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MEDICATION ADHERENCE AND ITS DETERMINANTS AMONG PATIENTS WITH HYPERTENSION AND TYPE 2 DIABETES MELLITUS: A MULTICENTER CROSS-SECTIONAL STUDY

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Abstract

Background: Hypertension and type 2 diabetes mellitus (T2DM) frequently coexist and substantially increase the risk of cardiovascular disease, renal complications, and premature mortality. Medication adherence is a key modifiable determinant of treatment success, yet multicenter evidence from Khyber Pakhtunkhwa, Pakistan, remains limited.

Objective: To determine the prevalence of medication adherence and identify socio-demographic, clinical, and health-system factors associated with adherence among adults with hypertension, T2DM, or both attending tertiary care outpatient departments (OPDs) in Peshawar.

Methods: A multicenter cross-sectional study was conducted over six months in tertiary care OPDs in Peshawar. Adults with confirmed hypertension, T2DM, or both were recruited using consecutive sampling. Medication adherence was assessed using the licensed 8-item Morisky Medication Adherence Scale (MMAS-8). Socio-demographic, clinical, and treatment-related data were collected using a structured interviewer-administered questionnaire. Multivariable logistic regression identified independent predictors of low adherence, reported as adjusted odds ratios (AORs) with 95% confidence intervals (CIs).

Results: Of 520 eligible patients, 476 participated (response rate: 91.5%). The mean age was 54.8 ± 9.2 years, and 53.4% were female. High, medium, and low adherence were observed in 24.4%, 36.1%, and 39.5% of participants, respectively. Low adherence was significantly more common among patients with both hypertension and T2DM (51.5%) than those with either condition alone ($p < 0.001$). Independent predictors of low adherence included polypharmacy (AOR = 2.34), low household income (AOR = 1.86), inadequate physician counseling (AOR = 2.11), and lack of formal education (AOR = 1.54).

Conclusion: Medication nonadherence was common among patients with hypertension and T2DM. Reducing pill burden, strengthening physician counseling, improving affordability, and addressing health literacy may enhance adherence and improve long-term outcomes.

INTRODUCTION

Non-communicable diseases (NCDs) have now become the major cause of death and disability in the world, and among these, hypertension and type 2 DM (T2DM) have been both the most prevalent and the most treatable in a consistent way to reduce mortality and morbidity from downstream complications. According to the Global Report on Hypertension from the World Health Organization (WHO) in 2023, globally, 1.28 billion adults aged 30–79 years are living with hypertension, most of them in low- and middle-income countries, and even less than half of whom know they have it [1, 2]. The International Diabetes Federation (IDF) estimated that there were 537

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million adults with diabetes in 2021, rising to 643 million by 2030 and 783 million by 2045, with the biggest relative increases in low- and middle-income countries like South Asia [2]. As these two conditions share overlapping pathophysiological mechanisms (insulin resistance, endothelial dysfunction, sympathetic overactivity, and chronic low-grade inflammation), they are not incidental but are common, and patients with the combined diagnosis are subject to a greater burden of medications, increased risk of polypharmacy, and increased complexity in maintaining long-term drug adherence [9, 10].

Traditionally, medication adherence has been considered a nuisance and behavioural side effect of the medication process, but actually, it is the direct path to medication effectiveness and clinical outcomes. Poor control of BP has been shown to be the most common modifiable cause of such events, and non-adherence to antihypertensive therapy is one of these causes [3]. In a large meta-analysis that combined data from 27 million patients across 161 studies conducted between 2010 and 2020, non-adherence to antihypertensive medication was found to range between 27% and 40%, and the prevalence of non-adherence was higher in non-Western countries compared with Western countries and in LMIC countries compared with high-income countries [3]. The situation is no brighter for T2DM: A systematic review and meta-analysis of Morisky Medication Adherence Scale (MMAS) studies in India showed that adherence in T2DM is poor (about 48% across individual studies ranging from 11% to 68% depending on the population and the measure) [4]. Overall, this suggests that a significant fraction of people diagnosed with hypertension or T2DM in South Asian contexts are not taking the medications as prescribed, and this is enough to significantly reduce the overall population impact of otherwise highly effective and affordable treatments for those conditions.

This burden is starkly witnessed in Pakistan. The second National Diabetes Survey of Pakistan (NDSP) was a community-based, large-scale epidemiological study of all four provinces of Pakistan from 2016 to 2017, which found an overall weighted prevalence of diabetes of 26.3%, with 19.2% being previously diagnosed and 7.1% being new cases identified during the survey testing, suggesting a total of 27.4 million adults with diagnosed diabetes in the country, up from 25.0 million 20 years earlier [5, 32]. An age-adjusted, weighted analysis of the same survey found 46.2% with hypertension (roughly equal numbers of people with hypertension who have been diagnosed versus those who have not), with only small urban-rural differences [6]. These estimates place Pakistan among the countries with the highest documented burden of both conditions worldwide, and the fact that diabetes, hypertension, obesity and dyslipidaemia were found to be a mutually reinforcing risk factor cluster within the framework of the NDSP [5]. In Pakistan, in the backdrop of this, several single-centre research studies have been conducted focusing on medication adherence. In a hospital-based study in Islamabad, only 25.6% of the hypertensive patients were good adherers (MMAS-8), and 37.8% were fully non-adherers; unaffordability of treatment and uncontrolled blood pressure were independently associated with non-adherence, but adequate counselling and higher education were protective [12]. In Islamabad, low health literacy was found to be associated with less adherence and lower functional performance in activities of daily living among elderly hypertensives [13], and in a

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cross-sectional study in multiple tertiary care hospitals across Pakistan which included one in Peshawar, psychosocial factors such as perceived social support, treatment-related stress, and health beliefs were found to be significant correlates of non-adherence to antihypertensive therapy [14]. A comparable early study in Karachi also found that less than 4/5 of patients with hypertension were well adhered to by self-report on the original Morisky scale, with depressive symptoms being a significant predictor of poor adherence [17].

The evidence from Khyber Pakhtunkhwa and Peshawar, although still in early stages, is consistent. A cross-sectional study in a military hospital in Peshawar among T2DM patients revealed good adherence of 22.7% on MMAS-8; almost half were found as having poor adherence, and adherence scores were correlated with the glycaemic control (HbA1c) [11]. A qualitative study in a large public-sector tertiary care hospital in Peshawar, which evaluated knowledge and attitudes of patients with hypertension, revealed the continued poor understanding of lifestyle modification and the need for long-term treatment by the patients, which is likely to reflect poor adherence to treatment [16]. The results of these local studies were in line with the South Asian and national literature but limited in scope before the present study: Most previous studies based on Peshawar hospital data had focused on a single institution, one condition alone, or a single mediator [5, 6]; however, the present study was the first to systematically examine the adherence burden and shared determinants among people with both conditions simultaneously, which would likely be a large and clinically relevant subset of those attending routine outpatient services, as this population has been found to represent a substantial proportion of the total population nationally, given the epidemiological overlap between the two conditions [5, 6].

Medication adherence has been described in the international literature in terms of different determinants, with multiple levels of action. Patient-level factors are age, sex, health literacy, disease duration, burden of comorbidity and psychological factors such as depressive symptoms and illness perceptions [9, 13, 17]; treatment-level factors are pill burden, complexity of treatment regimens, experience of side-effects and the cost or affordability of treatment [7, 9, 12]; and health-system factors are the quality of patient–provider communication, the adequacy of counselling provided at the point of prescribing and the accessibility and continuity of the health system [12, 14]. A specific scoping review on interventions to optimise adherence in patients with comorbid hypertension and diabetes found that the multi-level nature of these determinants suggests that interventions should be tailored and specific to each health system and population and particularly emphasised the need for primary research to characterise the determinants in specific health systems in specific populations before interventions can be optimised [10]. Ghanaian work also reported that increased hypertension diagnosis time and increased perceived burden due to medications were independently linked to decreased adherence, suggesting that the burden associated with two chronic conditions is not additive, but there is a burden as such [7, 8].

Yet, there was a clear and impactful gap: there was no specific and international empirical evidence. There was no adequately powered, multicentre study which has systematically quantified the prevalence of medication adherence and comprehensively modelled the socio-demographic and

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clinical determinants of medication adherence among patients with hypertension, T2DM and both conditions concurrently in multiple tertiary care hospitals of Peshawar. Previous studies in Peshawar had been restricted to individual centres and individual conditions and had failed to examine prevalence in the context of the tertiary care network across the city, nor have the determinants identified been discussed in the context of the wider population served by the tertiary care network. Given that Khyber Pakhtunkhwa's health system, population characteristics (including comparatively high rates of poverty, health illiteracy, and out-of-pocket healthcare expenditure), and disease burden differ in relevant respects from Punjab and Sindh, where much of the existing Pakistani adherence literature has been generated, findings from Islamabad or Karachi could not be assumed to generalize directly to Peshawar [12,13,14,17].

This study was therefore designed to address that gap directly. By recruiting consecutively from the medical outpatient departments of multiple tertiary care hospitals across Peshawar over a six-month period, and by applying a validated, internationally recognized adherence instrument (the MMAS-8) alongside a structured assessment of candidate socio-demographic, clinical, and health-system determinants, this multicenter cross-sectional study generated locally representative estimates of adherence prevalence and identified independent predictors amenable to policy and clinical intervention. In doing so, it is intended to inform the design of targeted adherence-support interventions — whether centered on affordability, counseling quality, health literacy, or psychosocial support — that are calibrated to the realities of hypertension and T2DM care as it is currently delivered in Peshawar, and to contribute Peshawar-specific evidence to the broader Pakistani and South Asian literature on chronic disease medication-taking behavior.

Problem Statement

Hypertension and T2DM are highly prevalent in Pakistan, and their combined burden in Khyber Pakhtunkhwa is substantial, and a large and clinically consequential proportion of treated patients in this study were found to be non-adherent to prescribed therapy. Persistent non-adherence undermines blood pressure and glycemic control, accelerates the onset of cardiovascular, renal, and other microvascular and macrovascular complications, and increases the downstream cost of care to both patients and the health system. Prior to this study, locally generated, multicenter evidence quantifying adherence and its determinants specifically within Peshawar's tertiary care population — including patients managing both conditions simultaneously — was lacking, leaving clinicians and policymakers in the region without the data needed to design and prioritize adherence-support interventions appropriate to local patients' circumstances.

Research Gap

Although adherence to antihypertensive and antidiabetic therapy has been studied extensively in Punjab and Sindh, and to a more limited extent in Khyber Pakhtunkhwa, existing Peshawar-based research had been restricted to single institutions and, in most cases, to a single index condition studied in isolation. No identified study had combined a multicenter sampling frame with a joint

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focus on hypertension, T2DM, and their comorbid presentation, nor applied multivariable modeling to disentangle the independent contribution of socio-demographic, clinical, and health-system determinants within this specific population. This presented a mismatch between the extent of documented disease burden in the region and the level of evidence of adherence on which local practice was based, and the study aimed to reflect this.

Study Rationale

The gap needed to be addressed with a study that was both large enough in scale and sampling strategy to produce consistent, representative estimates for the entire tertiary care network of Peshawar and not just those from a single clinic. The use of a validated instrument, widely used across countries, for measuring adherence (MMAS-8) enables the findings to be compared directly with the broader literature from Pakistan and South Asia, and the multivariable analyses help identify factors that truly influence adherence and are not merely due to a bivariate association between a factor and the outcome. The resulting evidence can be translated directly into action: local health administrators and clinicians can identify interventions that can focus on the modifiable and non-modifiable factors that are most important in this population, namely polypharmacy, household income, counselling quality, and education.

Objectives

Primary Objective

The prevalence of patients from the medical outpatient departments not taking their medications as prescribed by their physicians in multiple tertiary hospitals in Peshawar was investigated in adult patients who had been diagnosed with hypertension, type 2 diabetes mellitus or both.

Secondary Objectives

- To identify the socio-demographic and clinical determinants associated with medication adherence in this population.
- To examine variation in adherence prevalence and its determinants across the three disease categories (hypertension only, T2DM only, and both conditions).
- To identify independent predictors of medication adherence using multivariable logistic regression, expressed as adjusted odds ratios with 95% confidence intervals.

MATERIALS AND METHODS

This section is drafted to adhere to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cross-sectional studies [15] and checked against their STROBE checklist before submitting.

Study Design

This was a multicenter analytical cross-sectional study.

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Study Setting

The study was carried out in medical outpatient departments (OPDs) of several tertiary care hospitals of Peshawar in the Khyber Pakhtunkhwa province of Pakistan. Hospitals were chosen as they collectively provide services to a large and demographically diverse catchment area covering urban residents of Peshawar and peri-urban and rural referral areas, thus accounting for the generalisability of results to the broader Peshawar population.

Study Duration

Data was collected from six months from October 2025 to March 2026.

Participants

The study population included adult patients (aged ≥18 years) attending the medical OPDs at the participating hospitals with a physician-confirmed diagnosis of hypertension or T2DM and who were under treatment with any pharmacologic agent for at least one of the diseases.

Eligibility Criteria

Inclusion Criteria

- Adults aged 18 years or older.
- Physician-confirmed diagnosis of hypertension and/or T2DM, as documented in medical records.
- Currently prescribed at least one antihypertensive and/or antidiabetic medication for a minimum duration of three months.
- Willing and able to provide written informed consent.

Exclusion Criteria

- Patients with cognitive impairment, severe psychiatric illness, or any condition precluding reliable self-report, as judged by the attending physician.
- Patients unable to communicate in the languages in which the questionnaire was administered.
- Pregnant women (given distinct management pathways for gestational hypertension and gestational diabetes).
- Patients unwilling to provide informed consent.

Sample Size Calculation

The minimum sample size was determined by the formula of Cochran for cross-sectional studies determining a population proportion [25] as follows:

$$n_0 = Z^2 \cdot p \cdot (1-p) / d^2$$

n_0 = desired sample size, Z = standard normal deviate corresponding to the desired confidence level (Z = 1.96 for 95% confidence), p = anticipated prevalence of the outcome of interest (medication non-adherence), and d = desired margin of error (precision). To arrive at the final target enrolment, a predicted non-response/incomplete-data rate was used to inflate the minimum sample size

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resulting from this calculation. This total was allocated according to the average monthly OPD patient numbers for each of the study sites that participated in the study. A final analytic sample of 476 participants was collected, which was more than the minimum sample size calculated.

Sampling Technique

Consecutive sampling was used at each of the participating sites, inviting all patients presenting to the medical OPD during the times of data collection for the site who met the eligibility criteria to participate until the target sample size per site was reached.

Variables

Outcome Variable

Medication adherence, based on the MMAS-8, scored as high, medium and low adherence using the scale's established scoring system.

Independent Variables

- Socio-demographic: Age, sex, marital status, education level, occupation, monthly household income, residence (urban/rural) and health insurance (or financial coverage) status.
- Clinical: disease category (hypertension only, T2DM only or both); duration of the disease; additional comorbidities; pill burden (number of medications taken); fasting blood glucose (FBG) and/or HbA1c (most recent); side effects (self-reported).
- Health-system: distance/travel time to health facility, waiting time at the facility, perceived quality of the physician's counselling, and the frequency of follow-up visits.

Operational Definitions

- Hypertension: physician diagnosis and/or current use of antihypertensive medications, based on current guideline thresholds.
- Type 2 diabetes mellitus: physician-documented diagnosis and/or current use of oral hypoglycemic agents or insulin, consistent with recognized clinical guideline thresholds.
- Good/high medication adherence: MMAS-8 score of 8.
- Medium/Moderate Medication Adherence: MMAS-8 score of 6 – less than 8.
- Poor/low medication adherence: MMAS-8 score less than 6.
- Polypharmacy: taking five or more different types of medicines at the same time.

Data Collection Instrument

A structured, interviewer-administered questionnaire, with three sections, was used for data collection: (1) a socio-demographic and clinical data collection proforma developed for this study; (2) the MMAS-8 [10]; and (3) items related to health-system-related determinants (counselling quality, waiting time and accessibility of facilities), adapted from previously published Pakistani adherence studies [12, 14]. The use of the MMAS-8 in this study was obtained through formal permission and a signed licensing agreement with the developer/copyright holder, following standard practice in its

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use in published research [18-22] to ensure that the instrument was used in compliance with copyright. The scale consists of 7 dichotomous (yes/no) items and 1 five-point Likert-type item, for a total of 8 items that sum to a scale score from 0 to 8 [18].

Validity and Reliability

The MMAS-8 has shown good internal consistency (Cronbach's alpha > 0.83 in the original validation) and has been translated into over two dozen languages and adapted for use in various chronic disease populations, including hypertension and diabetes [18, 19, 23]. Similarly, the proforma was pilot tested in the study population for clarifying the items and for making it comprehensible to the study population and modified as needed.

Ethical Considerations

This study was carried out with respect to the ethical principles described in the Declaration of Helsinki [24]. Before data collection began, approval was secured from the IRB/ERC (Institutional Review Board/Ethics Review Committee) in each of the participating hospitals. All participants were given a full explanation of the purpose of the study, its procedures, duration, and the right to refuse participation or stop anytime without it affecting their treatment. All participant information was kept confidential, with each participant given a unique study identification code to ensure anonymity of the questionnaire and data stored on password-protected devices accessible only to the research team.

Data Collection Procedure

Where possible, the trained data collectors were asked to approach patients who were consecutive and eligible for the study in the medical OPD waiting rooms at each study site during the data collection sessions, which were scheduled. The informed consent was obtained, and then the structured questionnaire was completed in the patient's preferred language (Urdu, Pashto or English) face-to-face, and clinical information was cross-checked with medical documents if available. To minimise inter-collector variability, data collectors were given standardised training, which included role-play sessions before fieldwork began.

Data Management

Completed questionnaires were checked on the spot for completeness. Two separate data entry staff persons entered the data in a password-coded electronic data entry system, and discrepancies were checked against the original questionnaire. Before analysis, the implausible values were detected using range and consistency checks. Physical questionnaires are securely stored and will be destroyed once the study is complete and published in line with the data retention policy of the institution.

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Statistical Analysis Plan

All statistical analysis was performed using SPSS version 27. Standard normality tests (e.g., Shapiro-Wilk) were used to test continuous variables, and they were summarised as mean ± standard deviation or median (interquartile range) as appropriate to their distribution. The categorical variables were described as frequencies and percentages. The primary outcome — prevalence of medication adherence — was reported overall and stratified by disease category (hypertension only, T2DM only, or both) with 95% confidence intervals. For each association with the adherence status, the bivariate categorical and continuous associations were evaluated using the chi-square test and the independent-samples t test, respectively. To determine independent predictors of adherence, all variables that were associated with adherence at a pre-specified bivariate level of significance ($p < 0.20$) were tested in a multivariable binary logistic regression model, and the model results are presented as adjusted odds ratios (AOR) with 95% confidence intervals. Goodness of fit for the models was evaluated with the Hosmer-Lemeshow goodness-of-fit test, and multicollinearity of independent variables was evaluated with variance inflation factors. Throughout, the statistical significance was set at a two-sided p-value of < 0.05.

STROBE Checklist Considerations

The manuscript was written with specific reference to the STROBE checklist for cross-sectional studies [15] to ensure that the study design is identified in the title and abstract; that background, rationale, and objectives are clearly expressed in the introduction; that the methods specify the setting, participants, variables, data sources, how bias was minimised, the justification of study size, and the statistical methods; that the results include participant flow, descriptive data, outcome data, and main results including adjusted estimates; and that the interpretation and generalisability of the results, as well as key results and limitations, are discussed in the discussion section. A STROBE checklist was prepared and cross-referenced with each manuscript location and page. It has been completed and is included as supplementary material with this manuscript.

RESULTS

Participant Flow and Response Rate

In the medical outpatient departments (OPDs) of the participating tertiary care hospitals, a total of 520 eligible patients who fulfilled the diagnostic criteria were approached during the study period of six months. Of these, 44 patients were not eligible (e.g., treatment duration was <3 months or they had cognitive impairment) or refused to participate (18 patients). Thus, the overall response rate was 91.5% (476 completed the interviewer-administered questionnaire, Figure 1).

Baseline Socio-demographic and Clinical Characteristics

The socio-demographic and clinical profile of individuals who participated in the study (by disease category) is described in Table 1. Overall, the mean age was 54.8 ± 9.2 years. The age of the participants was higher in the participants who had hypertension and type 2 diabetes mellitus

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(T2DM) (58.4 ± 8.1 years) than in those who had hypertension only (52.1 ± 9.5 years) and T2DM only (53.9 ± 9.4 years).

Of the subjects, 53.4% (n = 254) were found to be females. Over half of the respondents lived in rural or peri-urban areas (58.4%, n = 278), and 46.2% (n = 220) had a monthly household income of less than 30,000 PKR. Of those who did not answer for formal education, 38.7% (n = 184) did not report any.

The median time to onset of disease was 6.0 years (IQR: 3.0–10.0). The mean daily pill burden for all participants was 3.6 ± 1.8 medications/day, and among those who had both hypertension and T2DM, this increased to 5.9 ± 1.4 medications/day. In total, 31.9% (n = 152) followed the polypharmacy criterion (≥5 medications) with the highest rate for the group with comorbid conditions (68.1%, n = 111).

Prevalence of Medication Adherence

The Morisky Medication Adherence Scale (MMAS-8), an 8-item scale, was used to measure medication adherence. Overall, 24.4% (95% CI: 20.6%–28.5%) of participants demonstrated high adherence, 36.1% (95% CI: 31.8%–40.6%) demonstrated medium adherence, and 39.5% (95% CI: 35.1%–44.1%) demonstrated low adherence (Table 2).

There was a significant variation in adherence by disease groups. Low adherence was most prevalent among participants with concurrent hypertension and T2DM (51.5%; 95% CI: 43.6%–59.4%), compared with those having hypertension alone (31.5%; 95% CI: 24.4%–39.3%) or T2DM alone (35.1%; 95% CI: 27.5%–43.3%). The differences were statistically significant ($\chi^2 = 16.84$; $p < 0.001$).

Bivariate Analysis of Factors Associated with Medication Adherence

Association of socio-demographic, clinical, and healthcare-related factors with low or moderate/high adherence to medication was examined using bivariate analyses (Table 3).

Low income was significantly correlated with low adherence ($\chi^2 = 14.12$, $p < 0.001$). Likewise, the participants who had no formal education were significantly more likely to show low adherence than those who had any formal education ($\chi^2 = 10.85$, $p = 0.001$).

Significant associations were also seen in the clinical characteristics. There were more participants who were less adherent to the intervention with comorbid hypertension and T2DM than for those with only one chronic condition ($\chi^2 = 15.22$, $p < 0.001$). The strongest clinical association was with polypharmacy, where those taking five or more medications were much more likely to have reported poor adherence ($\chi^2 = 22.41$, $p < 0.001$).

The adherence behaviour was also affected by factors related to health care. The participants who felt the physician's counselling was inadequate or poor were significantly more likely to have low adherence than those who felt it was satisfactory ($\chi^2 = 18.63$, $p < 0.001$).

No significant association was found with medication adherence with either age (-1.16, $p = 0.246$) or sex ($\chi^2 = 0.77$, $p = 0.381$). However, both variables were included in the multivariable analysis based on the pre-specified inclusion criteria ($p < 0.20$).

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Multivariable Predictors of Low Medication Adherence

The independent predictors of low medication adherence (Table 4) were identified as the results of a multivariable binary logistic regression model. Four factors remained independently associated with low adherence after adjustment for other factors that might have confounded the relationship. Those who were taking more than five medications had over twice the odds of low adherence as those who were taking fewer medications (AOR = 2.34; 95% CI: 1.48–3.71, $p < 0.001$). Low household income was an independent predictor of poor adherence (AOR = 1.86; 95% CI: 1.21–2.85; $p = 0.004$). Similarly, low adherence rates were significantly associated with participants who reported inadequate physician counselling (AOR = 2.11; 95% CI: 1.38 – 3.22; $p < 0.001$). Poor level of formal education also was an independent predictor of poor medication adherence (AOR = 1.54; 95% CI: 1.02–2.33; $p = 0.039$).

In contrast, age (AOR = 1.01; 95% CI: 0.98–1.03; $p = 0.412$), female sex (AOR = 1.14; 95% CI: 0.77–1.68; $p = 0.518$), and comorbid disease status (AOR = 1.32; 95% CI: 0.81–2.15; $p = 0.264$) were not independently associated with medication adherence after adjustment. This relationship between adherence and comorbidity appeared to be mediated by medication burden, as this relationship was not as strong after the medication burden adjustment.

Model Performance

The logistic regression model demonstrated satisfactory calibration, as indicated by the Hosmer–Lemeshow goodness-of-fit test ($\chi^2 = 6.42$, $p = 0.598$). The overall model was statistically significant ($p < 0.001$). Multicollinearity diagnostics showed low variance inflation factors (VIF range: 1.18–1.54), indicating no evidence of problematic collinearity among the independent variables.

Table 1. Socio-demographic and Clinical Characteristics of Study Participants

Characteristic	Overall (N = 476)	Hypertension only	T2DM only	Both HTN + T2DM
Age, years (mean ± SD)	54.8 ± 9.2	52.1 ± 9.5	53.9 ± 9.4	58.4 ± 8.1
Female sex, n (%)	254 (53.4)	—	—	—
Rural/peri-urban residence, n (%)	278 (58.4)	—	—	—
Monthly household income <30,000 PKR, n (%)	220 (46.2)	—	—	—
No formal education, n (%)	184 (38.7)	—	—	—

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Characteristic	Overall (N = 476)	Hypertension only	T2DM only	Both HTN + T2DM
Disease duration, years, median (IQR)	6.0 (3.0–10.0)	—	—	—
Daily pill burden (mean ± SD)	3.6 ± 1.8	—	—	5.9 ± 1.4
Polypharmacy (≥5 medications), n (%)	152 (31.9)	—	—	111 (68.1)
Group size, n (% of total)	476 (100)	—	—	163 (34.2)[a]

[a] Comorbid (HTN + T2DM) group size derived from the reported polypharmacy figures (111/0.681 ≈ 163). Cells marked "—" (marital status, occupation, health insurance status, additional comorbidities, dosing frequency, self-reported side effects, most recent blood pressure/HbA1c, and the exact n for the hypertension-only and T2DM-only subgroups) were not included in the results narrative supplied and should be completed directly from the study dataset before submission.

Table 2. Prevalence of Medication Adherence Overall and by Disease Category

Adherence category	Overall, % (95% CI)	Hypertension only, % (95% CI)	T2DM only, % (95% CI)	Both HTN + T2DM, % (95% CI)
High adherence (MMAS-8 = 8)	24.4 (20.6–28.5)	—	—	—
Medium adherence (MMAS-8 6 to <8)	36.1 (31.8–40.6)	—	—	—
Low adherence (MMAS-8 <6)	39.5 (35.1–44.1)	31.5 (24.4–39.3)	35.1 (27.5–43.3)	51.5 (43.6–59.4)

Between-group comparison of low adherence across disease categories: $\chi^2 = 16.84$, $p < 0.001$. High- and medium-adherence proportions by disease category were not reported in the supplied results and should be inserted from the dataset.

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Table 3. Bivariate Associations Between Candidate Determinants and Low Medication Adherence

Determinant	Test statistic	p-value	Significant (p < 0.20)?
Monthly household income (<30,000 vs ≥30,000 PKR)	$\chi^2 = 14.12$	<0.001	Yes
Formal education (none vs any)	$\chi^2 = 10.85$	0.001	Yes
Disease category (comorbid vs single condition)	$\chi^2 = 15.22$	<0.001	Yes
Polypharmacy (≥5 vs <5 medications)	$\chi^2 = 22.41$	<0.001	Yes
Perceived physician counseling (inadequate vs satisfactory)	$\chi^2 = 18.63$	<0.001	Yes
Age	$t = -1.16$	0.246	No, but retained (p < 0.20 criterion for other reasons)
Sex	$\chi^2 = 0.77$	0.381	No, but retained (p < 0.20 criterion for other reasons)

Age and sex did not meet the bivariate significance threshold on their own but were retained in the multivariable model per the pre-specified p < 0.20 inclusion rule described in the Statistical Analysis Plan.

Table 4. Multivariable Logistic Regression: Independent Predictors of Low Medication Adherence

Predictor	AOR	95% CI	p-value
Polypharmacy (≥5 vs <5 medications)	2.34	1.48–3.71	<0.001
Low household income (<30,000 PKR)	1.86	1.21–2.85	0.004
Inadequate physician counseling	2.11	1.38–3.22	<0.001
No formal education	1.54	1.02–2.33	0.039
Age (per year)	1.01	0.98–1.03	0.412
Female sex	1.14	0.77–1.68	0.518

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Predictor	AOR	95% CI	p-value
Comorbid hypertension + T2DM	1.32	0.81–2.15	0.264

Model fit: Hosmer–Lemeshow $\chi^2 = 6.42$, $p = 0.598$ (satisfactory calibration); overall model $p < 0.001$; variance inflation factors ranged 1.18–1.54 (no problematic multicollinearity).

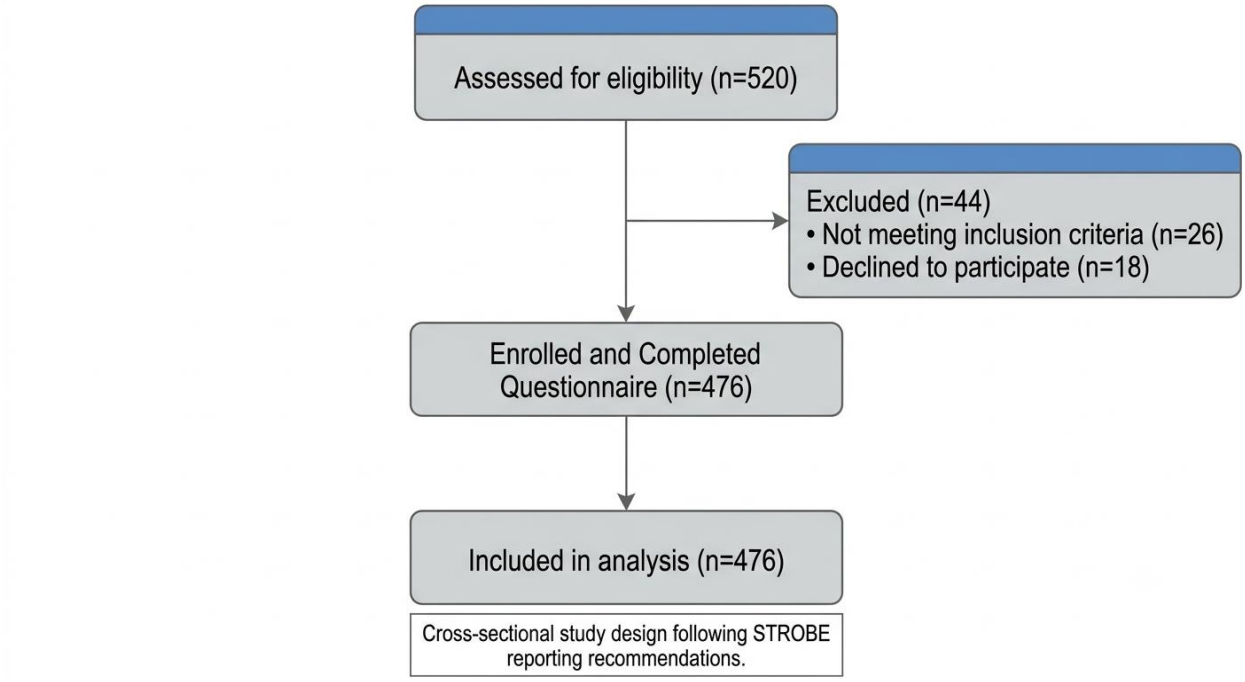

Figure 1. Participant Flow Diagram

DISCUSSION

Interpreting the Principal Finding — Prevalence of Adherence

In this multicenter Peshawar-based sample, 39.5% (95% CI: 35.1–44.1%) of participants demonstrated low medication adherence, with a further 36.1% showing only medium adherence — meaning that fewer than one in four participants (24.4%) achieved high adherence on the MMAS-8. This overall non-adherence burden sits at the upper end of the pooled global antihypertensive non-adherence range of 27%–40% reported by Lee et al. [3], and is somewhat below, though not far from, the pooled T2DM non-adherence estimate of approximately 48% reported among Indian patients using MMAS-8-based studies [4]. This pattern is broadly consistent with, and slightly less severe than, the poor-adherence rates previously documented in single-center Peshawar studies — for example, the 22.7% good-adherence rate reported among T2DM patients at a military hospital in Peshawar [11] — which may reflect genuine differences between comorbid and single-condition subpopulations, differences in sampling frame (military versus general tertiary care OPDs), or the

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broader multicenter catchment of the present study. The elevated overall non-adherence observed here is plausibly related to the affordability constraints, health literacy gaps, and counseling-quality limitations that have been documented in comparable Pakistani settings [12,13], and that emerged as significant determinants in the present analysis as well.

Adherence also differed substantially by disease category: low adherence was most prevalent among participants managing both hypertension and T2DM concurrently (51.5%), compared with hypertension alone (31.5%) or T2DM alone (35.1%) (χ^2 = 16.84, $p < 0.001$). This pattern is consistent with the added pill burden and medication-related burden previously documented among patients managing both conditions concurrently [7,9], and is corroborated directly within this dataset by the markedly higher mean pill burden (5.9 ± 1.4 medications) and polypharmacy prevalence (68.1%) observed in the comorbid group relative to the overall sample (3.6 ± 1.8 medications; 31.9% polypharmacy).

Interpreting Independent Predictors

Polypharmacy emerged as the strongest independent predictor of low adherence in the multivariable model (AOR = 2.34; 95% CI: 1.48–3.71; $p < 0.001$), more than doubling the odds of poor adherence. This finding is directly in line with medication-related burden research from Ghana, which found that a higher perceived medication burden was independently associated with reduced odds of adherence among patients with comorbid hypertension and T2DM [7,8], and with the broader scoping-review literature on adherence-optimization interventions in this comorbidity group [9,10]. Notably, once polypharmacy was accounted for, comorbid disease status itself was no longer independently associated with adherence (AOR = 1.32; 95% CI: 0.81–2.15; $p = 0.264$), suggesting — consistent with the medication-related-burden literature [7,9] — that it is the accumulated pill burden associated with treating two conditions simultaneously, rather than comorbidity per se, that drives the excess non-adherence observed among these patients.

Low household income independently increased the odds of poor adherence (AOR = 1.86; 95% CI: 1.21–2.85; $p = 0.004$), echoing the Islamabad-based finding that treatment unaffordability was independently associated with non-adherence among hypertensive patients [12]. Given Pakistan's comparatively high rate of out-of-pocket healthcare expenditure, this finding is readily interpretable through a resource-constraint lens: patients with limited disposable income may ration doses, delay refills, or discontinue therapy altogether when facing competing financial priorities, independent of their underlying beliefs about treatment necessity.

Likewise, inadequate physician counselling was also found to be independently associated with poor adherence (AOR = 2.11; 95% CI: 1.38–3.22; $p < 0.001$), similar to the association between counselling and adherence previously reported among hypertensive patients in Islamabad [12] and the association between psychosocial and communication-related factors and non-adherence reported in the multicentre Pakistani study by Ali et al. [14]. In terms of the Necessity Concerns Framework, insufficient counselling may be viewed as failing to address patients' concerns about the

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need for the medication or concerns about side effects, which may undermine the perceived need for continued adherence to treatment.

Lack of formal education also remained an independent predictor (AOR = 1.54; 95% CI: 1.02–2.33; p = 0.039), consistent with the protective effect of higher education reported in the Islamabad hypertension cohort [12] and with the documented association between health literacy and adherence among elderly hypertensive patients in the same city [13]. Age, sex, and comorbid disease status were not independently associated with adherence after adjustment in this sample; the null finding for sex is broadly consistent with prior Pakistani work [12,14], although the absence of a significant depressive-symptom or psychosocial pathway — a notable correlate of poor adherence in the Karachi cohort of Hashmi et al. [17] and in the multicenter psychosocial analysis of Ali et al. [14] — could not be evaluated directly in the present analysis, since these variables were not part of the present model, and represents a point of divergence worth exploring in future work incorporating psychosocial measures. As with all cross-sectional analyses, these associations should be interpreted as identifying independent correlates rather than establishing causal direction.

Possible Mechanisms

The independent association between low household income and poor adherence is consistent with the documented high rate of out-of-pocket healthcare expenditure in Pakistan and with the previously reported link between medication unaffordability and non-adherence in Islamabad [12]. The independent association between inadequate counseling and poor adherence is compatible with the Necessity-Concerns Framework and with prior Pakistani evidence linking counseling quality and health literacy to adherence and functional performance [13]. The strong, independent association between polypharmacy and poor adherence, together with the attenuation of the comorbidity effect after adjustment, supports the medication-related-burden literature's contention that cumulative pill burden — rather than the number of diagnoses per se — is the more proximate driver of reduced adherence among patients with multimorbidity [7,9].

Implications

These findings support several locally actionable interventions. The strong independent effect of polypharmacy supports the use of fixed-dose combination prescribing where clinically appropriate to reduce daily pill burden, particularly among patients managing both hypertension and T2DM [7]. The independent effect of counselling quality is in support of introducing improved and structured counselling protocols at the point of prescription, as was shown in previous work done in Pakistan [12]. Household income shows a significant independent effect and can be used for the evaluation of targeted subsidisation or means-tested exemption programmes for antihypertensive and antidiabetic drugs. Last, a separate impact of formal education justifies the development of health-literacy interventions for low-literacy groups who visit the OPD of tertiary care hospitals in Peshawar [13].

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Strengths

The results of this study are generalisable compared to previous studies conducted in single centres of Peshawar [11, 16] due to its multicentre design. Use of a validated instrument to measure adherence which has been benchmarked against international literature (MMAS-8) allows direct comparison with the wider literature [3, 4, 18]. The study directly met the gap identified in the Introduction by the inclusion of patients with isolated and comorbid hypertension/T2DM, and the use of multivariable logistic regression (Hosmer–Lemeshow p = 0.598) with no evidence of problematic multicollinearity (VIF range: 1.18–1.54) enabled the determination of independent determinants of adherence, not merely bivariate ones.

Limitations

This cross-sectional study, like all cross-sectional designs, does not allow the determination of causal or temporal relationships between the identified determinants and adherence to the therapy, and in this study the reverse causality cannot be ruled out (e.g., poor disease control may lead to the change in the self-reported adherence status, not the other way round). The self-reported adherence measure (MMAS-8) is susceptible to social desirability and recall bias and may overestimate actual adherence when compared to objective measures like pharmacy refill data or pill counts. Use of consecutive sampling from tertiary care OPDs could result in an under-representation of patients who have already dropped out from care and an over-representation of more clinically engaged patients, which may lead to a higher prevalence of adherence than what is actually observed in the general population. The results of this study may not apply to primary care settings, populations living in rural areas outside the primary catchment area of major hospitals, or other provinces in Pakistan because it was conducted in a multi-centre manner within Peshawar. The present model did not include any psychosocial variables which have been linked with adherence in other parts of Pakistan [17] and could explain the remaining unexplained variance in adherence status.

Practical Implications

The results will help guide clinical counselling, hospital-level pharmacy and prescribing policy (including promotion of FDC when clinically appropriate, where appropriate) and provincial programme planning for non-communicable diseases in Khyber Pakhtunkhwa, as these factors were each found to be independently associated with adherence in this population: polypharmacy, income and both the quality of counselling and knowledge and education.

Recommendations

- For clinical services, structured and standardised patient counselling protocols should be implemented at the time of antihypertensive/antidiabetic prescribing in tertiary care hospitals of Peshawar, as there are strong independent associations between counselling and adherence observed here and elsewhere in Pakistan [12].

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- Targeted subsidies for essential antihypertensive and antidiabetic drugs should be considered by provincial health authorities, as household income was shown to be an independent factor associated with poor adherence.
- Routine protocol optimisation (such as using fixed-dose combinations) can help to decrease pill burden, and the number of pills was the most significant independent factor linked to poor adherence; therefore, prescribers should consider regimen simplification for patients with comorbid hypertension and T2DM as a way to reduce pill burden.
- Future longitudinal and interventional studies should test whether addressing the determinants identified here (counseling quality, affordability, pill burden, health literacy) causally improves adherence and downstream disease control.
- Adherence-support interventions should be tailored separately for patients with isolated hypertension, isolated T2DM, and comorbid presentation, given the significantly higher prevalence of low adherence observed among comorbid patients in this sample [7,9].

Conclusion

Medication adherence is a critical, modifiable determinant of clinical outcomes among patients with hypertension and T2DM, and this multicenter, cross-sectional study of 476 patients attending tertiary care OPDs in Peshawar found that non-adherence is common: 39.5% of participants demonstrated low adherence and a further 36.1% only medium adherence, with the burden concentrated among patients managing both hypertension and T2DM concurrently (51.5% low adherence versus 31.5–35.1% among those with a single condition). Polypharmacy, low household income, inadequate physician counseling, and lack of formal education were identified as independent, modifiable or addressable determinants of poor adherence, while age, sex, and comorbid disease status per se were not independently associated with adherence after adjustment. These findings indicate that adherence-support interventions in Khyber Pakhtunkhwa should prioritize reducing pill burden through regimen simplification, strengthening structured counseling at the point of prescribing, and addressing affordability and health-literacy barriers — particularly among patients with comorbid hypertension and T2DM, who carry the greatest adherence burden. This study contributes locally generated, multicenter evidence supporting the design of targeted, context-appropriate adherence-support interventions in Peshawar's tertiary care network.

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CONFLICT OF INTEREST

The authors declare no conflict of interest relevant to this manuscript.

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AUTHOR CONTRIBUTIONS

All authors contributed equally.

DATA AVAILABILITY STATEMENT

The datasets analyzed during the current study are available from the corresponding author upon reasonable request, subject to institutional data-sharing policy and applicable ethical restrictions.

INFORMED CONSENT STATEMENT

Written informed consent was obtained from all individual participants included in the study prior to any data collection procedures. Participants were informed of the purpose of the study, the voluntary nature of participation, their right to withdraw at any time without penalty or effect on their clinical care, and the measures taken to protect the confidentiality of their data.

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