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Original Research Article

Assessment Of Quality of Life and Clinical Outcomes in Type 2 Diabetes: A Comparative Study of Metformin-Based Combination Therapies Using Sf-12

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Abstract: This study aimed to evaluate and compare the quality of life (QoL) and clinical outcomes among patients with type 2 diabetes mellitus (T2DM) receiving different metformin-based oral combination therapies using the SF-12 questionnaire. A cross-sectional observational study was conducted among 212 T2DM patients aged 18–80 years attending the outpatient department of a tertiary care hospital and receiving stable therapy for at least six months. Quality of life was assessed during patient counselling sessions, and clinical parameters including glycated haemoglobin (HbA1c) and body mass index (BMI) were recorded. Statistical analysis was performed using SPSS software to evaluate correlations between clinical variables and QoL domains. All assessed clinical parameters demonstrated a statistically significant inverse correlation with QoL scores, indicating poorer quality of life with worsening metabolic control. The strongest negative association was observed between HbA1c levels and the physical component of QoL, highlighting the impact of poor glycemic control on physical health. Among treatment regimens, the metformin plus SGLT-2 inhibitor combination demonstrated superior glycemic control and the highest QoL scores, followed by the DPP-4 inhibitor plus thiazolidinedione combination, while metformin plus sulfonylurea showed comparatively lower outcomes. The findings suggest that metformin combined with SGLT-2 inhibitors provides optimal clinical effectiveness and quality-of-life benefits, supporting the integration of patient-reported QoL measures into routine diabetes management for individualized therapy selection.This study emphasizes the importance of integrating QoL assessment into routine diabetes management to optimize therapeutic outcomes..

Keywords: Type 2 diabetes mellitus; Quality of life; SF-12 questionnaire; Metformin-based combination therapy; Glycemic control.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder that requires long-term pharmacotherapy, lifestyle modification, and continuous monitoring to achieve optimal glycemic control and prevent complications.[1]In clinical practice, diabetes management is guided by evidence-based guidelines, institutional protocols, and physician judgment, while also being influenced by factors such as treatment efficacy, safety, tolerability, and patient satisfaction. Adherence

to clinical guidelines is crucial for enhancing therapeutic outcomes and standardizing diabetes care.[2]However, the complex demands of diabetes management, including dietary restrictions, physical activity, medication adherence, and regularglucose monitoring, often impose a substantial burden on patients, negatively affecting their quality of life (QoL).[3,4]

The World Health Organization defines quality of life as an individual's perception of their position in life in the context of cultural values, goals, expectations, and concerns, and it is now recognized as an important health outcome.[5,6]Diabetes is known to significantly impair health-related quality of life (HRQoL), particularly in patients with poor glycemic

control, obesity, or associated comorbidities. The American Diabetes Association emphasizes a patient-centred approach that not only targets glycemic control and complication prevention but also prioritizes improvement in QoL.[7]

Several demographics, clinical, and psychosocial factors influence QoL in patients with T2DM, including age, gender, duration of illness, body mass index (BMI), glycated haemoglobin (HbA1c), treatment complexity, and psychological well-being.[8] Reliable assessment of QoL requires validated, multidimensional tools that are applicable across diverse populations. The SF-12 questionnaire, a concise and validated version of the SF-36, has been widely used to assess physical and mental health outcomes in chronic diseases.[9]

Previous studies have demonstrated the metabolic and functional benefits of newer oral antidiabetic combinations. An observational prospective pilot study assessing the combined use of dipeptidyl peptidase-4 (DPP-4) and sodium–glucose cotransporter-2 (SGLT-2) inhibitors in patients with type 2 diabetes mellitus reported significant reductions in HbA1c along with improvement in physical functioning, suggesting complementary and synergistic effects of this combination therapy. The authors emphasized that such combination regimens may contribute not only to improved glycemic control but also to the enhancement of patients' quality of life and functional status, thereby supporting the need for treatment strategies that extend beyond biochemical targets alone. However, evidence comparing different metformin-based combination therapies using standardized quality-of-life instruments remains limited.[10]

Previous evidence supports the clinical benefits of newer oral antidiabetic combination therapies. An observational prospective study evaluating combined dipeptidyl peptidase-4 (DPP-4) and sodium–glucose cotransporter-2 (SGLT-2) inhibitor therapy demonstrated significant reductions in HbA1c with improvement in physical functioning, suggesting complementary metabolic and functional benefits. These findings are reinforced by an updated systematic review and meta-analysis of 17 randomized controlled trials involving 7,588 participants, which reported superior glycemic control and modest weight reduction with SGLT-2/DPP-4 inhibitor combination therapy compared with monotherapy, without an increased risk of hypoglycemia. Importantly, the HbA1c-lowering effect was more pronounced in Asian populations, highlighting the relevance of these combinations in regional diabetes care.[11]

In this context, the present study was undertaken to comparatively evaluate clinical outcomes and quality of life across commonly prescribed metformin-based combination therapies using the SF-12 questionnaire, thereby addressing an important gap in patient-centered diabetes care.Therefore, this study was undertaken to assess and compare the quality of life and clinical outcomes among patients with T2DM receiving various metformin-based oral combination therapies, with the hypothesis that therapies providing better glycemic control and weight benefit would be associated with improved QoL.

MATERIALS AND METHODS

Study design and setting

A hospital-based, cross-sectional observational study was conducted in the Department of General Medicine of a teaching and general hospital in Hyderabad, India. Patients were recruited from the outpatient department.

Study population

Patients diagnosed with type 2 diabetes mellitus for at least six months before enrolment were included in the study.

Inclusion criteria

Patients aged 18–80 years with T2DM who were receiving oral hypoglycaemic agents for a minimum duration of three months, either as monotherapy or metformin-based combination therapy, were eligible for inclusion.

Exclusion criteria

Patients unwilling to participate, those with significant comorbid conditions such as malignancy, individuals with alcoholism, and patients with major psychiatric disorders were excluded from the study.

Sampling method and ethical considerations

Eligible patients attending the outpatient department were consecutively enrolled and categorized into different drug-combination groups. The study protocol was explained to all participants, and written informed consent was obtained before enrolment. Ethical approval for the study was obtained from the Institutional Ethics Committee.

Quality of Life AssessmentQuestionnaire

Health-related quality of life was assessed using the standardized SF-12 questionnaire, which evaluates eight domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health. Scores for each domain range from 0 to 100, with higher scores indicating better health status, except for the bodily pain domain, where higher scores reflect greater pain.Diabetes status was self-reported with the following options: (1) Yes, but not on medication, (2) Yes, on oral anti-diabetic medication (excluding

insulin), (3) Yes, on insulin, or a combination of options (2) and (3) for patients on both therapies.

Follow-up:
Every patient who was enrolled had already received structured diabetes education during earlier visits, with an average duration of three to six months.

Scoring of SF-12

Step 1: Data cleaning and item recoding
All questionnaire responses were checked for out-of-range values. Four items (GH1, BP2, MH3, and VT2) were reverse-coded to ensure that higher scores consistently represented better health.

Step 2: Creation of indicator variables
Indicator variables were generated for each response category except the best health state, resulting in 35 dummy variables.

Step 3: Weighting and aggregation
Each indicator variable was multiplied by its corresponding physical or mental regression weight and summed to generate Physical Component Summary (PCS-12) and Mental Component Summary (MCS-12) scores.

Step 4: Norm-based standardization
PCS-12 and MCS-12 scores were standardized using norm-based scoring with a mean of 50 and a standard deviation of 10.

Statistical analysis
Data were analysed using SPSS statistical software. Descriptive statistics were used to summarize demographic and clinical characteristics. Correlation analysis was performed to evaluate the association between clinical parameters and QoL domains. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 220 patients were approached, and out of them, 8 subjects were discontinued. Thus, the final sample size was 212. The data collected were analyzed to assess the demographic distribution across different therapy types. In the population under investigation, where demographic was assessed, it shows male predominance, whereas in the case of comparison of hypertension and dyslipidemia as the impact of clinical variables, HTN outnumbered the dyslipidemia. (Table 1)

Table.1: Influence of Demographic/Clinical Factors comorbidities (%)

Variable	Category	Percentage (%)
Gender	Male/ Female	55/45
Co morbidity-1	Hypertension	60
Co morbidity-2	Dyslipidemia	42

The improved glycemic management attained with metformin plus SGLT-2 inhibitor combination (HbA1c 7.2%), it reflects established clinical evidence supporting SGLT-2 inhibitors as preferred second-line agents. The combination of metformin + SGLT2 inhibitors shows the best clinical effectiveness against glycemic control. [Table 2]

Table.2: Clinical Effectiveness of Drug Combinations on Blood glucose and HbA1C

Drug Combination	HbA1c (%)	FBS (mg/dL)	PPBS (mg/dL)
Metformin + Sulfonylurea	7.8±0.32*	152.3±9.51*	204.6±18.3*
Metformin + SGLT-2 Inhibitor	7.2±.54**	143.8±10.86**	190.5±16.2***
DPP-4 Inhibitor + Thiazolidinedione	7.5±0.65**	148.1±11.66**	198.4±12.4*

(Data were significant values *p<0.05, ** p<0.01, *** p<0.001, vs control, diabetics treated combination groups)

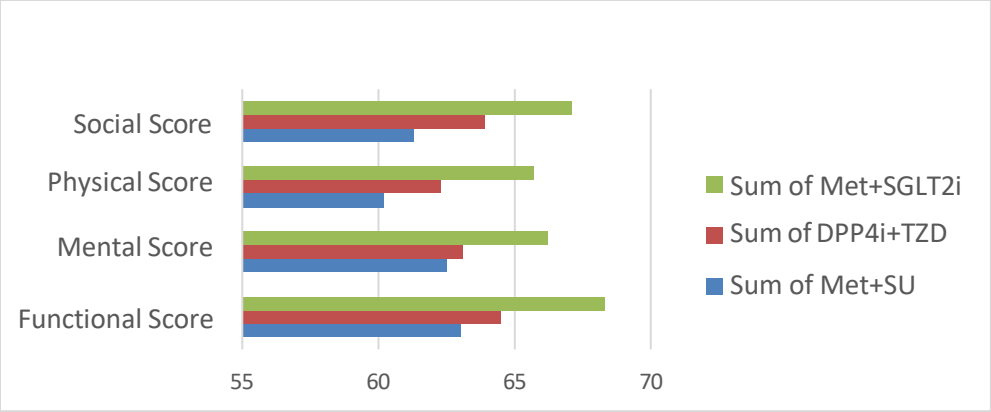
The safety analysis revealed the highest hypoglycemia risk is with metformin plus sulfonylurea (20%), compared to SGLT-2 inhibitor (6.7%) and DPP-4 plus thiazolidinedione (3.3%) combinations, confirming established

sulfonylurea safety concerns. Additionally, weight gain was more common with sulfonylurea therapy (16.7%) compared to SGLT-2 inhibitor regimens (3.3%). The DPP-4 plus TZD combination demonstrated the most advantageous safety profile with negligible adverse events.

Metformin plus SGLT-2 inhibitors showed good safety with only a small incidence of renal complications. Overall, metformin plus sulfonylurea exhibited the least favorable safety profile due to higher rates of hypoglycemia, GI disturbances, and weight gain.

The consistent superiority of metformin plus SGLT-2 inhibitor combinations across all quality-of-life domains (physical: 65.7, mental: 66.2, social: 67.1, functional: 68.3) compared to other combinations provides compelling evidence for patient-centered treatment selection. This finding is particularly significant given the strong relationship between medication burden and quality of life demonstrated by the progressive decline in total QoL ratings when the number of drugs increases (1 drug: 62.1±7.8; 2 drugs: 58.3±8.5; ≥3 drugs: 53.7±9.2). The combination of Met + SGLT2i shows the highest score in all the QoL domains, followed by DPP4i+TZD with intermediate scoring. Met+SU got the lowest score across all the QoL domains. [Fig- 1]

Fig-1: Impact on Quality of Life (QoL) with the drug therapy of antidiabetics



The correlation for all the variable pairs are negative, and statistically, it indicates a lower QoL score. The strongest association is between HbA1c & physical QoL (r = -0.41), indicating that physical health is most affected if there is a poor glucose/ glycemic control. [Table 3]

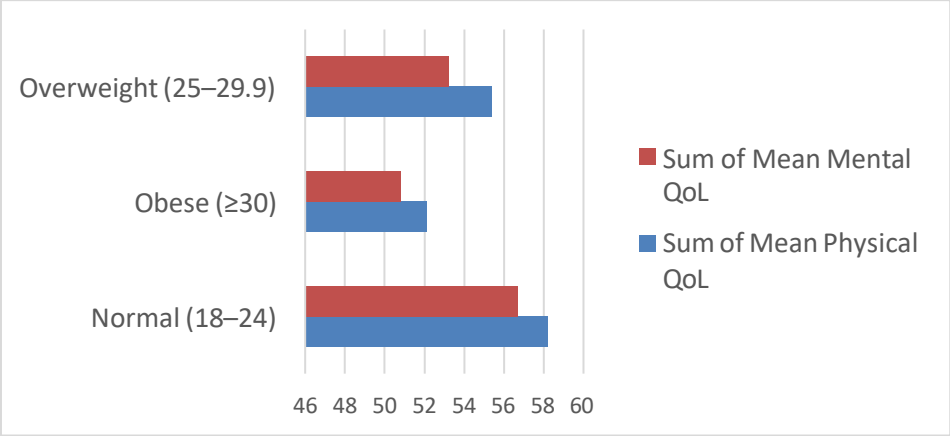
Table 3: Correlation Between Glycemic Control and QoL

Variable Pair	Correlation (r)	p-value
HbA1c vs. Physical QoL	-0.41	0.004
FBS vs. Functional QoL	-0.38	0.006
HbA1c vs. Mental QoL	-0.35	0.01
RBS vs. Social QoL	-0.3	0.015

This analysis reveals the inverse relationship between physical & mental health, that is, as the BMI increases, the QoL decreases.

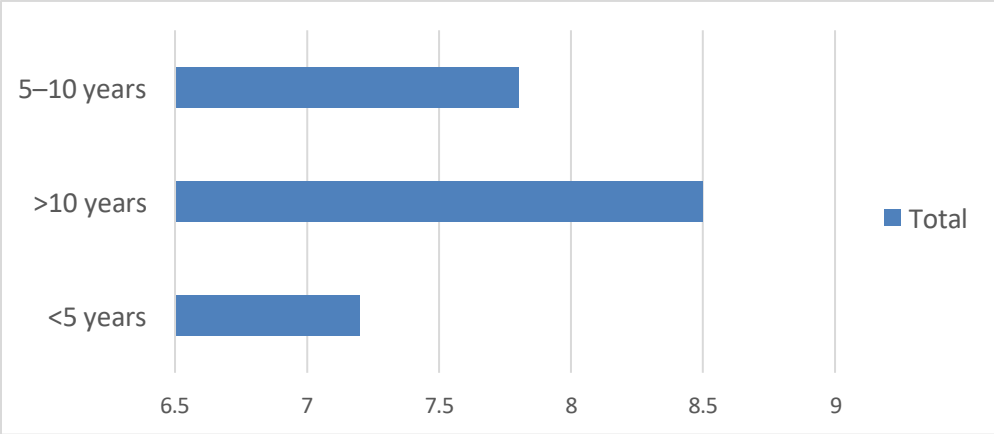
The population with normal BMI (18-24) exhibit highest QoL score as the BMI increases, that is,≥30. (fig-2)

Fig-2: QoL vs. BMI



When the relationship between the duration and HbA1c was assessed, it revealed direct proportionality(fig-3).

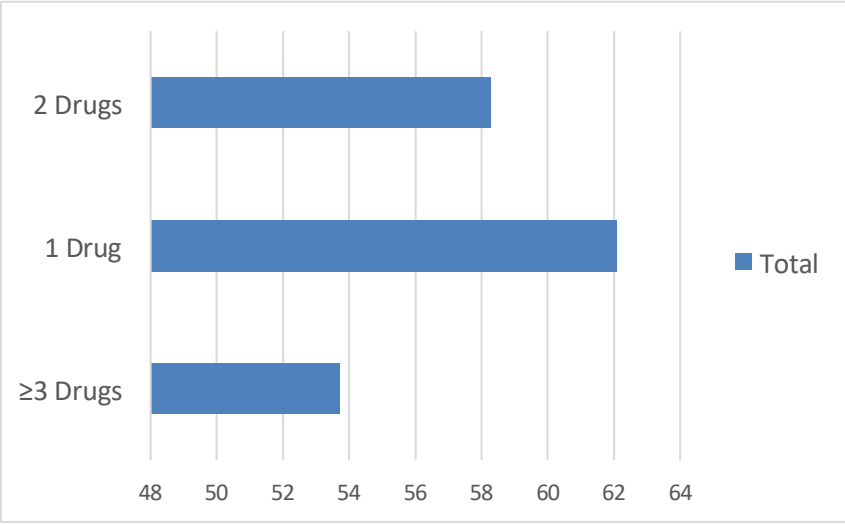
Fig-3: Duration and HbA1c



The patients on monotherapy, dual therapy, and polytherapy are assessed for quality of life, which shows that monotherapy reports a higher QoL.

This parameter exhibits an inverse relationship between the number of drugs &QoL. [Fig-4].

Fig-4: Number of Drugs vs QoL



The data of 212 diabetic patients, out of which 118 are males & 94 are females, were analyzed for the QoL. It shows males have slightly better QoL for both mental and Physical health.Males also have a marginally higher mean overall quality of life than females.

Table 4: QoL by Gender

Gender	n	Mean ±SDPhysical QoL	Mean±SD Mental QoL	Mean±SD Total QoL
Male	118	57.8±3.2*	56.2±3.3*	57±2.3*
Female	94	54.6±2.3*	52.9±3.6	53.8±3.8

(Data were significant values *p<0.05, QoL Vs. diabetics treated combination groups)

Table 5 : ANOVA / Correlation FOR QOL RESULTS

ANOVA	9.45	<0.001*	Significant (p < 0.001)
Pearson Correlation (r)	-0.38	<0.001*	Negative correlation (more drugs = lower QoL)

Table.6: Independent t-Test

QoL Domain	t-value	p-value	Interpretation
Physical Well-being	2.94	0.004*	Significant (p < 0.05)
Mental Well-being	2.67	0.009*	Significant (p < 0.05)
Total QoL Score	2.81	0.006*	Significant (p < 0.05)

(Data were significant values *p<0.05, QoL Vs. diabetics treated combination groups)

Table.7: ANOVA for BMI vs. QoL

QoL Domain	F-value	p-value	Interpretation
Physical Well-being	6.84	0.002*	Significant difference (p < 0.05)
Mental Well-being	5.12	0.008*	Significant difference (p < 0.05)

(Data were significant values *p<0.05, QoL Vs. diabetics treated combination groups)

DISCUSSION

Clinical Effectiveness and Glycemic Control

The present study demonstrates the consistent superiority of metformin combined with SGLT-2 inhibitors across glycemic, functional, and quality-of-life outcomes. These findings align with accumulating evidence favoring early combination therapy in type 2 diabetes to achieve durable glycemic control and reduce therapeutic inertia [12,13]. The observed 0.6% difference in HbA1c between the most and least effective regimens is clinically meaningful, as even modest reductions in HbA1c have been shown to significantly lower the risk of long-term microvascular and cardiovascular complications [14,15,16]. Beyond biochemical improvement, the significant inverse correlations between HbA1c and physical (r = −0.41) and mental (r = −0.35) QoL domains underscore the multidimensional impact of glycemic control on patient well-being, functional capacity, and psychosocial health.

Safety Profile Considerations

Variation in safety outcomes across treatment combinations highlights the importance of individualized therapeutic decision-making [17,18]. SGLT-2 inhibitor–based regimens demonstrated a lower incidence of hypoglycemia and minimal weight gain, which likely contributed to improved QoL and

higher treatment satisfaction. These safety advantages are particularly relevant in real-world settings, where fear of hypoglycemia and weight gain frequently compromise adherence and persistence with therapy [19,20,21]. The favorable tolerability profile of SGLT-2 inhibitors therefore enhances both clinical effectiveness and patient acceptability.

Quality of Life Outcomes and Treatment Expenditure
The observed negative association between medication burden and QoL ($r = -0.38$, $p < 0.001$) emphasizes the clinical value of simplified treatment regimens. Higher pill burden and complex dosing schedules are known to increase treatment fatigue, reduce adherence, and negatively impact patient perception of therapy [19,20,22]. SGLT-2 inhibitor–based combinations, particularly when used in fixed-dose formulations, may reduce regimen complexity, optimize adherence, and improve QoL while also potentially lowering long-term healthcare costs through complication prevention.

Demographic and Clinical Influences on Quality of Life

Gender-based differences in QoL scores, with females demonstrating lower physical and mental domain scores, are consistent with previously reported disparities in diabetes outcomes and psychosocial stressors [22,23,24]. Additionally, BMI-stratified analysis revealed significantly lower QoL scores among obese patients, reinforcing the negative impact of excess body weight on both physical functioning and psychological health. These findings support the preferential use of weight-neutral or weight-reducing therapies such as SGLT-2 inhibitors, which have demonstrated benefits across metabolic, functional, and patient-reported outcomes [25,26].

Activity Limitation and Functional Outcomes

A progressive improvement in functional status was observed across follow-up visits, with a marked reduction in severe activity limitation and a corresponding increase in patients reporting no limitation. These changes ($\chi^2 = 15.72$, $p = 0.003$) highlight the capacity of effective and well-tolerated diabetes management to reverse functional decline and enhance daily independence. Improved physical functioning may result from better glycemic control, weight reduction, reduced treatment side effects, and increased patient confidence in disease self-management [27,28].

Treatment Adherence and Long-Term Outcomes

Improved glycemic control was closely associated with better adherence, reduced complication burden, and enhanced QoL [29,30]. The superior outcomes observed with SGLT-2 inhibitor combinations likely reflect both their pharmacological efficacy and adherence advantages, including once-daily dosing, low hypoglycemia risk, and favorable metabolic effects [30,31,32]. Sustained adherence remains critical for long-term prevention of diabetes-related complications, emphasizing the importance of selecting therapies that align with patient preferences, tolerability, and lifestyle considerations.

CONCLUSION

This thorough research shows that the best option for managing type 2 diabetes across a number of outcome areas is a combination of metformin and SGLT-2 inhibitors. The combination consistently produced the best quality of life scores across all domains tested, demonstrated the most favorable safety profile with little weight gain (3.3%) and hypoglycemia (6.7%), and achieved improved glycemic control (HbA1c 7.2%). Since the observed differences in quality of life outcomes between men and women may reflect different treatment responses necessitating individualized therapeutic approaches, gender-specific considerations should guide treatment selection. Similarly, preferential use of weight-neutral or weight-reducing drugs, such as SGLT-2 inhibitors, is supported by the significant inverse association between BMI and quality of life.

The **temporal improvement in functional outcomes** observed across study visits demonstrates that the most effective therapy for diabetes can reverse activity limitations and improve patients' physical capabilities over time. **Clinical implications** include the recommendation for earlier initiation of SGLT-2 inhibitor-based combinations, particularly in patients with higher BMI or quality of life concerns. The superior benefit-risk profile of these combinations, combined with their positive impact on cardiovascular and renal outcomes established in large clinical trials, supports their position as preferred second-line therapy after metformin. **Future research** should focus on developing personalized treatment algorithms that incorporate quality of life assessments alongside traditional clinical parameters. Long-term studies examining the durability of these benefits and cost-effectiveness analyses considering both clinical outcomes and quality of life improvements would further inform evidence-based diabetes care practices.

ETHICAL APPROVAL

This study was approved by the Institutional Ethical Committee of Shadan Institute of Medical Sciences Teaching Hospital and Research Centre, Hyderabad, Telangana. With Ref no: 069/SIMS/Research/2023.

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Conflict Of Interest Statement

We declare no conflict of interest

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