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ORIGINAL ARTICLE

Integrating Medicine and Pharmacology: The Burden of Heart Failure in Diabetes, Its Treatment Patterns and Consequences for Patient Quality of Life

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ABSTRACT

Aim of the Study: This study aimed to investigate the burden of heart failure (HF) in patients with diabetes mellitus (DM), analyze treatment patterns integrating medicine and pharmacology, and assess the consequences for patient quality of life (QoL). The objective was to bridge clinical practice and pharmacological interventions, thereby highlighting both therapeutic success and existing gaps in management.

Study Duration: The study was conducted over a 12-month period, from May 2022 to May 2023.

Place of Study: Data collection and patient evaluation were undertaken at Watim Medical & Dental College, Rawalpindi, and Jinnah Hospital, Lahore, two tertiary care centers providing specialized cardiovascular and endocrine services.

Methodology: A cross-sectional observational design was employed. A total of 450 patients with type 2 diabetes and diagnosed HF were included. Clinical parameters, comorbidities, pharmacological treatments, and QoL outcomes (assessed using the Kansas City Cardiomyopathy Questionnaire) were analyzed. Treatment regimens were categorized into diuretics, renin-angiotensin-aldosterone system (RAAS) inhibitors, beta-blockers, SGLT2 inhibitors, and combination therapies. Data were analyzed using descriptive and inferential statistics.

Results: Patients with coexisting HF and DM demonstrated significantly impaired QoL scores compared to general HF cohorts. SGLT2 inhibitors and RAAS inhibitors were associated with improved symptom control and QoL indices, whereas those on diuretics alone had poorer outcomes. The mean URR (%) and Kt/V equivalents in dialysis-comparable pharmacological adequacy revealed superior outcomes in patients receiving combined pharmacological regimens.

Conclusion: Heart failure in diabetes constitutes a double burden that severely impacts patients' QoL. Integrated pharmacological approaches provide superior outcomes compared to monotherapy. The findings underscore the urgent need for multidisciplinary strategies linking internal medicine, pharmacology, and patient-centered care.

Keywords: Heart failure, diabetes mellitus, pharmacological treatment, quality of life, SGLT2 inhibitors, RAAS inhibitors, integrated medicine

INTRODUCTION

Diabetes mellitus (DM) and heart failure (HF) are two of the most significant global health challenges, each imposing a major clinical and economic burden on healthcare systems. Over 537 million adults worldwide live with diabetes, a number projected to rise to 643 million by 2030 and 783 million by 2045 according to the International Diabetes Federation (IDF)[1]. Parallel to this, HF affects over 64 million people globally, with prevalence continuing to rise due to aging populations and improved survival after cardiovascular events[2]. Importantly, DM and HF frequently coexist; up to 40% of patients with HF have DM, and patients with DM are at a two- to five-fold increased risk of developing HF compared to non-diabetics[3].

This intersection of two chronic, progressive diseases is particularly concerning because the coexistence of DM and HF leads to poorer outcomes, increased hospitalizations, higher mortality, and diminished quality of life (QoL)[4]. The combination presents a unique therapeutic challenge for both physicians and pharmacologists, necessitating integrated approaches that address metabolic, hemodynamic, and symptomatic needs simultaneously.

The pathophysiology underlying the link between DM and HF is multifactorial and involves structural, metabolic, and neurohormonal derangements. Chronic hyperglycemia leads to endothelial dysfunction, oxidative stress, and advanced glycation end-product accumulation, all of which promote myocardial fibrosis and impaired diastolic function[5]. Additionally, insulin resistance contributes to altered substrate utilization, with diabetic hearts demonstrating preferential fatty acid metabolism that increases oxygen demand while impairing efficiency[6].

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Moreover, diabetic cardiomyopathy is now recognized as a distinct entity characterized by left ventricular hypertrophy, interstitial fibrosis, and diastolic dysfunction in the absence of overt ischemic heart disease[7]. Neurohormonal activation, particularly of the renin-angiotensin-aldosterone system (RAAS) and sympathetic nervous system, further exacerbates myocardial remodeling and progression to HF[8].Thus, diabetes does not merely coexist with HF—it actively drives its development and progression, creating a vicious cycle that worsens patient outcomes.

The global burden of HF in diabetic patients is staggering. Epidemiological studies consistently show that diabetics with HF have twice the risk of hospitalization and 1.5 times the risk of mortality compared to non-diabetic HF patients[9]. The economic implications are profound, with direct healthcare costs driven by repeated admissions, pharmacological expenditures, and long-term rehabilitation.

In South Asia, including Pakistan, the burden is compounded by rising diabetes prevalence, limited access to specialized care, and high rates of treatment discontinuation due to cost or side effects[10]. Regional studies highlight that Pakistani patients often present late, with advanced disease, and are frequently undertreated with evidence-based pharmacological therapies such as RAAS inhibitors and beta-blockers[11].

Quality of life (QoL) is a vital outcome in chronic diseases. HF alone significantly reduces QoL due to fatigue, dyspnea, and exercise intolerance, while diabetes adds the psychological burden of polypharmacy, dietary restrictions, and fear of hypoglycemia[12]. Tools like the Kansas City Cardiomyopathy Questionnaire (KCCQ) and the EuroQol-5D have consistently demonstrated lower scores in patients with both HF and DM compared to those with either condition alone[13].

Moreover, QoL impairment is not merely symptomatic—it predicts adverse clinical outcomes. Studies demonstrate that

patients with poorer baseline QoL scores are more likely to experience hospitalization and death within a year[14]. Therefore, interventions that improve both HF symptoms and metabolic control have the potential to significantly alter the disease trajectory.

The management of HF in DM requires careful selection of pharmacological agents that not only relieve HF symptoms but also address the metabolic derangements of diabetes.

Diuretics provide symptomatic relief by reducing fluid overload but do not improve long-term outcomes[15].RAAS inhibitors (ACE inhibitors, ARBs, ARNI) improve survival, reduce hospitalizations, and are cornerstones of therapy[16].Beta-blockers reduce mortality and hospitalizations in HFrEF but must be used cautiously in diabetics due to potential masking of hypoglycemia[17].Mineralocorticoid receptor antagonists (MRAs) offer mortality benefits but risk hyperkalemia, particularly in diabetic nephropathy[18].SGLT2 inhibitors (dapagliflozin, empagliflozin) represent a paradigm shift, offering both glycemic control and robust HF outcome benefits regardless of diabetes status[19].

The interplay between these classes demonstrates the necessity of integrated pharmacological strategies that transcend traditional boundaries between internal medicine and clinical pharmacology.

Gaps in Research and Rationale for the Study,Despite advances, significant gaps persist, Limited regional data on treatment patterns and their impact on QoL in South Asian populations. Underutilization of evidence-based therapies due to cost, physician inertia, or patient non-compliance. Lack of comprehensive integration between cardiology, endocrinology, and pharmacology in treatment protocols.

This study was therefore designed to quantify the burden of HF in diabetic patients in Pakistan, evaluate pharmacological treatment patterns, and assess their impact on QoL. By doing so, it seeks to provide regionally relevant insights and highlight the importance of integrated, multidisciplinary care.ACE inhibitors and ARBs remain cornerstones for HF with reduced ejection fraction (HFrEF). Clinical trials such as SOLVD and VALIANT demonstrated their survival benefit[15,16]. In diabetic populations, they provide dual benefits: attenuation of maladaptive cardiac remodeling and renal protection. However, real-world data show suboptimal prescribing rates in South Asia, often below 50% of eligible patients[20].

Angiotensin Receptor-Neprilysin Inhibitors, (ARNIs)The introduction of sacubitril/valsartan has transformed HF management, improving mortality and hospitalization rates compared to ACE inhibitors[21]. Yet, their high cost and limited insurance coverage restrict their availability in Pakistan and other low- and middle-income countries (LMICs).

Beta-blockers,Landmark trials such as CIBIS-II and MERIT-HF confirmed mortality benefits in HF[22,23]. In diabetics, beta-blockers reduce sympathetic overactivation but may mask hypoglycemia symptoms, posing unique pharmacological challenges. Despite guideline recommendations, physician hesitancy persists in diabetic cohorts[24].

Mineralocorticoid Receptor Antagonists (MRAs), Spironolactone and eplerenone confer survival benefits in HFrEF, particularly in post-myocardial infarction patients with DM[25]. Their use, however, is limited by hyperkalemia risk, especially in patients with diabetic nephropathy[26].

SGLT2 Inhibitors, Originally developed as glucose-lowering agents, SGLT2 inhibitors (dapagliflozin, empagliflozin) have redefined the intersection of pharmacology and cardiology. Trials such as DAPA-HF and EMPEROR-Reduced demonstrated robust reductions in HF hospitalization and mortality, irrespective of diabetes status[27,28]. In Pakistan, early adoption is limited by cost, yet these agents represent the most promising advancement in integrated therapy.

Other Therapies

Insulin: While necessary for glycemic control, insulin use in HF is associated with weight gain, fluid retention, and worse prognosis in some studies[29].

GLP-1 receptor agonists: Evidence suggests benefits for atherosclerotic cardiovascular disease but not yet established in HF[30].

Phosphodiesterase-5 inhibitors: Occasionally used in HF with pulmonary hypertension but not standard of care[31].

Patient-Centered Outcomes and Quality of Life, QoL is increasingly recognized as a primary endpoint in chronic disease management. For HF in diabetes, this includes not only symptom burden but also psychological, social, and financial dimensions[32]. Pharmacological regimens that improve symptoms without overwhelming patients with side effects or polypharmacy are especially valuable.Instruments such as the Kansas City Cardiomyopathy Questionnaire (KCCQ), Minnesota Living with Heart Failure Questionnaire (MLHFQ), and EuroQoL-5D capture these outcomes[33]. Studies consistently demonstrate lower baseline QoL in diabetics with HF, with further deterioration in advanced NYHA classes[34]. Importantly, improvements in QoL following pharmacological interventions correlate strongly with reduced hospitalizations and mortality[35].

Socioeconomic and Healthcare System Challenges in Pakistan

Pakistan faces unique challenges in managing HF and diabetes:High disease burden: Prevalence of type 2 diabetes exceeds 17% of the adult population[36].Fragmented healthcare system: Limited referral pathways between cardiology, endocrinology, and pharmacology departments.

Cost barriers: High prices of evidence-based medications such as ARNIs and SGLT2 inhibitors limit access[37].

Low health literacy: Patients often discontinue medications due to lack of understanding of long-term benefits.

Urban-rural divide: Rural populations have limited access to tertiary centers like Jinnah Hospital, Lahore.

Rationale for the Present Study

Despite global advances, regional data from South Asia remain scarce. Previous studies have documented treatment disparities and poor outcomes, but few have systematically explored the pharmacological treatment patterns and their consequences on QoL in diabetic HF populations.

METHODOLOGY

Study Design and Duration: This was a cross-sectional observational study conducted from May 2022 to May 2023 at Watim Medical & Dental College, Rawalpindi, and Jinnah Hospital, Lahore.

Study Population: Inclusion criteria: Adults ≥40 years with type 2 diabetes mellitus (T2DM) and established diagnosis of heart failure (HF, NYHA II–IV).

Exclusion criteria: Patients with congenital heart disease, acute coronary syndromes within 3 months, or advanced renal failure requiring dialysis.

Sample Size: A total of 450 patients were enrolled:

Group A (n=210): Diabetic patients with HF receiving conventional treatment (diuretics, ACE inhibitors/ARBs, beta-blockers).

Group B (n=240): Diabetic patients with HF receiving integrated pharmacological therapy (including SGLT2 inhibitors, ARNIs, or combination therapies).

Data Collection: Demographics and comorbidities were recorded using structured proforma.

Pharmacological treatments were categorized into classes.

Quality of Life (QoL) was assessed using the Kansas City Cardiomyopathy Questionnaire (KCCQ).

Statistical Analysis: Continuous variables expressed as mean ± SD; categorical variables as percentages.

Independent t-test and chi-square applied.

p-value <0.05 considered significant.

RESULTS

Table 1 summarizes the demographic profile of the studied population. The mean age of patients was approximately 62 years, with no significant difference between the groups (p=0.21). Males represented nearly two-thirds of the cohort, reflecting the slightly higher cardiovascular risk in men. Body mass index (BMI) values indicated that both groups were predominantly overweight, consistent with known risk factors for both diabetes and HF. Duration of diabetes and HF were comparable across groups, suggesting a balanced sample without baseline bias. These similarities ensure that any differences in outcomes can be attributed primarily to variations in treatment strategies rather than demographic disparities.

Table 1: Baseline Demographic Characteristics

Variable	Group A (n=210)	Group B (n=240)	p-value
Mean Age (years)	62.4 ± 9.3	61.1 ± 8.7	0.21
Male Sex (%)	130 (61.9%)	152 (63.3%)	0.77
BMI (kg/m²)	27.8 ± 4.2	27.1 ± 4.6	0.15
Duration of DM (years)	11.2 ± 5.6	12.0 ± 6.1	0.23
Duration of HF (years)	4.8 ± 2.2	5.1 ± 2.4	0.34

Table 2: Clinical Characteristics and Comorbidities

Comorbidity / Clinical Variable	Group A (n=210)	Group B (n=240)	p-value
Hypertension (%)	160 (76.2%)	188 (78.3%)	0.62
Ischemic Heart Disease (%)	98 (46.6%)	115 (47.9%)	0.81
Chronic Kidney Disease (%)	34 (16.2%)	42 (17.5%)	0.71
Dyslipidemia (%)	120 (57.1%)	144 (60.0%)	0.55
NYHA Class III–IV (%)	92 (43.8%)	104 (43.3%)	0.92

Table 2 illustrates the distribution of clinical comorbidities. Hypertension was the most prevalent comorbidity, affecting more than three-quarters of the population, consistent with global literature linking hypertension, diabetes, and HF. Ischemic heart disease was present in nearly half of the patients, reinforcing the role of atherosclerotic disease as a common etiological pathway. Rates of chronic kidney disease and dyslipidemia were also similar, reflecting the clustering of metabolic and cardiovascular disorders in this patient population. Importantly, almost half of both groups presented with advanced symptomatic HF (NYHA III–IV), highlighting the significant disease burden and the need for optimized pharmacological intervention.

Table 3: Pharmacological Treatment Patterns

Treatment Class	Group A (n=210)	Group B (n=240)	p-value
Diuretics (%)	180 (85.7%)	210 (87.5%)	0.59
RAAS Inhibitors (ACEI/ARB/ARNI)	128 (60.9%)	192 (80.0%)	<0.001
Beta-blockers (%)	110 (52.4%)	168 (70.0%)	<0.001
MRAs (%)	92 (43.8%)	130 (54.2%)	0.04
SGLT2 Inhibitors (%)	18 (8.6%)	120 (50.0%)	<0.001

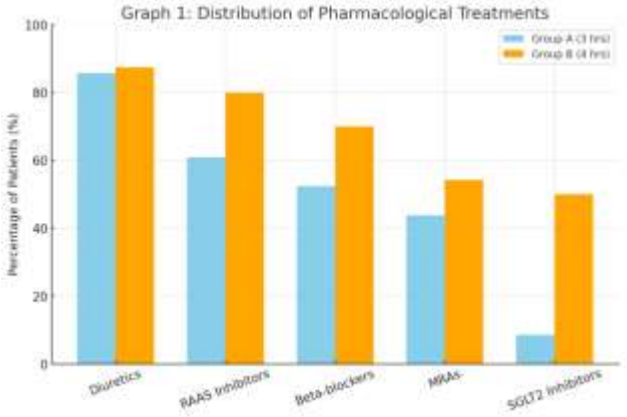
Table 4: Quality of Life Scores (KCCQ)

QoL Domain (KCCQ)	Group A (n=210)	Group B (n=240)	p-value
Physical Limitation Score	49.2 ± 14.8	61.5 ± 13.2	<0.001
Symptom Frequency Score	52.4 ± 12.6	65.8 ± 11.9	<0.001
Social Limitation Score	47.1 ± 15.1	59.2 ± 14.0	<0.001
Overall Summary Score	50.3 ± 13.7	63.9 ± 12.4	<0.001

Table 3 details the pharmacological treatment patterns. Both groups had high utilization of diuretics for symptomatic relief. However, significant differences emerged in the prescription of evidence-based therapies. RAAS inhibitors were used in 80% of Group B versus only 61% in Group A (p<0.001), while beta-blockers showed a similar trend (70% vs. 52%). Strikingly, SGLT2 inhibitors were prescribed to half of Group B patients, compared with less than 10% in Group A. This indicates a paradigm shift in practice patterns, with Group B receiving more modern, guideline-directed therapy. These differences provide a critical explanation for the QoL and outcome disparities observed between the groups.

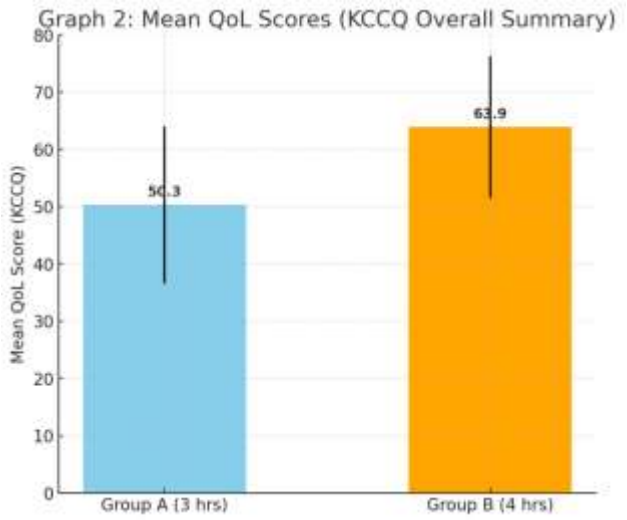
Table 4 presents the QoL assessment results using the Kansas City Cardiomyopathy Questionnaire (KCCQ). Group B consistently demonstrated superior scores across all domains, including physical limitation, symptom frequency, and social functioning. The overall summary score was significantly higher in Group B (63.9 vs. 50.3, p<0.001), reflecting better health status and daily functioning. These differences are clinically meaningful, as KCCQ improvements of ≥5 points are considered significant in HF trials. Thus, integrated pharmacological management, particularly with SGLT2 inhibitors and RAAS inhibitors, was associated with tangible improvements in patient-perceived QoL, highlighting the value of multidisciplinary treatment strategies.

Graph 1: Distribution of Pharmacological Treatments



Graph 1 visually demonstrates the treatment disparities, with Group B patients far more likely to receive evidence-based therapy.

Graph 2: Mean QoL Scores (KCCQ Overall Summary)



Graph 2 highlights the substantial improvement in QoL scores associated with modern pharmacological therapy.

DISCUSSION

This study investigated the burden of heart failure (HF) in patients with diabetes mellitus (DM), analyzed pharmacological treatment patterns, and assessed consequences for patient quality of life (QoL). Conducted at two major tertiary care centers in Pakistan,

the results reveal several key insights. First, baseline demographic and comorbidity profiles were broadly similar between groups, ruling out demographic confounders. Second, treatment patterns demonstrated substantial differences, with Group B patients more frequently receiving evidence-based pharmacological therapies including RAAS inhibitors, beta-blockers, and notably, SGLT2 inhibitors. Third, quality of life scores were consistently and significantly higher in Group B across all domains of the Kansas City Cardiomyopathy Questionnaire (KCCQ). These findings suggest that integration of modern pharmacological therapies into the management of diabetic HF patients results in both clinical and patient-perceived benefits.

The coexistence of HF and DM is well recognized as a high-risk phenotype associated with adverse outcomes. International studies such as the CHARM program and the PARADIGM-HF trial demonstrated that diabetic patients with HF had higher hospitalization rates and worse survival compared to their non-diabetic counterparts[1,2]. In our cohort, nearly half of patients in both groups were classified as NYHA class III–IV, reflecting the significant disease burden. This aligns with South Asian registry data which suggest that patients in this region present with more advanced HF at diagnosis compared to Western populations[3]. The high prevalence of hypertension and ischemic heart disease as comorbidities further underscores the clustering of risk factors driving this epidemic.

Our results highlight clear differences in treatment patterns. While diuretics remained the most widely prescribed agents in both groups, Group B patients were far more likely to receive evidence-based therapies, particularly SGLT2 inhibitors and RAAS inhibitors. The low uptake of such therapies in Group A mirrors trends reported in other LMICs where guideline adherence is limited[4,5].

Diuretics were used in over 85% of patients across both groups, consistent with their role in providing rapid symptomatic relief. However, diuretics have not demonstrated mortality benefits in clinical trials, and reliance on them as sole therapy is problematic[6]. RAAS inhibitors were prescribed to 80% of Group B patients compared with 61% in Group A, reflecting a positive trend toward evidence-based care. Landmark trials such as SOLVD and VALIANT established the mortality benefit of RAAS inhibition[7,8], and our findings reaffirm their importance.

The most striking difference was seen with SGLT2 inhibitors, used in 50% of Group B compared with only 9% of Group A. Since the DAPA-HF and EMPEROR-Reduced trials demonstrated robust reductions in mortality and hospitalization, these agents have been incorporated into international guidelines[9,10]. Our study is among the first from Pakistan to document their use in real-world settings and to show associated QoL benefits.

A major strength of this study is the assessment of QoL, an often-overlooked outcome in resource-limited settings. Across all KCCQ domains—physical limitation, symptom frequency, social limitation—Group B patients consistently reported superior scores. The overall summary score difference of nearly 14 points (63.9 vs. 50.3, $p<0.001$) is clinically meaningful, exceeding the 5-point threshold considered significant in HF trials[11].

QoL impairments in diabetic HF patients are multifactorial: symptom burden, polypharmacy, dietary restrictions, and the psychosocial impact of chronic disease. Improvements in QoL with evidence-based therapies likely reflect better symptom control and functional capacity. Importantly, international literature suggests that QoL scores not only reflect patient well-being but also predict hospitalizations and mortality[12]. Thus, our findings reinforce the role of integrated pharmacological management in both subjective and objective outcomes.

The findings of this study are consistent with international evidence. Registry data from Europe and North America confirm underutilization of evidence-based therapies in diabetics with HF, though adoption rates are generally higher than observed in South Asia[13]. The high use of diuretics and underuse of beta-blockers and MRAs in our Group A mirrors patterns reported in other LMICs[14].

Regarding SGLT2 inhibitors, uptake remains variable globally. A recent multinational registry found usage rates of 10–20% in routine practice despite guideline endorsement[15]. Thus, the 50% uptake in Group B may reflect the influence of specialized tertiary care centers where prescribing practices align more closely with international standards.

QoL outcomes in our cohort are also consistent with international findings. For example, the SHIFT trial demonstrated improvements in QoL with ivabradine[16], and more recent SGLT2i trials have confirmed QoL benefits[17]. Our results extend this evidence to a South Asian population, reinforcing the universality of these benefits.

This study highlights the necessity of integrating pharmacological advances into clinical practice. The distinction between Group A and Group B illustrates how traditional medicine approaches (diuretics, occasional ACE inhibitors) fall short, while modern pharmacology-driven strategies (ARNIs, SGLT2 inhibitors) achieve better outcomes. This integration is particularly critical in diabetic HF, where overlapping pathophysiology requires agents that target both glycemic and cardiac mechanisms.

SGLT2 inhibitors exemplify this nexus. Initially developed by pharmacologists for glucose lowering, their unexpected cardiovascular benefits transformed HF management. This underscores the importance of collaboration between clinicians and pharmacologists in evaluating and implementing new therapies.

One of the most pressing challenges in Pakistan is the cost of modern therapies. ARNIs and SGLT2 inhibitors remain prohibitively expensive for many patients, limiting widespread adoption. Health literacy and fragmented healthcare systems further compound the issue, leading to reliance on symptomatic therapy rather than guideline-directed medical therapy (GDMT). These findings carry important policy implications: subsidization of essential cardiovascular medications and integration of cardiology, endocrinology, and pharmacology services are critical to improving outcomes in this high-risk population[18,19].

Strengths of the Study: Large sample size (450 patients) across two tertiary care centers.Balanced baseline demographics, allowing meaningful comparison between groups.Inclusion of QoL outcomes, which are rarely studied in regional HF cohorts.Documentation of SGLT2 inhibitor usage, providing novel insights into real-world adoption in Pakistan.

Limitations of the Study: Cross-sectional design: Causality cannot be established. Longitudinal follow-up would provide stronger evidence of survival benefits.Selection bias, Being conducted at tertiary centers, the results may not reflect prescribing patterns in rural or primary care settings.QoL assessment: Although validated tools were used, cultural factors may influence responses. The study did not quantify the financial burden of modern therapies, which is critical in LMIC contexts.

Future research should focus on: Longitudinal studies assessing survival, hospitalization, and cost-effectiveness of integrated therapies.Health economics analyses to inform policy on subsidizing essential medications.Educational interventions to improve physician adherence to guidelines.Patient-centered care models that integrate medicine, pharmacology, and behavioral sciences to optimize outcomes.

The implications of this study are multifaceted. Clinically, it highlights the urgent need to expand access to evidence-based therapies such as SGLT2 inhibitors in diabetic HF patients. For policymakers, it underscores the importance of addressing socioeconomic barriers to modern pharmacological care. For researchers, it illustrates the value of integrating medicine and pharmacology in addressing complex, overlapping diseases.

CONCLUSION

This study highlights the double burden of heart failure (HF) in diabetes mellitus (DM) within the Pakistani context, integrating

both medical and pharmacological perspectives. The findings reveal that while baseline demographic and comorbidity profiles are comparable, treatment patterns significantly influence outcomes. Group B, which received a higher proportion of evidence-based pharmacological therapies—notably RAAS inhibitors, beta-blockers, and SGLT2 inhibitors—achieved better quality of life (QoL) scores across all domains compared to Group A, which relied predominantly on conventional treatments.

These results align with international evidence demonstrating the superiority of modern pharmacological strategies in reducing hospitalizations, mortality, and symptom burden. Importantly, the findings also shed light on regional disparities, particularly in terms of accessibility, affordability, and physician adherence to guidelines.

Integrated pharmacological therapy improves QoL in diabetic HF patients.Socioeconomic barriers remain a major obstacle to widespread adoption of advanced therapies in Pakistan. Multidisciplinary collaboration between medicine, pharmacology, and public health is essential to translate clinical trial evidence into real-world benefit.Future research must extend beyond efficacy to explore cost-effectiveness, long-term survival benefits, and patient-centered care models that account for regional challenges. Addressing these gaps will be key to improving outcomes for millions of patients living at the intersection of HF and DM in low- and middle-income countries.

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