence of diabetic nephropathy, contributes significantly to the prevalence of ESKD, estimated to be between 20-50% in both type 1 and type 2 diabetes[2]. Prolonged uncontrolled diabetes damages kidney blood vessels, impairing their waste filtration function and high blood pressure exacerbates this damage by increasing pressure within the kidney's filtering system[5]. Managing T2DM, particularly in the context of CKD, necessitates careful consideration of the pharmacology of anti-diabetic agents, the duration of diabetes, and the impact of chronic hypoglycemia on renal function. Nephrologists often prescribe Dipeptidyl Peptidase-4 (DPP-4) inhibitors, or gliptins, which enhance glucose-dependent insulin secretion by increasing active levels of incretin peptides such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptides (GIP)[6]. Linagliptin, a newer DPP-4 inhibitor approved in 2011, stands out for not requiring dose adjustment in patients with reduced renal function. Its unique molecular structure, based on xanthine, differs from other DPP-4 inhibitors and its long half-life (over 184 hours) supports a once-daily dosing regimen[7]. The RENOBOND survey 2, conducted within the Indian healthcare context, aimed to elucidate nephrologists' perspectives on the efficacy and safety of Linagliptin in managing T2DM patients with renal impairment. This survey provides valuable insights into the knowledge and attitudes of nephrologists in India regarding the prescription of Linagliptin.

Objectives: The primary objective of this survey is to evaluate the real-world, in-clinic perspectives of nephrologists regarding the selection of Linagliptin for its efficacy and safety in managing Type 2 Diabetes Mellitus (T2DM) patients with renal impairment. This study aims to capture the criteria and considerations nephrologists use in their clinical practice when prescribing Linagliptin for these patients.

MATERIALS AND METHODS

Design and Setting: This was a cross-sectional survey targeting nephrologists across various regions of India. The survey was conducted in-clinic to gather authentic, real-time data. A structured questionnaire was developed to assess the efficacy and safety of Linagliptin in managing T2DM patients with renal impairment.

Study Period: The survey was conducted over a period of two months, from November 21, 2023, to January 30, 2024.

Participants: A total of 292 nephrologists, all holding postgraduate qualifications in nephrology, participated in the survey.

Survey Instrument: The survey instrument was a specially designed questionnaire comprising 15 multiple-choice questions. The questions were crafted to assess nephrologists' knowledge, attitudes and perceptions regarding Linagliptin. The survey covered various aspects such as:

- Efficacy of Linagliptin in managing T2DM with renal impairment.
- Preferences and recommendations for Linagliptin use. Use of Linagliptin in co-morbid conditions.
- Dosage and formulation preferences.
- Overall choice and decision-making criteria for Linagliptin in clinical practice.

Data Analysis: Descriptive statistics were used to summarize the qualitative data, with results presented as numbers (n) and percentages (%) for each category of response. The data was graphically represented using bar diagrams. The denominator for calculating the proportion of responses to a particular question was the total number of participants who responded to that question, with the 'n' appropriately indicated in each graph.

RESULTS AND DISCUSSIONS

The survey conducted among 292 nephrologists across India provided comprehensive insights into the efficacy and safety profile of Linagliptin in the management of

Type 2 Diabetes Mellitus (T2DM) patients with renal impairment. The survey had a varied regional participation, with the majority (31.86%) of nephrologists being from the South Zone, followed by 22.03% from the West Zone, 19.66% from the North Zone, 14.24% from the East Zone and 12.20% from the Central Zone (Table 01).

Effectiveness and Safety: The majority of nephrologists (61.22%) perceived Linagliptin as highly effective, while 31.29% considered it moderately effective, resulting in an overall effectiveness endorsement of 92.51% (Fig 3.1). Additionally, 96.60% of nephrologists acknowledged Linagliptin's distinct advantages over other oral antidiabetic drugs (OADs), and 98.98% concurred that Linagliptin is safe for long-term use.

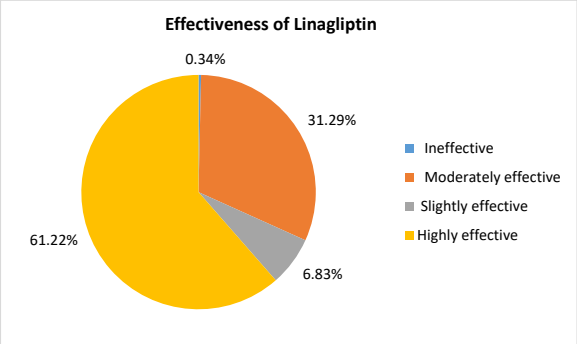

Fig 3.1: Effectiveness of Linagliptin in T2D Patients with Renal Impairment (n=292)

First-Line Therapy: A substantial majority (74.15%) of nephrologists regarded Linagliptin as the first-line drug of choice among DPP-4 inhibitors for managing T2DM in patients with renal impairment (Fig 3.2).

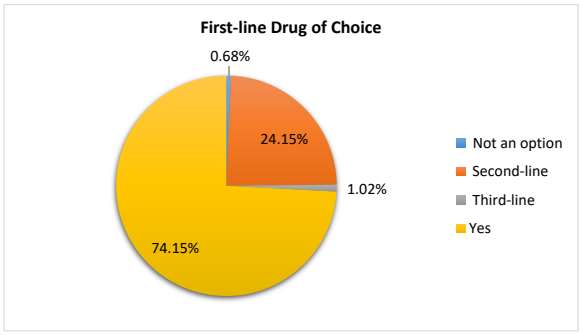

Fig. 3.2: First-line Drug of Choice by Nephrologists (n=292)

Prescription Practices: Nearly half of the nephrologists (48.30%) frequently prescribed Linagliptin to T2DM patients with renal impairment, and 32.65% prescribed it very frequently, leading to 80.95% of nephrologists prescribing Linagliptin in more than 50% of such patients (Fig 3.3). Regarding patient demographics, 49.32% of nephrologists had 25-50% of their patients on Linagliptin, 27.21% had 50-75% and 11.56% had more than 75% of their patients on the drug (Fig 3.4).

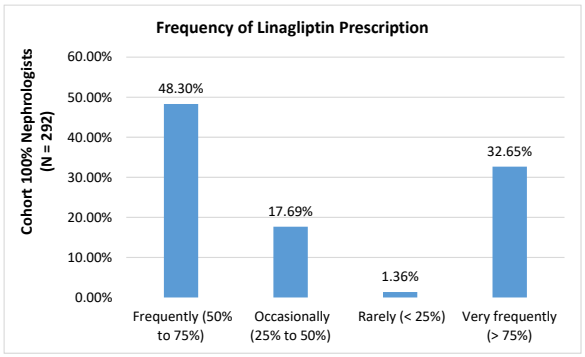

Fig 3.3: Frequency of Prescription of Linagliptin by Nephrologists (n=292)

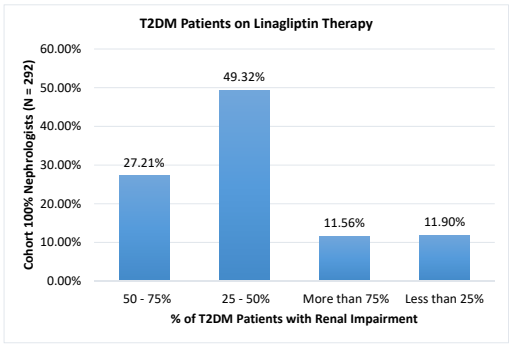

Fig. 3.4: T2DM Patients on Linagliptin Therapy (n=292)

Dosing and Monotherapy: Most nephrologists (60.88%) followed a standard dosage of Linagliptin regardless of renal function, while 36.73% based their dosing on creatinine clearance (Fig 3.5). Linagliptin monotherapy provided sufficient glycemic control for 43.88% of T2DM patients with renal impairment (Fig 3.6).

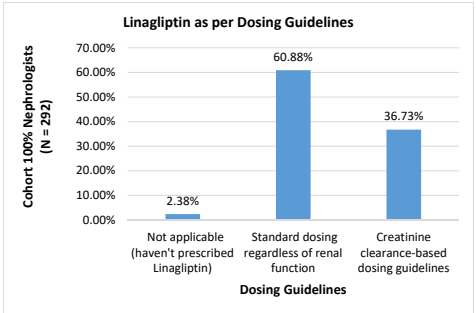

Fig. 3.5: Linagliptin Dosing Guidelines (n=292)

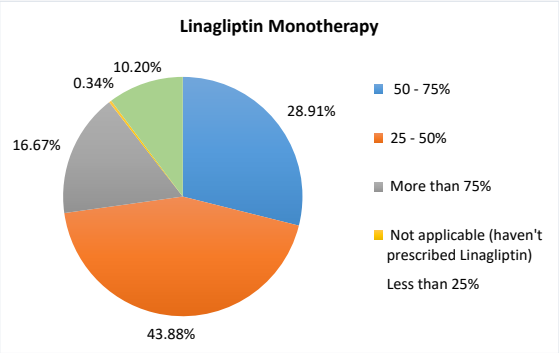

Fig. 3.6: Linagliptin Use as Monotherapy by Nephrologists (n=292)

Combination Therapy: Gliclazide was the most preferred OAD to be co-prescribed with Linagliptin in patients with mild to moderate and moderate to severe CKD (Fig. 3.7). Linagliptin was also widely prescribed (79.25%) across various patient subsets, including the elderly, those with multiple comorbidities and those at different stages of renal impairment (Fig 3.8).

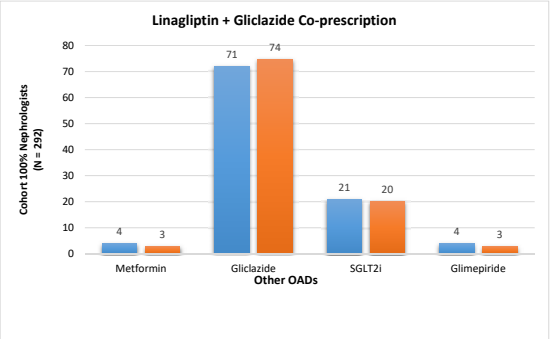

Fig. 3.7: Co-Prescription of Linagliptin with Other Oral Anti Diabetic Drugs in CKD (in %) (n=292)

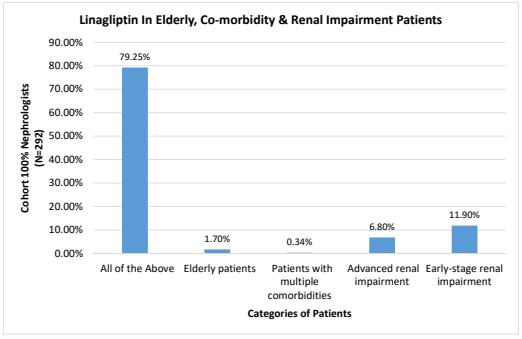

Fig. 3.8: Prescription of Linagliptin in Elderly, Co-morbid and Renal Impairment Patients (n=292)

Formulation Preference: A majority of nephrologists (64.63%) preferred prescribing Linagliptin as single tablets, though there is an increasing acceptance of fixed-dose combinations to reduce pill burden and improve compliance (Fig 3.9).

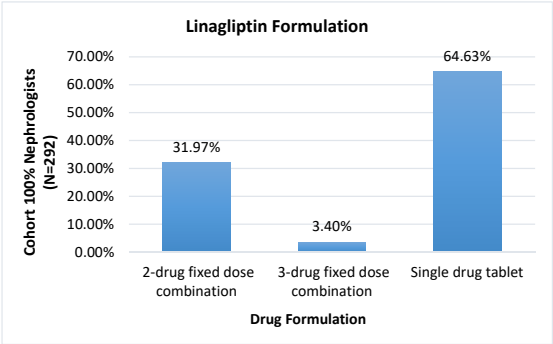

Fig. 3.9: Preferred Choice of Linagliptin Formulation (n=292)

Belief in Existing Evidence: A significant proportion of nephrologists (74.49%) expressed confidence in the current data supporting Linagliptin's safety and efficacy, indicating that further research might not be necessary for its continued use in this patient population. However, a minority expressed a need for additional research.

Peer Recommendation: Linagliptin was recommended by 83.67% of nephrologists to their peers and colleagues (Fig. 3.10).

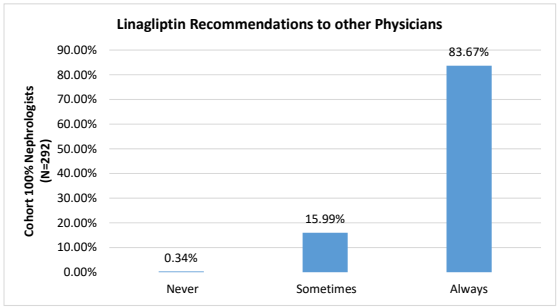

Fig. 3.10: Recommendation of Linagliptin to Other Doctors

The survey findings underscore Linagliptin's pivotal role in the management of T2DM patients with renal impairment in India. Its renoprotective benefits are attributed to the inhibition of DPP-4 activity and the subsequent elevation of active GLP-1 levels, which confer antioxidative and antiapoptotic effects on renal tissues.

Effectiveness and Safety: Linagliptin's effectiveness and safety, as reported by nephrologists, align with its pharmacokinetic profile, which involves minimal renal excretion and a primary elimination through the hepatobiliary system. This non-renal route of

elimination (~5% renal excretion) is particularly advantageous for patients with impaired renal function, allowing consistent dosing without the need for adjustments based on renal function[1,2].

First-Line Therapy and Prescription Practices: The widespread endorsement of Linagliptin as a first-line therapy reflects its efficacy in glycemic control and its favorable safety profile compared to other DPP-4 inhibitors. The high frequency of Linagliptin prescriptions in clinical practice is indicative of its acceptance and the trust nephrologists place in its therapeutic benefits[3].

Dosing and Monotherapy: The uniform approach to dosing, irrespective of renal function, simplifies its use in clinical settings, reducing the risk of dosing errors. The significant proportion of nephrologists using Linagliptin monotherapy suggests confidence in its ability to achieve adequate glycemic control without the need for additional medications[4].

Combination Therapy: The preference for combining Linagliptin with Gliclazide leverages the complementary mechanisms of action of these drugs, enhancing glycemic control while mitigating the risk of hypoglycemia. This combination is particularly beneficial for patients who do not achieve target glucose levels with monotherapy[5].

Formulation Preference and Patient Compliance: The preference for single-tablet formulations, along with the growing acceptance of fixed-dose combinations, highlights the emphasis on patient convenience and compliance. Reducing pill burden is crucial for improving adherence to treatment regimens, especially in elderly patients with multiple comorbidities[6,7].

Belief in Existing Evidence: The confidence expressed by nephrologists in the current evidence supporting Linagliptin's use suggests a well-established trust in its clinical benefits. However, the call for further research by a minority indicates a continuous pursuit of optimal therapeutic strategies[8].

Peer Recommendation: The high rate of peer recommendations further validates Linagliptin's established role in the therapeutic landscape for T2DM patients with renal impairment.

CONCLUSION

Overall, this survey highlights Linagliptin's status as the first-line treatment choice among nephrologists for managing T2DM patients with renal impairment. Its efficacy, safety and renoprotective effects make it a preferred therapeutic option. Linagliptin's mechanism of action through DPP-4 inhibition and the elevation of active GLP-1 levels provide significant advantages in slowing the progression of renal disease in T2DM patients. The consistent positive feedback from nephrologists underscores its critical role in clinical practice, emphasizing the need for continued utilization and exploration of its benefits in this patient population.

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