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EXPLORE THE LATEST ADVANCEMENT IN DIABETES MANAGEMENT INCLUDING NEW MEDICATION AND LIFESTYLE INTERVENTIONS

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Abstract

Background: *Diabetes mellitus is the chronic metabolic disease, which is marked by the constant increase in glucose level because of the impairment of insulin secretion, its action, or both. Current developments have altered the development of the management of diabetes, with new pharmacological agents, technology, and personalized lifestyle interventions being highlighted to help patients manage their glycemic control, reduce complications, and overall improve their quality of life.*

Objectives: *To assess the effectiveness of new drugs and lifestyle changes on glycemic control, cardiovascular, and quality of life in patients with type 2 diabetes mellitus in a tertiary care environment.*

Study Design: *A prospective study.*

Place and duration of study*: From July 2024 to December 2024 General Medicine Department, Bolan Medical Complex Hospital Quetta.*

Methods: *The study actually comprised of a prospective study of 120 diabetic patients in a tertiary care hospital. Structured questionnaires (that measured demographics, medication type, adherence to lifestyle and glycemic control) were used to collect data. Laboratory parameters such as fasting blood glucose and HbA1c were measured. Statistical tests were done in SPSS version 24.0 and $p < 0.05$ was used as the statistical significance.*

Results: *One hundred and twenty patients (54.6 ± 10.8 years on average; 58 men) were involved. There was a significant improvement in glycemic control (GLP-1 receptor agonists and SGLT2 inhibitors demonstrated a mean HbA1c of 6.8 ± 0.7 vs. the conventional therapy (7.9 ± 1.0): $p = 0.001$). Fasting glucose levels (102.4 ± 18.2 mg/dL) of patients who adhered to structured diet and exercise program were better as compared to non-adherent patients (126.7 ± 21.3 mg/dL), $p = 0.002$. There was an improvement in cardiovascular parameters and lower BMI in the group that has undergone pharmacologic plus lifestyle*

interventions.
Conclusion: *Coupled with a structured lifestyle intervention, the combination of high-technology antidiabetic drugs, including GLP-1 receptor agonists and SGLT2 blockers, has a significant effect on glycemic control and cardiovascular outcomes. The focus on patient education, constant glucose level monitoring, and personalized treatment approaches can be also used to improve disease management in the long-term and minimize diabetes-related complications. The combination of pharmacotherapy and lifestyle modification is the keystone of the optimal care of diabetes.*

Introduction:

Diabetes mellitus (DM) is a long-lasting metabolic condition where a person experiences hyperglycemia due to a failure of insulin secretion or a series of mechanisms of the insulin-combating hormone. It is still among the most important health issues in the world as International Diabetes Federation (IDF) reports that in 2021 some 537 million adults experienced diabetes, which is expected to increase to 643 million by 2030 unless current trends are managed [1]. T2DM is the closest related type of diabetes, as it is also related to obesity, sedentary living, and dietary imbalances and comprises almost 9095% of all cases of diabetes [2]. Prolonged hyperglycemia also causes microvascular and macrovascular problems such as renal pathology, eye pathology, neuropathy, and heart disease, and results in a significant morbidity and mortality among individuals in the entire world [3]. The last ten years witnessed an incredible change in management of diabetes. Metformin, sulfonylureas, and insulin, which are the traditional agents used to control glucose levels, are currently being supplemented with newer classes of pharmacologic agents that affect several pathophysiological processes of diabetes. Among them, sodium-glucose cotransporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have become the new front runners in both improving glycemic control and providing substantial cardiovascular and renal protection [4]. Recent study has also averted to the possibility of dual and triple incretin-based therapy, including tripeptide, which is a combination of GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptor agonism, which has shown greater weight loss and glycemic control than standard regimens [5].A number of large-scale cardiovascular outcome trials (CVOTs), like EMPA-REG OUTCOME and LEADER have demonstrated cardiovascular mortality and heart failure hospitalization reduction in patients treated with these agents [Moreover, oral GLP-1 and insulin once-weekly preparations have enhanced compliance and satisfaction [6]. Alongside pharmacological developments, lifestyle interventions have been re-established as some of the key strategies in managing diabetes. Caloric restriction, dietary changes, and consistent physical exercise can help to weight loss and considerably increase insulin sensitivity and can even lead to remission in early cases of T2DM [7]. The Diabetes Remission Clinical Trial (DiRECT) has indicated that close to 50 percent of the participants showed lasting remission after a structured low-calorie diet program [8]. There is also interest in time-restricted feeding and intermittent fasting as methods of improving glycemic parameters and not raising the risk of hypoglycemia. The further use of technology, such as continuous glucose monitoring (CGM) and automated insulin delivery, enables patients to reach personalized glycemic goals with a minimum of hypoglycemia. The American Diabetes Association (ADA) standards of care 2025 recommend that all patients under insulin therapy and selected non-insulin-therapy be evaluated to use CGM to maximize the effect. In these changing modalities, it is still necessary to consider the efficacy of more recent pharmacological treatment along with lifestyle changes. The proposed study will evaluate the effects of contemporary drug regimen and lifestyle change on the glycemic control,

anthropometric measurements, and cardiovascular outcomes in a tertiary care environment when used in patients with T2DM [9].

Methods:

The present study is a prospective one that was carried out From July 2024 to December 2024 General Medicine Department, Bolan Medical Complex Hospital Quetta. One hundred and twenty patients with type 2 diabetes mellitus were recruited using non probability consecutive sampling. Demographic data, type of medication and adherence to lifestyle modifications were recorded after informed consent was obtained and duration of diabetes was recorded. Parameters in the laboratory such as fasting blood glucose (FBG), glycated hemoglobin (HbA1c), lipid profile, and body mass index (BMI) were taken. The patients taking GLP-1 receptor agonists, SGLT2 inhibitors, or the traditional oral antidiabetic drugs (OADs) were compared on glycemic and cardiovascular outcomes.

Inclusion Criteria:

Included were adults between 30 and 70 years with a known diagnosis of insulin-resistant type 2 diabetes mellitus of over one year, who are on stable pharmacologic therapy, and would be willing to take part.

Exclusion Criteria:

The study excluded patients with type 1 diabetes, gestational diabetes, hepatic or renal failure, active malignancy, pregnant patients, and those not willing to consent to participate in the study.

Ethical Approval Statement:

After receiving ethical approval of the Institutional Review Board of Bolan Medical Complex Hospital Quetta the study was carried out. All participants signed an informed consent that was written before their enrollment, making the consent confidential, and sticking to the Declaration of Helsinki ethical principles.

Data Collection:

Demographic data, length of the disease, treatment regimen, physical activity, and diet compliance were recorded with the help of a structured questionnaire. Biochemical analyses were done by drawing blood samples after overnight fasting. Measurement of anthropometric parameters was done through standardized methods and all data were tabulated and checked by the trained clinical personnel.

Statistical Analysis:

The SPSS version 24.0 was used to analyze data. The quantitative variables were in terms of mean, standard deviation, whereas the qualitative variables were in terms of frequencies and percentages. Group comparison was done using student t-test and chi-square test and the p-value less than 0.05 was taken as statistically significant in all tests.

Results:

The sample size was 120 patients with type 2 diabetes, 70 of them males (58.3%), 50 females (41.7) with an average age of 54.6 +10.8 years. Among them, 48 (40%) were taking conventional oral antidiabetic medications, 42 (35%) SGLT2 inhibitors and 30 (25) GLP-1 receptor agonists. The patients who received newer therapies had better glycemic control, the mean HbA1c being 6.8/0.7 percent versus 7.9/1.0 percent in conventional group ($p = 0.001$). The mean fasting glucose was 104.2 +/-17.6 mg/ dL and 128.9 +/- 22.3 mg/dL respectively ($p = 0.002$). Females on combination therapy experienced cardiovascular (reduction of systolic blood pressure and improvement of HDL levels) and lifestyle modification (reduction of BMI) compared to non-adherent patients (26.8 ± 3.4 kg/m 2 vs 29.5 ± 4.2 kg/m 2, $p = 0.004$). No significant hypoglycemic incidents were complained of. In general, the combination of the pharmacologic and lifestyle interventions showed better metabolic results than either the intervention.

Table 1: Demographic Characteristics of Study Participants (n = 120)

Variable	Total (n=120)	Male (n=70, 58.3%)	Female (n=50, 41.7%)	p-value
Mean Age (years)	54.6 ± 10.8	55.2 ± 10.5	53.8 ± 11.3	0.412
BMI (kg/m²)	28.3 ± 4.1	27.9 ± 3.9	28.8 ± 4.3	0.318
Duration of Diabetes (years)	7.6 ± 3.4	7.9 ± 3.2	7.2 ± 3.7	0.285
Family History of DM	78 (65%)	42 (60%)	36 (72%)	0.174
Hypertension Present	66 (55%)	36 (51%)	30 (60%)	0.287
Smokers	28 (23%)	26 (37%)	2 (4%)	<0.001*

Table 2: Distribution of Antidiabetic Treatment Modalities

Treatment Group	Number of Patients (%)	Mean HbA1c (%)	Mean FBG (mg/dL)	p-value (vs Conventional)
Conventional OADs (Metformin ± Sulfonylurea)	48 (40%)	7.9 ± 1.0	128.9 ± 22.3	Reference
SGLT2 Inhibitors	42 (35%)	6.9 ± 0.8	106.3 ± 19.4	0.002*
GLP-1 Receptor Agonists	30 (25%)	6.8 ± 0.7	104.2 ± 17.6	0.001*
Combination (OAD + SGLT2/GLP-1)	18 (15%) †	6.5 ± 0.6	101.5 ± 16.2	0.001*

Table 3: Comparison of Lifestyle Adherence and Glycemic Outcomes

Lifestyle Parameter	Adherent (n=72, 60%)	Non-Adherent (n=48, 40%)	p-value
Mean BMI (kg/m²)	26.8 ± 3.4	29.5 ± 4.2	0.004*
Mean HbA1c (%)	6.7 ± 0.8	7.8 ± 0.9	0.001*
Mean FBG (mg/dL)	102.4 ± 18.2	126.7 ± 21.3	0.002*
Regular Exercise ≥150 min/week	62 (86%)	18 (37%)	<0.001*
Dietary Compliance (Low-carbohydrate diet)	58 (81%)	20 (42%)	<0.001*
Medication Adherence	68 (94%)	36 (75%)	0.018*

Table 4: Cardiovascular and Metabolic Parameters Across Treatment Modalities

Parameter	Conventional OADs	SGLT2 Inhibitors	GLP-1 RAs	Combination Therapy	p-value
Systolic BP (mmHg)	136.2 ± 15.3	129.6 ± 12.4	128.1 ± 11.8	126.4 ± 10.9	0.021*
Diastolic BP (mmHg)	86.4 ± 8.2	82.8 ± 7.6	81.5 ± 7.1	80.6 ± 6.8	0.034*
HDL-C (mg/dL)	42.6 ± 8.5	48.2 ± 9.1	50.4 ± 9.5	52.8 ± 8.8	0.012*
LDL-C (mg/dL)	119.5 ± 24.8	105.6 ± 22.2	102.4 ± 20.8	98.3 ± 19.6	0.018*
Triglycerides	172.3 ± 34.5	148.6 ± 28.9	145.8 ±	138.2 ± 25.6	0.029*

(mg/dL)			26.4		
Weight Reduction (kg)	0.8 ± 1.2	3.2 ± 1.8	3.6 ± 1.7	4.1 ± 1.9	

Discussion:

The current study has shown that the integrated approach of using new antidiabetic drugs like GLP-1 receptor agonists and SGLT2 inhibitors with planned lifestyle change programs resulted in better glycemic and cardiometabolic results relative to the usual oral antidiabetic treatment. The results are consistent with the worldwide trends that focus on personalized and multi-modes management of type 2 diabetes mellitus (T2DM). The findings of the LEADER and SUSTAIN-6 trials, in which liraglutide and semifluid reduced the mean HbA1c and cardiovascular mortality rates [10], are supported by our finding that patients who used GLP-1 receptor agonists had mean HbA1c of 6.8 ± 0.7%. Equally, the glycemic and weight outcomes of SGLT2 inhibitors in this case are similar to the EMPA-REG OUTCOME and DECLARE-TIMI 58 studies that reported large decreases in heart failure and renal disease progression hospitalization [11]. This was supported by a meta-analysis of 2024 by Yamada et al. which established that combined incretin and SGLT2 therapy is additively beneficial on glycemia, weight, and blood pressure with no excess hypoglycemia [12]. The new paradigm of weight-centric diabetes management is also represented in our results. Those who followed diet and physical-activity regimens experienced significant BMI loss (26.8 -0.3 kg/m2 compared with 29.5 -0.5 kg/m 2, p = 0.004). The Direct 5-year follow-up also reported similar results having found sustained remission in 36% of participants who had continued to lose 10 kg weight loss [13]. According to recent results of SURMOUNT-2 trials, tripeptide a dual GIP/GLP-1 receptor agonist produced average body-weight loss of 12 15% with strong A1c lowering, endorsing the dual-incretin strategy in the management of obesity and glycemic control [14]. The parameters of cardiovascular parameters like blood pressure and lipid profile also improved significantly in our study among participants that were treated with newer pharmacotherapy. This is in line with the CANVAS and DAPA-HF trials that demonstrated the cardioprotective nature of SGLT2 inhibitors even in non-diabetic groups [15]. In addition, recent findings also show that GLP-1 receptor agonists regulate endothelial activities and inflammatory processes, thus, on top of glucose-reducing effects, they have anti-atherogenic properties [16]. Changes in lifestyle have been a crucial part of diabetes management. Hu et al. (2023) conducted a randomized controlled trial which indicated that the insulin sensitivity increased by 25% and reduced HbA1c by 0.8% in six months in participants using structured exercise programs that included aerobic and resistance training [17]. Time-constrained feeding and intermittent fasting are also promising; Jamshed et al. found a decrease in the glycemic variability and oxidative stress in adults with T2DM after an 8-hour eating window [18]. Among our group members, lifestyle-sensitive participants demonstrated significantly smaller values of HbA1c and fasting glucose, which supports the cumulative value of behavioral interventions in combination with pharmacologic treatment. The further contribution to integrated diabetes management is technological advances. New technologies such as continuous glucose monitoring (CGM) and automated insulin delivery (AID) systems have changed the way glycemic monitoring and self-management is conducted in patients. Multicenter analysis by Bergen Stal et al. has shown that the use of CGM decreases HbA1c by 0.8 percent and time-in-range by 18 percent compared to traditional self-monitoring. ADA 2025 guidelines suggest CGM even in the non-insulin users that are chosen to maximize therapy titration and adherence [19]. Although the study has its strengths, such as a real-life hospital-based design and the comparison of pharmacologic categories, it has some limitations to be considered. The cross-sectional design restricts causation and sample size (n=120) might be

inadequate to indicate wider population diversity. Longer and more longitudinal-based studies, that would include continuous follow-up and patient-reported outcomes would give greater evidence on the long-term sustainability of these benefits. However, the study highlights a clinically important shift towards combined care which focuses on glycemic regulation, cardiovascular care, and the quality of life of the patient. The combination of modern incretin-based regimens with SGLT2 and lifestyle and technological interventions as an addition to the latter is a paradigm shift in the management of T2DM. The future studies need to be narrowed down to precision-medicine techniques that involve genetic, behavioral, and metabolic profiling to personalize therapy further [20]. Finally, our results support the idea that the use of new pharmacologic drugs with lifestyle change produces the best metabolic and cardiovascular results. Implementation of such a multidimensional approach can help improve the rates of remission of diabetes, decrease the incidence of complications and correspond to the international objective of an individual, result-oriented diabetes care.

Conclusion:

Combined with structured lifestyle interventions, the use of new pharmacologic agents, especially GLP-1 receptor agonists and SGLT2 inhibitors, can be used to improve glycemic control, cardiovascular outcomes, and the quality of life of patients with type 2 diabetes mellitus significantly. It is a multidimensional, evidence-based method that is the future of the overall management of diabetes.

Limitations:

The current study had limitations regarding the design (cross-sectional) and a rather small sample (limited to causal interpretation and generalizability). Self-reported adherence to lifestyle can bring about a recall bias. This study requires future longitudinal studies that are larger with randomized controlled designs to confirm the findings in different populations.

Future Findings:

Future study must examine the area of individualized, precision-based diabetes management using genomic, metabolic, and behavioral profiling. Further evaluation of the sustainability of remission, digital health integration, and real-world cost-effectiveness of combined pharmacologic and lifestyle interventions can further streamline the contemporary treatment of diabetes and enhance the treatment results worldwide.

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Authors Contributions

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