

Quality of Life in People with Type 2 Diabetes on Metformin–Sitagliptin Combination Therapy: A Questionnaire-Based Cross-Sectional Study

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Abstract

Background: Diabetes mellitus is a major public health challenge in India, contributing significantly to morbidity and reduced quality of life (QOL). Metformin remains the cornerstone of pharmacological therapy, while dipeptidyl peptidase-4 (DPP-4) inhibitors such as sitagliptin are increasingly prescribed as add-on agents. Despite well-established efficacy and safety, evidence on QOL outcomes with this drug combination remains limited. This study assessed QOL in individuals with type 2 diabetes mellitus (T2DM) receiving metformin–sitagliptin therapy and explored the association between sitagliptin dose and QOL. **Materials and Methods:** A cross-sectional study was conducted among 80 adults with T2DM attending the Department of Endocrinology, Government Medical College, Thiruvananthapuram, and the Indian Institute of Diabetes, Pulayanarkotta. Eligible participants (≥ 18 years) on metformin (≥ 1000 mg) plus sitagliptin (50–100 mg) were recruited after informed consent. Baseline demographic, clinical, and laboratory details were documented. QOL was assessed at 12 weeks using the WHOQOL-BREF questionnaire in Malayalam or English. Domain scores were transformed to a 0–100 scale and classified as poor, intermediate, or good QOL. **Results:** The mean age of participants was 56 ± 9.06 years, with 60% male. Median scores in physical, psychological, social, and environmental domains indicated an overall moderate QOL. Participants receiving sitagliptin 100 mg demonstrated higher mean domain scores compared to 50 mg, though the differences did not reach statistical significance. **Conclusion:** Metformin–sitagliptin therapy was associated with moderate QOL in people with T2DM. The WHOQOL-BREF questionnaire proved reliable for assessment in this population. While no statistically significant dose-dependent differences were observed, a trend toward improved QOL with 100 mg sitagliptin was noted. Larger, longitudinal studies are warranted to confirm these findings and elucidate drug-specific influences on QOL.

Keywords: Type 2 diabetes mellitus, Metformin, Sitagliptin, DPP-4 inhibitors, Quality of life, WHOQOL-BREF.

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INTRODUCTION

Diabetes mellitus represents a major public health challenge in India, with an estimated 89.8 million adults (20–79 years) diagnosed in 2024.^[1] The burden is particularly high in South India, where prevalence has reached 16.03%, with Kerala ranked second only to Pondicherry.^[2] Metformin remains the cornerstone of type 2 diabetes mellitus (T2DM) therapy and is one of the most extensively studied oral hypoglycemic agents. Its primary mechanisms include suppression of hepatic gluconeogenesis, enhancement of peripheral glucose uptake, and improvement of insulin sensitivity, thereby reducing insulin resistance. Over several decades, robust clinical evidence has confirmed its efficacy in achieving durable glycemic control without significant risk of weight gain or hypoglycemia. Owing to this favorable efficacy–safety profile, metformin continues to be recommended as the first-line pharmacological agent at T2DM diagnosis.^[3]

Dipeptidyl peptidase-4 (DPP-4) inhibitors constitute another important class of oral glucose-lowering drugs. These agents enhance glucose-dependent insulin secretion and act through a mechanism distinct from sulfonylureas.^[4] Sitagliptin, a widely used DPP-4 inhibitor, has

demonstrated proven efficacy and safety as add-on therapy to metformin in individuals with T2DM.^[5–9]

Although recent nationwide data on antidiabetic drug utilization are limited, a study from Ahmedabad in 2013 reported metformin use in 87.7% and DPP-4 inhibitor use in 10.5% of individuals with T2DM [10]. Beyond glycemic control, diabetes is associated with diverse complications such as retinopathy, neuropathy, cardiovascular disease, and diabetic foot. Moreover, psychological comorbidities including depression and anxiety adversely affect daily functioning and psychosocial well-being, thereby reducing quality of life (QOL).^[11]

In view of the rising prevalence of diabetes and its multidimensional impact on health, QOL assessment has

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emerged as a critical outcome in chronic disease management.^[11] Despite the widespread use of metformin–sitagliptin combination therapy, there is a paucity of research examining QOL in this subgroup. This cross-sectional study was therefore designed to evaluate the overall QOL of individuals with T2DM receiving metformin and sitagliptin combination therapy.

MATERIALS AND METHODS

Study Design and Setting: This cross-sectional study was conducted from December 2018 to December 2019 in the Department of Endocrinology, Government Medical College, Thiruvananthapuram, and the Indian Institute of Diabetes, Pulayanarkotta. Eligible participants were recruited after obtaining written informed consent. Baseline data collected included sociodemographic characteristics, clinical diagnosis, treatment history, anthropometric parameters (weight, height, abdominal circumference), comorbidities, and laboratory investigations such as fasting blood sugar (FBS), postprandial blood sugar (PPBS), lipid profile, and glycated hemoglobin (HbA1c). Quality of life (QOL) was assessed at 12 weeks using the pre-validated WHOQOL-BREF questionnaire.

Participants: Adults aged ≥ 18 years with T2DM receiving metformin (≥ 1000 mg) in combination with sitagliptin (50–100 mg), who had complete laboratory records (FBS, PPBS, HbA1c, and lipid profile), and were able to understand and respond to the WHOQOL-BREF questionnaire (Malayalam or English version) were included. Exclusion criteria were: T2DM patients treated with other oral antidiabetic drug combinations or insulin, those managed with diet and exercise alone, patients with renal complications, and individuals with type 1 diabetes mellitus.

Variables: QOL was assessed using the WHOQOL-BREF questionnaire, which consists of 26 items: two covering overall QOL and general health, and 24 grouped into four domains—physical health, psychological health, social relationships, and environmental health. Responses were rated on a 5-point Likert scale (1–5).

Sample Size: A sample size of 80 was determined based on the study by Subodhkumar et al,^[12] which compared efficacy, safety, and treatment satisfaction of glimepiride versus sitagliptin in combination with metformin in T2DM.

Statistical Analysis: Descriptive statistics were applied, with results presented as mean $\pm$ standard deviation (SD). Mean domain scores were calculated and transformed into standardized scores ranging from 0 to 100, as per WHOQOL-BREF guidelines. Scores ≤ 25 th percentile indicated poor QOL, ≥ 75 th percentile indicated good QOL, and intermediate scores reflected moderate QOL.

Ethical Approval: The study protocol was reviewed and approved by the Institutional Research Committee and the Institutional Human Ethics Committee of Government Medical College, Thiruvananthapuram.

RESULTS

Patient demographics

The age of the study population ranged from 18 – 80 years. The mean age was 56 ± 9.06 years. Among the 80 patients included in the study, 2.5% were less than 40 years. 52 patients (65%) belonged to the age group of 40 – 59 years. 32.5% belonged to an age group of 60 – 80 years. 60% of study participants were male. Mean duration of diabetes was 7.1 years. 58.7% patients were on metformin 1000 mg and 76.2% patients were on sitagliptin 100 mg. Other demographics have been presented in [Table 1].

Table 1: Patient demographics

Variables	Frequency
Age (mean $\pm$ SD)	56 ± 9.06
Male [No. (%)]	48 (60%)
Female [No. (%)]	32 (40%)
Duration of diabetes (years)	7.1 ± 3.57
Patients on Metformin 1000mg (%)	58.7
Patients on Metformin 2000mg (%)	41.2
Patients prescribed on Sitagliptin 50mg (%)	23.7
Patients prescribed on Sitagliptin 100mg (%)	76.2
HbA1c (mean $\pm$ SD)	7.6 ± 1.0

Among the study group, higher proportion of patients (38.75%) were prescribed 2000 mg of Metformin and 100 mg of Sitagliptin, followed by 1000 mg of Metformin and 100 mg

of Sitagliptin among 37.5%. Only 2 patients (2.5%) were prescribed 2000 mg of Metformin and 50 mg of Sitagliptin [Table 2].

Table 2: Patients on different doses of metformin and sitagliptin combination

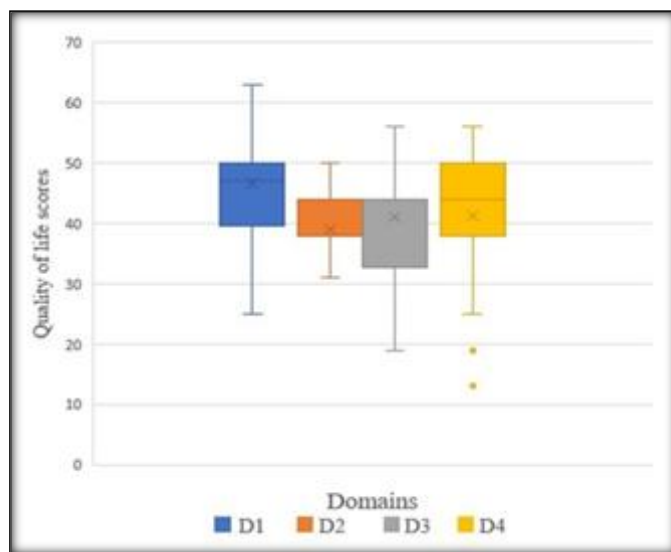
Dose (mg)		Patients [No. (%)]
Metformin	Sitagliptin	
1000	50	17 (21.25)
1000	100	30 (37.5)
2000	50	2 (2.5)
2000	100	31 (38.75)

Table 3: Association between drug dosage and QOL

Domains	Dose of Sitagliptin (Mean ± SD)		p-value
	50 mg	100 mg	
Domain 1	44.44 ± 8.53	47.42 ± 8.20	0.721
Domain 2	38.00 ± 5.66	39.26 ± 5.13	0.560
Domain 3	38.28 ± 10.09	41.95 ± 9.42	0.184
Domain 4	39.00 ± 9.46	41.95 ± 9.51	0.822

Patient QOL

Domain wise interquartile range varied from 39.50 to 50.00 (median=47.00), and from 38 to 44 (median = 38.00), and from 32.75 to 44 (median = 44.00), and from 38 to 50 (median = 44.00) in the physical, psychological, social and environmental domains respectively (Figure 1). The median scores of the all the four domains lies between 25th and 75th percentile indicating an overall moderate QOL [Figure 1].

**Figure 1: Quality of life scores of participants across four domains**

D1(Physical domain), D2(Psychological domain), D3(Social domain), D4(Environmental domain)

The domains of QOL were analysed for the determinant-dosage of Sitagliptin. In all domains a dose of 100 mg Sitagliptin showed a comparatively higher mean than 50 mg of Sitagliptin, but there was no statistically significant association [Table 3].

DISCUSSION

In this cross-sectional study of 80 individuals with T2DM receiving metformin–sitagliptin combination therapy, overall QOL after 12 weeks was found to be moderate across physical, psychological, social, and environmental domains. To the best of our knowledge, this is among the first studies in India to specifically assess QOL in people on this combination regimen using the WHOQOL-BREF scale. Previous studies from India have demonstrated heterogeneous results regarding QOL in T2DM populations, likely reflecting regional, demographic, and healthcare delivery differences. A rural South Indian study involving 100 participants reported

that more than 60% had good physical and psychological QOL, while environmental domain scores reached 85%, suggesting that diabetes did not substantially impair QOL when assessed with the WHOQOL-BREF questionnaire.^[13] In contrast, a study from Patna, which compared 124 T2DM patients with 124 healthy controls, reported higher mean QOL scores among the diabetic group (77.8 vs. 75; $p = 0.015$), with significantly higher scores across multiple domains.^[14] Conversely, other findings point toward greater impairment in diabetes. A Western Indian study of 114 participants found that uncontrolled T2DM was associated with significantly poorer QOL compared with controlled disease.^[15] Similarly, an Eastern Indian study involving 306 patients reported that males, urban residents, younger adults (<60 years), and overweight individuals had better QOL, underlining the influence of sociocultural and health system disparities on patient-reported outcomes. These results also highlight the importance of integrating mental health and lifestyle interventions into diabetes management to improve overall well-being.^[16] It is noteworthy that while several Indian studies have examined overall QOL in T2DM, they did not focus on drug-specific analysis. Prior clinical trials have consistently demonstrated the efficacy and safety of sitagliptin–metformin therapy in improving glycemic outcomes.^[7–9] Although these benefits may indirectly suggest a favorable influence on QOL, quantitative evidence from validated QOL instruments has been lacking. In the present study, participants receiving sitagliptin 100 mg showed slightly higher mean QOL scores compared with those receiving 50 mg, but the differences did not reach statistical significance. To our knowledge, no prior studies have directly evaluated sitagliptin dose–response relationships in relation to QOL outcomes using the WHOQOL-BREF tool. Larger, multicentric, and longitudinal studies are warranted to confirm these observations and to clarify whether higher doses of sitagliptin may confer incremental improvements in QOL among people with T2DM.

CONCLUSION

The present study demonstrated that individuals with T2DM receiving metformin–sitagliptin combination therapy experienced an overall moderate quality of life across physical, psychological, social, and environmental domains. The WHOQOL-BREF questionnaire proved to be a practical and reliable tool for assessing patient-reported outcomes in this setting. Although no statistically significant differences were observed between sitagliptin doses, participants receiving 100 mg consistently achieved higher mean domain scores, suggesting a possible but unconfirmed dose–response effect. These findings reinforce the importance of integrating

QOL evaluation into routine diabetes care, beyond conventional glycemic targets. Larger, multicentric, and longitudinal studies are needed to establish robust evidence on the impact of antidiabetic drug dosage on health-related QOL and long-term patient well-being.

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Conflicts of interest

There are no conflicts of interest.

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