JHWCR JOURNAL OF HEALTH, WELLNESS AND COMMUNITY RESEARCH 3007-0570

https://doi.org/10.61919/yvc56606

Original Article

Effect of Medication Adherence on Therapeutic Response to Antihypertensive Regimens in Newly Diagnosed Hypertensive Patients

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"Cite this Article" Received: 08 March 2026; **Accepted**: 27 April 2026; **Published**: 22 May 2026

Author Contributions: AWA and ST contributed to concept and design; IRG and SAS contributed to data collection; MAS contributed to analysis; FN contributed to drafting and critical revision. **Ethical Approval** was obtained by the Respective Institution. **Informed Consent**: Written informed consent was obtained from all participants; **Conflict of Interest**: The authors declare no conflict of interest. **Funding**: No external funding; **Data Availability**: Available from the corresponding author on reasonable request; **Acknowledgments**: N/A.

ABSTRACT

Background: Hypertension remains a major contributor to cardiovascular morbidity, yet early blood pressure control is often limited by poor medication adherence and delayed treatment adjustment. Objective: To evaluate the effect of medication adherence on early therapeutic response among newly diagnosed hypertensive patients started on first-line antihypertensive therapy. Methods: This prospective cohort study was conducted in selected tertiary care hospitals of Karachi, Pakistan. Newly diagnosed adult hypertensive patients were followed for 12 weeks after initiation of first-line antihypertensive treatment. Patients were categorized as adherent or non-adherent based on medication-taking behavior during follow-up. Outcomes included blood pressure control at 12 weeks, systolic and diastolic blood pressure reduction, dose escalation, side effects, and therapeutic inertia. Results: Of 220 enrolled patients, 208 completed follow-up; 126 (60.6%) were adherent and 82 (39.4%) were non-adherent. Blood pressure control was achieved in 78 adherent patients (61.9%) compared with 24 non-adherent patients (29.3%) (OR 3.93, 95% CI 2.16–7.13; $p < 0.001$). Adherent patients had greater systolic reduction (18.6 ± 9.4 vs 8.9 ± 10.1 mmHg; $p < 0.001$) and diastolic reduction (11.2 ± 6.8 vs 5.1 ± 7.0 mmHg; $p < 0.001$). Dose escalation and therapeutic inertia were more frequent among non-adherent patients. Conclusion: Medication adherence was strongly associated with better early blood pressure control and fewer treatment adjustments. Keywords: Hypertension, Medication Adherence, Antihypertensive Therapy, Therapeutic Response, Therapeutic Inertia, Blood Pressure Control, Karachi.

INTRODUCTION

Hypertension remains one of the most important modifiable contributors to cardiovascular morbidity, stroke, heart failure, chronic kidney disease, and premature mortality worldwide. Although effective antihypertensive medicines are widely available, optimal blood pressure control continues to be difficult to achieve in routine clinical practice, particularly during the early phase after diagnosis. Contemporary hypertension guidelines emphasize that successful management depends not only on selecting an appropriate first-line antihypertensive regimen but also on regular follow-up, timely treatment adjustment, and sustained medication adherence (1–3). In clinical settings, uncontrolled blood pressure after treatment initiation may therefore reflect inadequate pharmacological response, poor adherence, delayed therapeutic intensification, or a combination of these factors.

Medication adherence is a central determinant of therapeutic response in hypertension because even evidence-based first-line regimens cannot produce stable clinical benefit if doses are missed, interrupted, or discontinued. Adherence includes initiation of treatment, correct daily implementation, and persistence over time, all of which are particularly vulnerable in newly diagnosed patients because hypertension is often asymptomatic and patients may stop medication once they feel well. International evidence has consistently linked poor adherence with uncontrolled blood pressure, higher cardiovascular risk, increased healthcare utilization, and adverse long-term outcomes (30–36). However, adherence is not merely a patient-level behavior; it interacts with prescribing decisions, follow-up structure, adverse-effect counseling, treatment cost, and patient understanding of disease chronicity.

Therapeutic inertia is another major barrier to blood pressure control and refers to the failure to initiate, intensify, or modify treatment when blood pressure remains above target despite clinical indication for adjustment (4–12). In routine outpatient practice, therapeutic inertia may occur because clinicians are uncertain whether uncontrolled readings represent true treatment failure or irregular medication use. This uncertainty is clinically important because a non-adherent patient may be misclassified as having inadequate drug response and may receive unnecessary dose escalation, whereas an adherent but uncontrolled patient may remain undertreated if treatment intensification is delayed. Therefore, adherence and therapeutic inertia should be evaluated together rather than as isolated barriers to hypertension control.

The early months after hypertension diagnosis represent a critical period in which treatment beliefs, adherence habits, and clinician–patient follow-up patterns are established. During this phase, patients are introduced to long-term medication, learn to interpret blood pressure changes, experience or fear side effects, and develop expectations about whether treatment is necessary despite absence of symptoms. A favorable early response may reinforce adherence, whereas poor counseling, adverse effects, cost burden, or weak follow-up may promote early discontinuation. Evidence also suggests that adherence and persistence may vary across antihypertensive drug classes and treatment complexity, further influencing early therapeutic outcomes (34,35).

In Pakistan, hypertension prevalence is substantial, while awareness, adherence, and control remain suboptimal. Local studies have identified several barriers to antihypertensive adherence, including limited disease knowledge, forgetfulness, financial constraints, pill burden, symptomatic use of medication, fear of adverse effects, and inadequate follow-up support (13–25,27,28). Karachi provides an important setting for evaluating this problem because its tertiary hospitals serve a socioeconomically diverse population and manage large numbers of newly diagnosed hypertensive patients. Existing local evidence has documented poor adherence and low hypertension knowledge, but prospective data examining how adherence influences early therapeutic response, dose escalation, and therapeutic inertia in newly diagnosed patients remain limited (15–18,23,24).

The present study was therefore designed to evaluate the effect of medication adherence on early therapeutic response among newly diagnosed hypertensive adults started on first-line antihypertensive therapy in selected tertiary care hospitals of Karachi. Using a prospective cohort approach, the study compared adherent and non-adherent patients in terms of blood pressure control at 12 weeks, mean reduction in systolic and diastolic blood pressure, dose escalation, adverse-effect profile, and therapeutic inertia. The primary research question was whether newly diagnosed hypertensive patients who remain adherent to first-line therapy achieve superior blood pressure control at 12 weeks compared with non-adherent patients. The study hypothesis was that medication adherence is independently associated with better early blood pressure control and lower requirement for dose escalation after adjustment for relevant baseline clinical factors.

MATERIALS AND METHODS

This study was conducted as a prospective cohort study among newly diagnosed adult hypertensive patients attending outpatient medical clinics of selected tertiary care hospitals in Karachi, Pakistan. A prospective design was selected because the objective was to observe treatment response after initiation of first-line antihypertensive therapy and to relate subsequent blood pressure outcomes to medication-taking behavior during follow-up. Each enrolled patient was followed for 12 weeks after treatment initiation, with scheduled assessments at baseline, week 4, week 8, and week 12. The overall study period was 12 months and included recruitment, follow-up visits, data verification, data entry, and statistical analysis.

The study population comprised adults aged 18 years or above with a fresh diagnosis of hypertension who were started on first-line antihypertensive treatment during the index visit or within the preceding two weeks. Eligible patients were recruited consecutively from outpatient departments after confirmation of diagnosis and treatment initiation by the treating physician. Patients were included if they were newly diagnosed, had not previously used antihypertensive medication, were willing to provide written informed consent, and were available for scheduled follow-up. Patients were excluded if they had secondary hypertension, pregnancy-induced hypertension or pre-eclampsia, severe organ failure or terminal illness, serious psychiatric illness interfering with communication, inability to provide reliable responses, or unwillingness to complete follow-up. These criteria were applied to maintain a clinically homogeneous cohort of treatment-naïve patients in whom early response to first-line therapy could be evaluated.

The sample size was calculated to detect a clinically meaningful difference in blood pressure control between adherent and non-adherent patients at 12 weeks, using a 95% confidence level and 80% statistical power. A margin was added for anticipated loss to follow-up, and 220 patients were enrolled to preserve adequate analytical power. Non-probability consecutive sampling was used because patients were recruited as they presented to outpatient clinics during the study period. Of the 220 enrolled participants, 208 completed the 12-week follow-up and were included in the final complete-case analysis.

At baseline, demographic and clinical information was collected using a structured data collection form. Recorded variables included age, gender, marital status, educational level, occupation, monthly income, smoking status, body mass index, family history of hypertension, baseline systolic and diastolic blood pressure, comorbid conditions, prescribed first-line antihypertensive regimen, drug dose, and dosing frequency. Blood pressure was measured using a standard sphygmomanometer or validated digital blood pressure device available in the hospital setting. Patients were seated quietly for at least five minutes before measurement. Two readings were recorded at a short interval and averaged; when readings differed substantially, a third reading was taken and the average of the two closest readings was used. The same measurement approach was followed during subsequent visits to improve internal consistency.

Follow-up assessments were conducted at 4, 8, and 12 weeks. At each visit, current systolic and diastolic blood pressure, missed doses, treatment continuation, dose changes, regimen modification, side effects, achievement of target blood pressure, and clinician response to uncontrolled blood pressure were recorded. Medication adherence was assessed using structured, non-judgmental questioning supported by review of prescription refill behavior, medication strips, or prescriptions where available. Patients were asked whether they had missed tablets, delayed doses, stopped medication because they felt well, or avoided medication because of adverse effects. For operational classification, patients who took their prescribed antihypertensive medication on most treatment days during follow-up and did not report frequent interruption or unsupervised discontinuation were categorized as adherent, whereas those who frequently missed doses, stopped medication without medical advice, or failed to follow the prescribed schedule were categorized as non-adherent.

The primary outcome was blood pressure control at 12 weeks. Secondary outcomes included mean reduction in systolic blood pressure, mean reduction in diastolic blood pressure, dose escalation, addition or switching of antihypertensive therapy, reported side effects, and therapeutic inertia. Therapeutic response was defined by reduction in blood pressure and achievement of target blood pressure by the final follow-up visit. Dose escalation was defined as an increase in drug dose, addition of another antihypertensive medication, or switch to a stronger regimen due to inadequate control. Therapeutic inertia was defined as absence of treatment intensification or modification despite persistently uncontrolled blood pressure during follow-up when clinical intensification was expected. This definition was applied consistently at scheduled visits by reviewing blood pressure status and documented treatment decisions.

To reduce measurement bias, blood pressure measurement procedures were standardized across visits, data were collected on predesigned forms, and study staff were oriented regarding consent, interview technique, follow-up documentation, and blood pressure recording. Adherence questions were asked in a non-judgmental manner to reduce social desirability bias. To address potential confounding, baseline variables known to influence blood pressure control, including age, gender, baseline blood pressure, body mass index, diabetes mellitus, family history of hypertension, and initial treatment type, were recorded for comparison and planned adjusted analysis. Data forms were checked regularly for missing values and internal consistency before entry into the electronic database. Each participant was assigned a unique study identification number to maintain confidentiality and enable accurate follow-up tracking.

Data were entered and analyzed using SPSS version 26. Continuous variables such as age, body mass index, systolic blood pressure, and diastolic blood pressure were summarized as mean and standard deviation. Categorical variables such as gender, adherence status, blood pressure control, dose escalation, side effects, and therapeutic inertia were summarized as frequencies and percentages. Baseline comparability between adherent and non-adherent groups was assessed using independent-sample t-tests for normally distributed continuous variables and chi-square tests for categorical variables.

Within-group change in blood pressure from baseline to follow-up was assessed using paired t-tests. Between-group differences in blood pressure reduction were examined using independent-sample t-tests. Categorical outcome differences were tested using chi-square tests. Logistic regression analysis was planned to estimate the association between adherence and blood pressure control at 12 weeks after adjustment for relevant demographic and clinical covariates. A p-value below 0.05 was considered statistically significant.

Ethical approval was obtained from the relevant institutional ethical review committee before initiation of the study. Written informed consent was obtained from all participants after explanation of study objectives, follow-up requirements, voluntary participation, confidentiality, and the right to withdraw without effect on clinical care. No invasive procedure was performed as part of the research, and all treatment decisions remained under the authority of the treating physician. Participant confidentiality was maintained throughout data collection, storage, and analysis by using coded study identifiers rather than personal identifiers in the analytical dataset.

RESULTS

A total of 220 newly diagnosed hypertensive patients were enrolled, of whom 208 completed the 12-week follow-up and were included in the final analysis. Among these participants, 126 patients (60.6%) were classified as adherent and 82 patients (39.4%) as non-adherent. Baseline demographic and clinical characteristics were broadly comparable between groups, with small between-group differences in age, baseline systolic blood pressure, baseline diastolic blood pressure, body mass index, diabetes mellitus, family history of hypertension, and initial treatment type.

Table 1. Baseline Characteristics of Study Participants by Adherence Status

Variable	Adherent (n = 126)	Non-Adherent (n = 82)	Total (n = 208)	Mean Difference/ Effect Estimate
Age, years	50.2 ± 11.1	49.1 ± 12.3	49.8 ± 11.6	MD 1.1, 95% CI −2.19 to 4.39
Male, n (%)	70 (55.6)	48 (58.5)	118 (56.7)	—
Female, n (%)	56 (44.4)	34 (41.5)	90 (43.3)	—
Baseline SBP, mmHg	154.8 ± 10.7	155.9 ± 11.3	155.2 ± 10.9	MD −1.1, 95% CI −4.18 to 1.98
Baseline DBP, mmHg	96.4 ± 7.8	97.1 ± 8.2	96.7 ± 8.0	MD −0.7, 95% CI −2.94 to 1.54
BMI, kg/m²	27.3 ± 4.2	27.9 ± 4.7	27.5 ± 4.4	MD −0.6, 95% CI −1.85 to 0.65
Family history of hypertension, n (%)	68 (54.0)	40 (48.8)	108 (51.9)	—
Diabetes mellitus, n (%)	24 (19.0)	18 (22.0)	42 (20.2)	—
Started on monotherapy, n (%)	89 (70.6)	60 (73.2)	149 (71.6)	—
Started on combination therapy, n (%)	37 (29.4)	22 (26.8)	59 (28.4)	—

At baseline, the adherent and non-adherent groups showed clinically similar blood pressure profiles. Mean baseline systolic blood pressure was 154.8 ± 10.7 mmHg in adherent patients and 155.9 ± 11.3 mmHg in non-adherent patients, with a mean difference of −1.1 mmHg. Mean baseline diastolic blood pressure was also comparable between adherent and non-adherent groups, 96.4 ± 7.8 mmHg versus 97.1 ± 8.2 mmHg, respectively. These findings indicate that subsequent differences in therapeutic response were unlikely to be explained by major baseline imbalance in blood pressure severity.

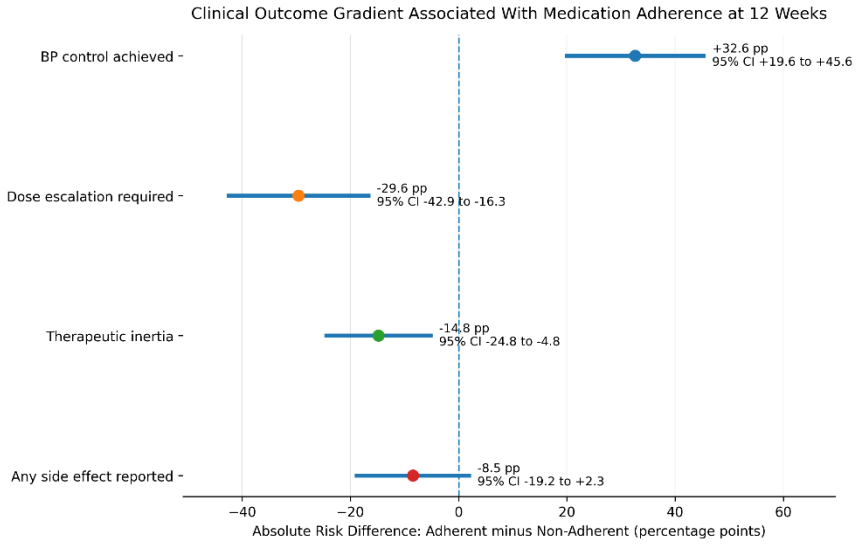

Figure 1 Clinical Outcome Gradient Associated With Medication Adherence at 12 Weeks

Table 2. Treatment Outcomes at 12 Weeks by Medication Adherence Status

Outcome Variable	Adherent (n = 126)	Non-Adherent (n = 82)	p-value	Effect Estimate
Controlled BP, n (%)	78 (61.9)	24 (29.3)	<0.001	OR 3.93, 95% CI 2.16–7.13
Uncontrolled BP, n (%)	48 (38.1)	58 (70.7)	<0.001	OR 0.25, 95% CI 0.14–0.46
Mean reduction in SBP, mmHg	18.6 ± 9.4	8.9 ± 10.1	<0.001	MD 9.7 mmHg, 95% CI 6.97–12.43
Mean reduction in DBP, mmHg	11.2 ± 6.8	5.1 ± 7.0	<0.001	MD 6.1 mmHg, 95% CI 4.18–8.02
Dose escalation required, n (%)	38 (30.2)	49 (59.8)	<0.001	OR 0.29, 95% CI 0.16–0.52
Therapeutic inertia, n (%)	9 (7.1)	18 (22.0)	0.002	OR 0.27, 95% CI 0.12–0.64
Any side effect reported, n (%)	17 (13.5)	18 (22.0)	0.108	OR 0.55, 95% CI 0.27–1.15

At 12 weeks, blood pressure control was achieved in 78 adherent patients (61.9%) compared with 24 non-adherent patients (29.3%), showing a statistically significant difference between groups. Adherent patients had approximately 3.9-fold higher odds of achieving blood pressure control than non-adherent patients. The adherent group also demonstrated a greater mean systolic blood pressure reduction, with a between-group mean difference of 9.7 mmHg, and a greater mean diastolic blood pressure reduction, with a mean difference of 6.1 mmHg.

Dose escalation was required in 38 adherent patients (30.2%) compared with 49 non-adherent patients (59.8%), indicating that treatment intensification was substantially more frequent among non-adherent

participants. Therapeutic inertia was also more common in the non-adherent group, occurring in 18 patients (22.0%) compared with 9 patients (7.1%) in the adherent group. Side effects were reported by 17 adherent patients (13.5%) and 18 non-adherent patients (22.0%); however, this difference did not reach statistical significance. Overall, the results indicate that medication adherence was strongly associated with better early therapeutic response, lower dose escalation, and reduced therapeutic inertia among newly diagnosed hypertensive patients.

Figure 1, Medication adherence showed a clinically meaningful outcome gradient at 12 weeks: adherent patients had a 32.6 percentage-point higher probability of blood pressure control than non-adherent patients (95% CI: 19.6 to 45.6), while also showing a 29.6 percentage-point lower risk of dose escalation (95% CI: −42.9 to −16.3) and a 14.8 percentage-point lower occurrence of therapeutic inertia (95% CI: −24.8 to −4.8). The reduction in reported side effects was smaller and statistically less certain at −8.5 percentage points (95% CI: −19.2 to 2.3), suggesting that adherence was most strongly associated with therapeutic effectiveness and treatment-decision outcomes rather than adverse-effect reporting.

DISCUSSION

The present prospective cohort study demonstrates that medication adherence is strongly associated with early therapeutic response among newly diagnosed hypertensive patients receiving first-line antihypertensive treatment in tertiary care hospitals of Karachi. Although adherent and non-adherent patients had comparable baseline systolic and diastolic blood pressure values, their clinical trajectories separated substantially during follow-up. By 12 weeks, blood pressure control was achieved in 61.9% of adherent patients compared with 29.3% of non-adherent patients, with adherent participants showing nearly fourfold higher odds of achieving target control. This finding supports the hypothesis that regular medication use is a major determinant of early blood pressure response after treatment initiation and that poor adherence can substantially reduce the apparent effectiveness of otherwise appropriate antihypertensive regimens (30–36).

The magnitude of blood pressure reduction further reinforces the clinical importance of adherence. Adherent patients achieved a mean systolic blood pressure reduction of 18.6 mmHg compared with 8.9 mmHg among non-adherent patients, while mean diastolic reduction was 11.2 mmHg versus 5.1 mmHg, respectively. These differences are not only statistically significant but also clinically meaningful because even modest reductions in systolic and diastolic pressure are associated with lower cardiovascular risk. The findings are consistent with international evidence showing that sustained antihypertensive medication use improves blood pressure control and reduces cardiovascular morbidity and mortality (30,31,36). In newly diagnosed patients, this early response may be especially important because successful initial control can strengthen confidence in treatment and support long-term persistence.

A key implication of this study is that non-adherence may be misinterpreted as pharmacological treatment failure. Dose escalation was required in 59.8% of non-adherent patients compared with 30.2% of adherent patients, despite similar baseline blood pressure profiles. This suggests that irregular medication intake may have contributed to persistent hypertension and prompted clinicians to intensify therapy when the underlying problem was not necessarily inadequate drug efficacy. Such a pattern can lead to unnecessary polypharmacy, higher treatment cost, greater adverse-effect burden, and reduced patient trust. Previous studies have similarly cautioned that treatment intensification without adherence assessment may distort clinical decision-making in hypertension care (8,11).

Therapeutic inertia also emerged as an important finding. It was more frequent among non-adherent patients, occurring in 22.0% compared with 7.1% of adherent patients. This may reflect clinical uncertainty: when blood pressure remains uncontrolled but adherence is unclear, clinicians may hesitate to intensify treatment because they are unsure whether the poor response reflects true therapeutic failure or inconsistent medication use. Conversely, if adherence is not assessed systematically, truly

adherent patients who require intensification may remain undertreated. These findings support the view that adherence and therapeutic inertia are interdependent barriers rather than separate problems in hypertension management (4–12).

Side effects were reported more frequently among non-adherent patients, although the difference was not statistically significant. This pattern is still clinically relevant because even mild adverse effects such as dizziness, fatigue, cough, ankle swelling, or increased urination may influence medication-taking behavior. Patients who are not adequately counseled may skip doses or stop treatment without consulting their physician. This highlights the need for proactive counseling at treatment initiation, including explanation of expected side effects, reassurance about mild symptoms, and clear instructions about when to seek medical advice (31,32).

The findings are particularly relevant for Pakistan, where hypertension control remains poor and barriers to adherence are common. Previous local studies have reported that limited disease knowledge, financial constraints, forgetfulness, fear of side effects, symptomatic medication use, and weak continuity of care contribute to poor antihypertensive adherence (13–25,27,28). The present study adds prospective evidence from Karachi, showing that these adherence-related challenges translate into measurable differences in early blood pressure control, dose escalation, and therapeutic inertia. In busy tertiary care settings, routine adherence screening may therefore be one of the most practical ways to improve treatment outcomes.

The study has several strengths. Its prospective design allowed assessment of treatment response after initiation of therapy rather than relying only on retrospective records. The focus on newly diagnosed patients is also important because adherence behavior is still forming during this period. In addition, the study assessed both patient-related and clinician-related barriers by examining medication adherence alongside dose escalation and therapeutic inertia. However, limitations should be acknowledged. Adherence assessment relied partly on self-report, which may overestimate actual medication use because of recall error or social desirability bias. The follow-up duration was limited to 12 weeks, so long-term persistence, cardiovascular outcomes, and sustained blood pressure control could not be evaluated. The hospital-based setting may also limit generalizability to primary care and rural populations. Finally, although adjusted analysis was planned, future studies should present multivariable models more fully to confirm whether adherence remains independently associated with control after accounting for demographic and clinical covariates.

Overall, this study indicates that early hypertension control cannot be improved by prescription alone. Effective management requires simultaneous attention to medication-taking behavior, side-effect counseling, follow-up reliability, and timely clinical intensification when indicated. Incorporating simple adherence screening into routine visits before dose escalation may help distinguish true treatment failure from irregular medication use and may reduce both unnecessary intensification and therapeutic inertia.

CONCLUSION

Medication adherence was strongly associated with early therapeutic response among newly diagnosed hypertensive patients started on first-line antihypertensive therapy in tertiary care hospitals of Karachi. Patients who adhered to treatment achieved substantially higher blood pressure control, greater systolic and diastolic blood pressure reduction, lower dose escalation, and less therapeutic inertia than non-adherent patients. These findings suggest that poor adherence can mimic treatment failure and complicate clinical decision-making, while delayed intensification may further compromise control in patients who remain hypertensive. Routine adherence assessment, patient education, side-effect counseling, and structured follow-up should therefore be integrated into early hypertension care to improve therapeutic outcomes and reduce avoidable treatment failure.

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