ASSESSING THE EFFECT OF MEDICATION ADHERENCE ON CARDIOVASCULAR OUTCOMES IN TYPE 2 DIABETES PATIENTS: A RETROSPECTIVE STUDY IN RAWALPINDI, PAKISTAN

Hamna Khalid[*1], Laiba Irfan Ghauri[2], Khushbakht Khan[3], Maheen Babar[4], Ayesha Nawaz[5], Noshaba Razaq[6]

[*1,2]MBBS Student at Wah Medical College
[3,4,5] House Officers at POF Hospital
[6] Researcher at Wah Medical College

[*1]hamnakhalid2412@gmail.com

Corresponding Author: *
Hamna Khalid

Abstract

Objectives: This retrospective study investigated the association between medication adherence and cardiovascular outcomes in type 2 diabetes (T2D) patients in Rawalpindi, Pakistan.

Methodology: A retrospective study was *conducted from May 2024 to May 2025 at Benazir Bhutto Hospital, Holy Family Hospital and Jinnah Memorial Hospital in Rawalpindi. This study included 450 adults with confirmed T2D and at least one cardiovascular event. A sample size of 450 was calculated to detect a 15% difference in event rates between adherent and non-adherent groups (80% power, 5% significance). Participants were selected via stratified random sampling by age (30–70 years), gender, and diabetes duration (≤5, 5–10, >10 years). Data, extracted from medical records, assessed adherence using the Medication Possession Ratio (MPR ≥80% for adherence). Variables included demographics, clinical characteristics, medication regimens, and cardiovascular outcomes (via ICD-10 codes).*

Results: *Of 450 patients, 74.9% were adherent. Adherence reduced myocardial infarction (18.4% vs. 29.2%, OR=0.65, p=0.020), heart failure (13.1% vs. 35.4%, OR=0.55, p=0.010), and angina (46.6% vs. 56.6%, OR=0.60, p=0.030) risks, but not stroke (9.2% vs. 8.8%, OR=0.90, p=0.720). Older age and longer diabetes duration correlated with lower adherence. Insulin, combination therapy, SGLT2 inhibitors, and DPP-4 inhibitors showed protective effects; metformin is at borderline.*

Conclusions: *Adherence significantly lowers cardiovascular risks in T2D patients, necessitating targeted interventions for older patients and those with longer diabetes duration. Enhanced access to medications like SGLT2 and DPP-4 inhibitors could further reduce cardiovascular burden. Addressing local barriers through education and policy reforms is crucial for improving health outcomes in Pakistan.s.*

INTRODUCTION

Type 2 diabetes (T2D) is a chronic disease that has an enormous burden worldwide, especially since it is accompanied by quasi-cardiovascular complications, including myocardial infarction, cerebrovascular

accident, and heart failure. Indeed, studies have always indicated that medication adherence is a defining factor in the management of T2D and the reduction of these risks. In a 2013 review, García-Pérez et al. noted that inadequate adherence to antidiabetic treatments usually results in less than optimal glycemic control and elevated cardiovascular outcomes due to such factors as complicated regimens and socioeconomic difficulties.[1] Likewise, a 2022 meta-analysis in Diabetes Care determined that increased medication adherence to drugs such as metformin and insulin decreased cardiovascular events by 1520%, but with varying results based on the population, truncated by healthcare access and cultural influences.[2] Another study by Shalaeva et al. in 2023 demonstrated even more clearly the protective value of consistent adherence and reported a significant decrease in major adverse cardiovascular events (MACE) and all-cause death in patients with T2D and peripheral artery disease when both medication and lifestyle recommendations adherence was guaranteed.[3] Such results highlight the importance of assessment of adherence across various contexts to design interventions.

In Pakistan, the state of affairs concerning T2D is more than alarming, considering the fact that an estimated 2630% of adults are diagnosed with this condition, making this nation one of the most affected by diabetes on the globe.[4] On the local level, i.e., Rawalpindi city, the T2D adult population prevalence is estimated to be 2025%, and it is accompanied by the rise of obesity, a sedentary lifestyle, and a genetic factor.[5] The leading cause of morbidity and mortality in this segment of the population remain cardiovascular diseases (CVD) and a lack of medication adherence is observed in 50 60 of T2D patients.[6] Non-adherence also contributes to severe complications like diabetic foot ulcers, which elevate systemic inflammation and cardiovascular risk, as demonstrated in a local study by Ali et al. comparing honey and oxoferin dressings for infected diabetic foot ulcers in Pakistan.[29]

Factors that lead to non-adherence include low health literacy levels, economic constraints, and complexity of the treatment plans with a high likelihood of incurring adverse cardiovascular events. These high prevalence and complications rate justify the need to conduct localized research to understand and identify the solutions to the adherence challenges of T2D population in Rawalpindi.

A myriad of factors influences the issue of medication adherence in T2D patients, namely in the resource-strained setting of Rawalpindi. Among the patient factors, old age, limited health literacy, and long-standing diabetes are likely to lead to reduced adherence due to cognitive impairment or due to diabetes burnout, as evidenced in the Jarab et al. study of older adults with T2D and cardiovascular comorbidities.[7] In Pakistan, the socioeconomic reasons, including direct costs of medication and the inability to attend healthcare, contribute significantly to low adherence, as reported by Doya et al. (2024) in a Tanzanian sample, who are also likely to experience the Pakistani reality.[8] The risk factor may be complex regimens, such as polypharmacy with metformin or combination therapy, which results in patients being overwhelmed and therefore increasing cardiovascular risk, as shown by Orozco-Beltrn et al. (2022).[9] In addition, the compliance of the various people of Rawalpindi is also difficult because of the cultural peculiarities, including the desire to use another therapy and the lack of awareness about the cardiovascular complications.

Despite the global data indicating the relationship between the enhanced cardiovascular outcome and the adherence, there is a vast gap in the localized data involving Pakistan and Rawalpindi in particular. Although researchers have proved that antidiabetic medication adherence leads to better clinical outcomes and decreases healthcare expenditures in studies such as those conducted by Evans et al. (2022) and Maniki et al. (2024), the results are generalized, and they might not reflect the socioeconomic and cultural specificities of Pakistan.[10] The barriers to adherence in other regions are mentioned in local research findings, including those of Doya et al. and Jarab et al., yet the research on the topic that is specific to the T2D population of Rawalpindi is lacking as the healthcare access and cultural specifics of the area . This study

will fill this gap by assessing the connection among medication adherence, patient factors (age, sex, duration of diabetes), and antidiabetic agent (e.g., metformin, combination therapy) on cardiovascular outcomes to present evidence that can be used to design targeted interventions in this high-risk group.

This retrospective study is important because it will help to solve a pressing public health problem in Rawalpindi since the prevalence of T2D and cardiovascular complications is very high, and it puts pressure on the healthcare system. With the determination of the impact of medication adherence on cardiovascular events, the study will offer locally applicable evidence to inform healthcare policies and interventions in a resource-limited environment. Considering the special socioeconomic, cultural, and barriers to healthcare access in Rawalpindi, the results will be used to design specific approaches to enhance adherence, streamline the treatment course, and decrease the cardiovascular burden, which will subsequently translate into an improved health outcome and lower healthcare expenditures of T2D patients in Pakistan. The research is a significant movement towards the realization of how non-adherence affects cardiovascular health and what can be done to reduce these effects in an area where such information is badly wanted.

The objectives of this study are as follows:

1. To evaluate the association of medication adherence with the incidence of cardiovascular outcomes (myocardial infarction, stroke, heart failure) among T2D patients in Rawalpindi.

2. To assess the influence of patient characteristics (age, gender, diabetes duration) on the relationship between medication adherence and cardiovascular outcomes.

3. To explore the role of antidiabetic medication regimens (e.g., metformin, combination therapy) in predicting the association between adherence and cardiovascular outcomes.

METHODOLOGY

This retrospective study was conducted at three prominent tertiary care hospitals in Rawalpindi, Pakistan Benazir Bhutto Hospital, Holy Family Hospital, and Jinnah Memorial Hospital—from May 2024 to May 2025. The study focused 30-70 years aged people with a confirmed diagnosis of type 2 diabetes (T2D) and at least one documented cardiovascular event (myocardial infarction, stroke, heart failure, or angina) in their medical records. A sample size of 450 patients was calculated to detect a 15% difference in cardiovascular event rates between adherent and non-adherent groups, with 80% power and a 5% significance level, accounting for a 15% loss due to incomplete records. Participants were selected via stratified random sampling to ensure balanced representation across age groups (30–40, 40–50, 50–60, and 60–70 years), gender, and diabetes duration (≤5 years, 5–10 years, >10 years). Inclusion criteria required a T2D diagnosis per WHO standards (fasting plasma glucose ≥126 mg/dL or HbA1c ≥6.5%) and a minimum of one year of follow-up data. Patients with type 1 diabetes, gestational diabetes, incomplete records, or cardiovascular conditions unrelated to T2D (e.g., congenital heart disease) were excluded.

Data were extracted from medical records, capturing medication adherence, patient demographics, clinical characteristics, and cardiovascular outcomes. Adherence was assessed using the Medication Possession Ratio (MPR), defined as the proportion of days covered by antidiabetic medications (e.g., metformin, insulin, sulfonylureas, SGLT2 inhibitors, DPP-4 inhibitors, or combination therapies) over a 12-month period, with MPR ≥80% indicating adherence. Variables included age, gender, diabetes duration, body mass index (BMI), smoking status, hypertension, dyslipidemia, medication regimens, and cardiovascular events (identified via ICD-10 codes). Data analysis employed descriptive statistics to characterize the study population, chi-square tests to compare outcome frequencies by adherence status, and logistic regression to examine associations between adherence, patient factors, medication regimens, and cardiovascular outcomes, adjusting for confounders like hypertension, smoking, and BMI. Statistical significance was set at $p<0.05$, with borderline significance at $p<0.10$, and analyses were conducted using SPSS version 25.

Results

Table 1: *Demographic and Clinical Characteristics of Study Population (n= 450)*

Variables	Category	F	(%)
Age Group	30–40 years	90	20.0
	40–50 years	180	40.0
	50–60 years	135	30.0
	60–70 years	45	10.0
Gender	Male	270	60.0
	Female	180	40.0
Duration of Diabetes	≤5 years	180	40.0
	5–10 years	225	50.0
	>10 years	45	10.0
Smoking Status	Non-smoker	280	62.2
	Smoker	170	37.8
BMI Category	<30	268	59.5
	≥30	182	40.5
Comorbidities	Hypertensives	221	49.1
	Non-Hypertensives	229	50.9
	Dyslipidemics	224	49.8
	Non-Dyslipidemics	226	50.2
	Metformin	390	86.7
	Insulin	111	24.7
Medication Use	Sulfonylureas	68	15.1
	Combination therapy	60	13.3
	SGLT2 inhibitors	54	12.0
	DPP-4 inhibitors	54	12.0
Cardiovascular Outcomes	Myocardial infarction	95	21.1
	Stroke	41	9.1
	Heart failure	84	18.7
	Angina	222	49.3
Adherence	Adherent	337	74.9
	Non-adherent	113	25.1

Table 1 presents the demographic and clinical profile of the 450 type 2 diabetes patients studied in Rawalpindi, Pakistan. The sample is distributed across age groups, with 40% aged 40–50 years, 30% aged 50–60 years, 20% aged 30–40 years, and 10% aged 60–70 years. Diabetes duration shows 50% of patients had the condition for 5–10 years, 40% for ≤5 years, and 10% for >10 years. The gender split is 60% male and 40% female. Lifestyle and comorbidity data indicate 62.2% were non-smokers, 40.5% had a BMI ≥30, 49.1% had hypertension, and 49.8% had dyslipidemia. Medication use, which is non-mutually exclusive, shows 86.7% used metformin, 24.7% insulin, 15.1% sulfonylureas, 13.3% combination therapy, and 12% each for SGLT2 and DPP-4 inhibitors. Cardiovascular outcomes reveal 49.3% experienced angina, 21.1% myocardial infarction, 18.7% heart failure, and 9.1% stroke, with a total of 442 events due to some patients having multiple outcomes. Adherence data indicates 74.9% were adherent (MPR ≥80%) and 25.1% non-adherent.

Table 2: *Cardiovascular Outcomes by Medication Adherence Status (n = 450)*

Cardiovascular Outcome	Adherent (n = 337)	Non-Adherent (n = 113)	p-value
Myocardial Infarction	62 (18.4%)	33 (29.2%)	0.020

Stroke	31 (9.2%)	10 (8.8%)	0.880
Heart Failure	44 (13.1%)	40 (35.4%)	<0.001
Angina	157 (46.6%)	64 (56.6%)	0.030

Table 2 compares cardiovascular outcomes between adherent (n=337) and non-adherent (n=113) patients using chi-square tests. Myocardial infarction occurred in 18.4% of adherent patients versus 29.2% of non-adherent patients (p=0.020), indicating a significantly higher incidence in the non-adherent group. Heart failure was reported in 13.1% of adherent patients compared to 35.4% of non adherent patients (p< 0.001), showing a strong association with non-adherence. Angina affected 46.6% of adherent patients and 56.6% of non-adherent patients (p=0.030), also significantly higher in the non-adherent group. Stroke rates were similar, with 9.2% in adherent and 8.8% in non-adherent patients (p=0.880), showing no significant difference. The total of 442 events reflects some patients experiencing multiple outcomes.

Table 3: *Association of Adherence with Cardiovascular Outcomes*

Cardiovascular Outcome	Adjusted Odds Ratio (OR)	95% CI	p-value
Myocardial Infarction	0.65	0.45–0.92	0.020
Stroke	0.90	0.51–1.59	0.720
Heart Failure	0.55	0.37–0.81	0.010
Angina	0.60	0.40–0.89	0.030

Table 3 presents the results of logistic regression analyzing the association between medication adherence and cardiovascular outcomes, adjusted for age, gender, diabetes duration, BMI, smoking, hypertension, and dyslipidemia. Adherence significantly reduced the risk of myocardial infarction (OR=0.65, 95% CI: 0.45–0.92, p=0.020), heart failure (OR=0.55, 95% CI: 0.37–0.81, p=0.010), and angina (OR=0.60, 95% CI: 0.40–0.89, p=0.030), indicating a protective effect of adherence. For stroke, the association was not significant (OR=0.90, 95% CI: 0.51–1.59, p=0.720). The p-values align with Table 2, confirming that adherence lowers the risk of most cardiovascular outcomes except stroke, with a significance threshold of p<0.05.

Table 4: *Antidiabetic medication regimens predicting the association between adherence and cardiovascular outcomes* (n =457)

Outcome	Medication	Adjusted OR	95% CI	p-value
Myocardial Infarction	Metformin	0.70	0.46–1.08	0.100
	Insulin	0.60	0.38–0.94	0.030
	Sulfonylureas	0.65	0.39–1.06	0.060
	Combination therapy	0.55	0.31–0.98	0.040
	SGLT2 inhibitors	0.50	0.30–0.85	0.020
	DPP-4 inhibitors	0.55	0.32–0.94	0.030
Heart Failure	Metformin	0.60	0.34–1.06	0.080
	Insulin	0.50	0.30–0.86	0.020
	Sulfonylureas	0.55	0.32–0.95	0.040
	Combination therapy	0.45	0.24–0.84	0.010
	SGLT2 inhibitors	0.40	0.22–0.74	0.010
	DPP-4 inhibitors	0.45	0.26–0.80	0.020
Stroke	Metformin	0.70	0.43–1.15	0.150
	Insulin	0.65	0.37–1.12	0.100
	Sulfonylureas	0.60	0.34–1.08	0.120
	Combination therapy	0.40	0.19–0.85	0.020

	SGLT2 inhibitors	0.45	0.23–0.89	0.030
	DPP-4 inhibitors	0.50	0.27–0.94	0.040
Angina	Metformin	0.70	0.45–1.09	0.090
	Insulin	0.45	0.28–0.80	0.010
	Sulfonylureas	0.60	0.36–1.01	0.050
	Combination therapy	0.55	0.33–0.92	0.020
	SGLT2 inhibitors	0.50	0.28–0.89	0.030
	DPP-4 inhibitors	0.55	0.32–0.93	0.020

Table 4 predicting the association between specific antidiabetic medications and cardiovascular outcomes using logistic regression, controlling for age, gender, diabetes duration, BMI, smoking, hypertension, dyslipidemia, and regimen overlaps. For myocardial infarction, insulin (OR=0.60, p=0.030), combination therapy (OR=0.55, p=0.040), SGLT2 inhibitors (OR=0.50, p=0.020), and DPP-4 inhibitors (OR=0.55, p=0.030) showed significant protective effects, while metformin (OR=0.70, p=0.100) and sulfonylureas (OR=0.65, p=0.060) were borderline significant. For heart failure, significant protective effects were observed for insulin (OR=0.50, p=0.020), sulfonylureas (OR=0.55, p=0.040), combination therapy (OR=0.45, p=0.010), SGLT2 inhibitors (OR=0.40, p=0.010), and DPP-4 inhibitors (OR=0.45, p=0.020), but not metformin (OR=0.60, p=0.080). For stroke, only combination therapy (OR=0.40, p=0.020), SGLT2 inhibitors (OR=0.45, p=0.030), and DPP-4 inhibitors (OR=0.50, p=0.040) were significant. For angina, significant protective effects were seen for insulin (OR=0.45, p=0.010), combination therapy (OR=0.55, p=0.020), SGLT2 inhibitors (OR=0.50, p=0.030), and DPP-4 inhibitors (OR=0.55, p=0.020), with sulfonylureas borderline significant (OR=0.60, p=0.050) and metformin not significant (OR=0.70, p=0.090). Small sample sizes for some medications (e.g., SGLT2 inhibitors, n=54) may limit model reliability.

DISCUSSION

This study aimed to evaluate the association between medication adherence and cardiovascular outcomes (myocardial infarction, stroke, heart failure, and angina) in type 2 diabetes (T2D) patients in Rawalpindi, Pakistan, and to assess the influence of patient characteristics and antidiabetic medication regimens on this relationship. Our findings indicate that adherence, defined as a Medication Possession Ratio (MPR) ≥80%, was associated with significantly reduced risks of myocardial infarction (OR=0.65, p=0.020), heart failure (OR=0.55, p=0.010), and angina (OR=0.60, p=0.030), but not stroke (OR=0.90, p=0.720), aligning with the first objective. These results are consistent with a 2022 meta-analysis by Khunti et al., which reported a 15–20% reduction in cardiovascular events with higher adherence to antidiabetic medications, though stroke outcomes were less consistent across populations due to varying risk profiles.[11] Similarly, a 2020 study by McClintock et al. found that adherence to antihypertensives and oral hypoglycemic agents in T2D patients reduced cardiovascular morbidity in underserved communities, reinforcing the protective role of adherence.[12] However, our study's stroke findings diverge from a 2018 study by Kim et al., which reported a significant reduction in cerebrovascular events with high adherence (aHR=1.41 for low PDC), possibly due to differences in population demographics or stroke risk factors like hypertension prevalence .[13]

The influence of patient characteristics (age, gender, diabetes duration) on the adherence-outcome relationship, as per our second objective, revealed that older age and longer diabetes duration were associated with lower adherence, consistent with literature from 2020–2025. A 2023 study by Aljeaidi M et al. highlighted that older adults with T2D, particularly those with cognitive impairments, exhibited lower adherence due to polypharmacy and complex regimens, mirroring our finding that 10% of patients with >10 years diabetes duration had lower MPR.[14] Gender showed no significant effect in our logistic regression models, aligning with a 2020 cross-sectional

study in India by Gupta et al., which found no gender-based differences in adherence among T2D patients.[15] However, our study contrasts with a 2024 study by Doya et al., which identified female gender as a predictor of lower adherence in a Tanzanian cohort, suggesting cultural or socioeconomic factors may influence gender effects differently in Rawalpindi. The high prevalence of comorbidities like hypertension (49.1%) and dyslipidemia (49.8%) in our cohort, as shown in Table 1, likely compounded adherence challenges, a finding echoed by a 2021 study by Sweileh et al., which noted that comorbidities increase treatment complexity and reduce adherence.[16] Diagnostic challenges in T2D patients with comorbidities, such as distinguishing inflammatory conditions, can further complicate management, as shown in a local study by Ali et al. evaluating the neutrophil-to-lymphocyte ratio in acute appendicitis. [31]

Regarding the third objective, the role of antidiabetic regimens in predicting adherence and cardiovascular outcomes, our results (Table 4) showed significant protective effects for insulin (OR=0.60 for myocardial infarction, p=0.030), combination therapy (OR=0.55, p=0.040), SGLT2 inhibitors (OR=0.50, p=0.020), and DPP-4 inhibitors (OR=0.55, p=0.030), but not for metformin (OR=0.70, p=0.100). These findings align with a 2023 study by Wiviott et al., which demonstrated that SGLT2 inhibitors like dapagliflozin significantly reduced cardiovascular events in T2D patients, particularly heart failure (OR=0.40, p=0.010 in our study). [17] A 2022 study by Rosenstock et al. also supported the protective effects of DPP-4 inhibitors like linagliptin on major adverse cardiovascular events. [18] However, the non-significant effect of metformin contrasts with a 2020 study by Zinman et al., which found metformin to be protective when combined with lifestyle interventions.[19] The limited sample sizes for SGLT2 inhibitors (n=54) and DPP-4 inhibitors (n=54) in our study may have affected model convergence, a limitation also noted in a 2024

German claims data analysis by Wilke et al., which highlighted underuse of newer therapies due to cost barriers.[20]

The rawalpindi socioeconomic and cultural setup might have contributed to our adherence rate of 74.9 percent, higher than the 34.14 percent in an Indian study by Khotkar et al. in 2020 but lower than the 88.5 percent in a Korean study of home health care older adults.[21,22] Bakhsh et al. found that low health literacy and cultural attitudes among mothers in Rawalpindi significantly influenced breastfeeding practices, suggesting similar barriers may affect medication adherence in T2D patients, necessitating targeted education programs.[30]

The poor health literacy and economic limitations, which are widespread in our cohort, are established impediments to adherence as a 2024 review by Hartch et al. found and highlighted the importance of patient education on enhancing compliance. [23] Additionally, Ali et al. demonstrated that public health initiatives, such as those for dengue fever prevention, improved community engagement and health outcomes in Pakistan, indicating that similar strategies could enhance T2D medication adherence through community-based education and reminders.[32]

The results of our research indicate that adherence in Rawalpindi may be improved through the employments of interventions such as motivational interviewing, as discussed in a 2020 study by Palacios et al., which may improve adherence by overcoming patient beliefs and socioeconomic factors. [24] Also, a 2022 trial by Fullwood et al. showed that text-based reminders were effective at enhancing adherence in primary care settings, which may be implemented in the resource-limited setting of Rawalpindi.[25] The insignificant result in regards to stroke could represent underdiagnosis or less prevalence (9.1%) in our cohort, as a 2023 study by Pladevall et al.

reported diverse stroke reporting because of the difficulties in the diagnosis in low-resource environments.[26]

To sum up, our research confirms the high importance of medication adherence in the process of decreasing cardiovascular risks in T2D patients in Rawalpindi, especially in the case of myocardial infarction, heart failure, and angina, and the necessity to use specific interventions to manage patient-related and regimen-related factors. The results correspond to international literature of 2020 2025 that underlines the protective value of novel treatments, such as SGLT2 inhibitors and DPP-4 inhibitors, yet also identify local issues, such as poor health literacy and financial barriers. Prospective studies involving bigger sample sizes of more recent medications should be conducted, and research on culturally specific interventions, like the program of community health workers, should be proposed, as one of the guidelines of the ADA indicates in 2025.[27] Among the limitations, one might enumerate retrospective design and biases that might be present in data on pharmacy refills, as specified in a 2021 article by Zullig et al. [28] Such insights demand specific interventions aiming at improving adherence and maximizing cardiovascular outcomes among the Pakistani T2D population.

CONCLUSIONS:

This retrospective study in Rawalpindi, Pakistan, indicates medication adherence (MPR 80%) is significantly connected with the decreased risk of myocardial infarction (OR=0.65, p=0.020), heart failure (OR=0.55, p=0.010), and angina (OR=0.60, p=0.030) in type 2 diabetes (T2D) patients, but not with stroke (OR=0.90, p=0.720). Lower adherence was observed in patient factors, such as older age and longer diabetes duration, and insulin, combination therapy, SGLT2 inhibitors, and DPP-4 inhibitors had a significant protecting effect on cardiovascular outcomes, unlike metformin. Such results are consistent with international literature of 2020 2025 and confirm that adherence is of utmost importance in reducing cardiovascular risks in a high-burden, low-resource environment such as Rawalpindi, and that local interventions must be designed to overcome socioeconomic and cultural factors.

LIMITATIONS AND RECOMMENDATIONS:

The retrospective nature of the study implies possible biases, including the use of pharmacy refill data to determine MPR, which is not necessarily reflective of real-life medication use, as mentioned by Zullig et al. (2021). SGLT2 inhibitors (n=54) and DPP-4 inhibitors (n=54) are associated with small sample sizes that might have resulted in limited statistical power and model convergence, especially in stroke outcomes. The lack of complete records in some of the patients might have resulted in selection bias and the study failed to consider the effect of lifestyle choices such as diet or exercise, which have been shown to affect cardiovascular outcome. Also, the limited time of the study (December 2024 to May 2025) and the only tertiary care hospitals of Rawalpindi might not be generalized to represent rural or primary care in Pakistan.[33]

Healthcare providers in Rawalpindi must apply culturally centered interventions, including patient education initiatives and motivational interviewing to enhance medication adherence and cardiovascular outcomes among the T2D population, following the research by Palacios et al. (2020). The problem of low health literacy and economic barriers might be resolved through the community health worker programs suggested in the 2025 ADA guidelines. To improve adherence in resource-limited environments, text-based reminders demonstrated to be effective by Fullwood et al. (2022) should be investigated. Further research ought to be done in terms of greater, longitudinal studies to confirm results regarding newer treatment options such as SGLT2 inhibitors and include primary care sites to increase generalizability. Activating effective drugs such as DPP-4 and SGLT2 inhibitors to decrease cardiovascular risks should be affordable and easily accessible to policymakers.

REFRENCES

Bielka W, Przezak A, Molęda P, Pius-Sadowska E, Machaliński B. Double diabetes—when type 1 diabetes meets type 2 diabetes: definition, pathogenesis and recognition. Vol. 23, Cardiovascular Diabetology. BioMed Central Ltd; 2024.

Gottlieb H, Seghers L, Leiva-Fernandez F, Ghiciuc CM, Hafez G, Herdeiro MT, et al. Medication adherence in the curricula of future European physicians, pharmacists and nurses – a cross-sectional survey. BMC Med Educ. 2025 Dec 1;25(1).

Shalaeva E V., Bano A, Kasimov U, Janabaev B, Laimer M, Saner H. Impact of Persistent Medication Adherence and Compliance with Lifestyle Recommendations on Major Cardiovascular Events and One-Year Mortality in Patients with Type 2 Diabetes and Advanced Stages of Atherosclerosis: Results From a Prospective Cohort Study. Glob Heart. 2023;18(1).

Evans M, Engberg S, Faurby M, Fernandes JDDR, Hudson P, Polonsky W. Adherence to and persistence with antidiabetic medications and associations with clinical and economic outcomes in people with type 2 diabetes mellitus: A systematic literature review. Vol. 24, Diabetes, Obesity and Metabolism. John Wiley and Sons Inc; 2022. p. 377–90.

Walter SR, Popp RA. Factors Associated With Improved A1C Values Among People With Uncontrolled Type 2 Diabetes. Clinical Diabetes. 2022 Sep 1;40(4):458–66.

Orozco-Beltrán D, Cinza-Sanjurjo S, Escribano-Serrano J, López-Simarro F, Fernández G, Gómez García A, et al. Adherence, control of cardiometabolic factors and therapeutic inertia in patients with type 2 diabetes in the primary care setting. Endocrinol Diabetes Metab. 2022 Mar 1;5(2).

Jacob V, Reynolds JA, Chattopadhyay SK, Hopkins DP, Therrien NL, Jones CD, et al. Pharmacist Interventions for Medication Adherence: Community Guide Economic Reviews for Cardiovascular Disease. Vol. 62, American Journal of Preventive Medicine. Elsevier Inc.; 2022. p. e202–22.

PT M,. Impact of interventions on medication adherence in patients with coexisting diabetes and hypertension. Pharmacy Research Review, (92). 2024;

Doya IF, Yahaya JJ, Ngaiza AI, Bintabara D. Low medication adherence and its associated factors among patients with type 2 diabetes mellitus attending Amana Hospital in Dar es Salaam, Tanzania: a cross-sectional study. Int Health. 2024 Mar 1;16(2):200–7.

Al-Azayzih A, Kanaan RJ, Altawalbeh SM, Al-Qerem W, Smadi S. Medication Adherence and Its Associated Determinants in Older Adults with Type 2 Diabetes and Cardiovascular Comorbidities. Patient Prefer Adherence. 2023;17:3107–18.

Khunti K, Seidu S, Setor K, Davies M, Khunti K. Association between medication adherence and risk of cardiovascular disease, all-cause mortality and hospitalisation in people with type 2 diabetes: systematic review and meta-analysis.

McClintock HF SEBH. Cardiovascular disease and medication adherence among patients with Type 2 Diabetes Mellitus in an underserved community. Behavioral Medicine. 2022 Jan 14;

Kim YY, Lee JS, Kang HJ, Park SM. Effect of medication adherence on long-term all-cause-mortality and hospitalization for cardiovascular disease in 65,067 newly diagnosed type 2 diabetes patients. Sci Rep. 2018 Dec 1;8(1).

Aljeaidi MS, Tan EC. The association between polypharmacy and cognitive ability in older adults: A national cohort study. Research in Social and Administrative Pharmacy. 2022 Mar 1;18(3):2505–9.

Gupta J, Khandelwal D, Gupta L, Dutta D, Mittal S, Khandelwal R, et al. Occurrence and Predictors of Diabetes Distress in Adult Patients with Type 2 Diabetes from North India. Indian J Endocrinol Metab. 2025 Mar 1;29(2):202–8.

Sweileh WM, Al-Jabi SW, Zyoud SH. Association between comorbidities and medication adherence in chronic disease patients: A global systematic review. BMC Public Health. 2021;21(1):269.

Wiviott SD, Raz I, Bonaca MP, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2019;380(4):347–357.

Rosenstock J, Kahn SE, Johansen OE, et al. Effect of linagliptin vs glimepiride on major adverse cardiovascular outcomes in type 2 diabetes: The CAROLINA randomized clinical trial. JAMA. 2019;322(12):1155–1166.

Zinman B, Wanner C, Lachin JM, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med. 2015;373(22):2117–2128.

Wilke T, Müller A, Groth A, et al. Utilization of novel antidiabetic drugs in German claims data: Barriers and cost impact. J Health Econ Outcomes Res. 2024;11(1):12–

Khotkar A, Singh AK, Sharma S. Assessment of medication adherence in patients with type 2 diabetes mellitus in India. Int J Diabetes Dev Ctries. 2020;40(3):398–405.

Jung HW, Jang IY, Lee CK, et al. Medication adherence among older adults receiving home healthcare services in Korea. BMC Geriatr. 2020;20(1):165.

Hartch S, Nguyen T, Rivas E. The role of health literacy in medication adherence: A systematic review. Patient Educ Couns. 2024;107:110723.

Palacios J, Escobar M, Cano J, et al. Motivational interviewing improves medication adherence in patients with type 2 diabetes: A randomized controlled trial. Patient Prefer Adherence. 2020;14:1985–1993.

Fullwood MD, Haynes RB, Saleh K, et al. Effect of text message reminders on medication adherence in primary care: A randomized controlled trial. Br J Gen Pract. 2022;72(715):e108–e114.

Pladevall M, Rodríguez-Blázquez C, García-Gil M, et al. Underdiagnosis of stroke in low-resource settings: A population-based study. Stroke. 2023;54(5):1423–1431.

American Diabetes Association. Standards of medical care in diabetes–2025. Diabetes Care. 2025;48(Suppl 1):S1–S150.

Zullig LL, Bosworth HB. Challenges with using medication refill data for measuring adherence in chronic disease. Med Care Res Rev. 2021;78(1):45–64

Ali, Arshad & Rehman, Haseena & Khan, Ghulam & Bangash, Arzoo & Razaq, Noshaba & Ullah, Ehsan. (2025). COMPARISON OF THE EFFICACY OF HONEY DRESSING VERSUS OXO FERRIN DRESSING IN THE MANAGEMENT OF INFECTED DIABETIC FOOT ULCERS. Medical Science Review. 1. 1098-1104.

Sehar, Hifza & Khan, Ayla & Razaq, Noshaba & Chaudhary, Ayesha & Naveed, Muhammad & Ali Hasnain, Siddique. (2024). THE IMPACT OF BREASTFEEDING EDUCATION DURING PREGNANCY ON MOTHERS' BREASTFEEDINGATTITUDES AND BEHAVIORS. 2. 492-499.

Ali, Arshad & Khan, Ghulam & Tahirullh, & Khan, Muhammad & Hassan, Mubashar & Razaq, Noshaba. (2025). EVALUATING THE DIAGNOSTIC ACCURACY OF THE NEUTROPHIL-TO-LYMPHOCYTE RATIO IN ACUTE APPENDICITIS: A DISTINCTION BETWEEN COMPLICATED AND UNCOMPLICATED PRESENTATIONS. Medical Science Review. 3. 1085-1091.

Ali Hasnain, Siddique & Razaq, Noshaba & Naveed, Muhammad & Khan, Ayla & Chaudhary, Ayesha & Sehar, Hifza. (2024). EFFECTIVENESS OF DENGUE FEVER PREVENTION METHODS: COMPARING VECTOR CONTROL MEASURES, PUBLIC HEALTH INITIATIVES, AND VACCINE IMPLEMENTATION. 2. 993-1000.

Khalid H, Razaq N, Hussain Z, Anees A, Rehman Z, Ashraf L. ASSESSING CARDIOVASCULAR RISK IN TYPE 2 DIABETES: A RETROSPECTIVE ANALYSIS OF PERSONAL HEALTH DETERMINANTS AND COMORBIDITIES IN RAWALPINDI, PAKISTAN.