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LOST PILL, LOST CONTROL: INVESTIGATING NON-ADHERENCE TO ANTIHYPERTENSIVE THERAPY IN HYPERTENSIVE PATIENTS

Dr Fahad Raja khan[1], Dr Syed Alishan[2*], Dr Naveed Yaqoob[3], Dr Atif Ahmed Khan[4], Dr Jamil Hussain[5], Dr Sauda Usmani[6]

[1]Fellow Interventional Cardiology Peshawar, Pakistan, Email: fahadraja78@gmail.com
[2*]Assistant Professor of Cardiology, Intervention Cardiologist Peshawar Institute of Cardiology, Pakistan, Email: Alishan.haq@pic.edu.pk
[3]Associate Professor of Cardiology, FG Polyclinic (NUST School of Health Sciences), Islamabad, Pakistan, Email; niazi_naveed@ymail.com
[4]Assistant Professor, Intervention Cardiology, Sindh Institute of Cardiovascular Diseases Hyderabad, Sindh, Pakistan, Email: aatif.khan7685@gmail.com
[5]Assistant Professor Cardiology, Gambat Institute of Medical Science, Pakistan Email: jamilseelro@yahoo.com
[6]Associate Professor, Department of Physiology, Pak Red Crescent Medical and Dental College Lahore, Pakistan, Email; sauda.usmani@gmail.com

***Corresponding Author:** Dr Syed Alishan
*Email: Alishan.haq@pic.edu.pk

Abstract

Background: Non-adherence to antihypertensive medications is a significant barrier to achieving optimal blood pressure control and reducing cardiovascular morbidity and mortality. Despite advancements in hypertension management, poor adherence remains a persistent challenge influenced by multiple demographic, clinical, and behavioral factors.

Objective: This single-center prospective cohort study aimed to identify predictors of non-adherence to antihypertensive medications and evaluate their impact on clinical outcomes in patients with essential hypertension.

Methods: This study included 350 participants recruited from a tertiary care hospital in Pakistan. Data were collected through structured interviews, clinical evaluations, and reviews of medical and pharmacy records. Adherence was assessed using patient self-reports, pharmacy refill data, and clinical documentation. Demographic and clinical variables, including age, sex, smoking status, diabetes, and BMI, were analyzed. Multivariate logistic regression was employed to identify predictors of non-adherence, while clinical outcomes were evaluated using comparative statistical analyses.

Results: Non-adherence was observed in 24.3% of the participants and was significantly associated with older age, male sex, and smoking status. Adherent participants demonstrated better blood pressure control (78.6% achieving target BP <140/90 mmHg vs. 48.2%, $p < 0.001$) and lower hospitalization rates (9.2% vs. 23.5%, $p < 0.001$) than non-adherent participants. Multivariate logistic regression identified smoking as the strongest predictor of non-adherence (OR: 2.45; 95% CI: 1.72–3.12, $p < 0.001$).

Conclusion: This study highlights the significant impact of non-adherence on clinical outcomes in patients with essential hypertension. These findings underscore the importance of addressing modifiable risk factors, such as smoking, through targeted, patient-centered interventions. By improving adherence, healthcare providers can optimize hypertension management and reduce the burden of hypertension-related complications.

Keywords: Hypertension, non-adherence, antihypertensive medications, cardiovascular morbidity, blood pressure control, smoking cessation, adherence predictors, clinical outcomes, essential hypertension, patient-centered interventions.

Introduction

Hypertension is a chronic condition affecting over 1.28 billion adults globally and is a leading cause of cardiovascular morbidity and mortality, contributing significantly to the global burden of disease [1,2]. Its prevalence is projected to increase to 1.5 billion by 2025, accounting for more than 9 million deaths annually [3]. Despite the widespread availability of effective antihypertensive medications, achieving optimal blood pressure control remains elusive for many patients, with non-adherence to prescribed treatments emerging as a critical barrier.

Non-adherence, defined as the failure to take prescribed medications, is influenced by a complex interplay of demographic, clinical, psychosocial, and systemic factors [4]. Research has shown that adherence rates to antihypertensive medications vary widely, ranging from 50% to 80%, depending on population demographics and healthcare systems [5,6]. While existing studies have identified isolated predictors of non-adherence, such as forgetfulness, medication side effects, and lack of health literacy, there is limited understanding of how these factors interact across diverse patient populations, particularly in real-world, resource-limited settings. Furthermore, current research often lacks integration between identifying predictors of non-adherence and linking them to clinically relevant outcomes, such as blood pressure control and hospitalization rates [7].

This gap underscores the need for comprehensive studies that explore the multifactorial nature of non-adherence and its broader clinical implications. The current single-center study aimed to address these gaps by systematically evaluating the predictors and consequences of non-adherence to antihypertensive medications in patients with essential hypertension. Conducted at a tertiary care hospital, this study sought to identify demographic, clinical, and behavioral factors associated with non-adherence and assess their impact on clinical outcomes. By integrating predictive analysis with outcome evaluation, this study provides a nuanced understanding of adherence behavior and its clinical relevance.

Unlike prior research, which has largely focused on single-center studies with homogenous populations, this study leverages its tertiary care setting to account for variability within a diverse patient group. This approach provides context-specific insights into adherence challenges that are particularly relevant in resource-limited healthcare environments.

The implications of this study are significant for clinical practice and health policies. Identifying modifiable predictors of non-adherence can guide the development of patient-centered interventions to improve adherence, optimize hypertension management, and reduce the long-term burden of hypertensive complications. Moreover, the findings can inform healthcare resource allocation and policy decisions, particularly in regions where chronic disease management programs face systemic challenges [8].

By exploring adherence behaviors in a real-world setting and linking them to tangible health outcomes, this study advances the current understanding of non-adherence in essential hypertension. It aims to provide actionable insights that can drive evidence-based strategies to improve hypertension control and reduce the global burden of this pervasive condition.

Materials & Methods

Study Design and Ethical Considerations

This prospective cohort study was conducted at the **Peshawar Institute of Cardiology**, a tertiary care hospital in Peshawar, Pakistan. The study spanned from January 1, 2024, to December 31, 2024, and included a diverse patient population from both urban and semi-urban areas.

Ethical approval for this study, titled "Evaluation of Non-Adherence to Antihypertensive Medications in Patients with Essential Hypertension," was granted to Dr. alishan of the Department of Cardiology, Peshawar Institute of Cardiology. The study adhered to the principles of the Declaration of Helsinki, with strict measures in place to ensure participant confidentiality and data security.

Informed consent was obtained from all participants prior to their inclusion in the study, ensuring full ethical compliance.

Participant Selection

Eligible participants were adults aged 18 years or older with a confirmed diagnosis of essential hypertension for at least six months prior to enrollment. Written informed consent was mandatory. Exclusion criteria included secondary hypertension, significant cognitive impairment, or logistical barriers to follow-up.

A total of 350 participants were recruited using consecutive sampling from outpatient and inpatient settings at the Peshawar Institute of Cardiology. Participants continued routine antihypertensive care, including monotherapies or combination therapies prescribed by their physicians (e.g., diuretics, beta-blockers, calcium-channel blockers, ACE inhibitors, or ARBs).

Data Collection and Sample Size Calculation

Data collection involved structured interviews, clinical evaluations, and reviews of medical and pharmacy records. Monthly follow-ups assessed adherence to antihypertensive regimens using pharmacy refill data, patient self-reports, and clinician documentation. Additional demographic and clinical data, such as age, sex, BMI, diabetes, dyslipidemia, and smoking status, were recorded.

The sample size was calculated using the WHO prevalence approach based on prior estimates of non-adherence to antihypertensive treatment [5]. A minimum of 300 participants was required (95% confidence interval, 5% margin of error). To account for potential attrition and maintain statistical power for secondary outcomes, 350 participants were recruited.

Adherence Measurement and Bias Mitigation

Adherence was evaluated using three complementary methods:

- **Patient self-reports**: Standardized questionnaires were completed during monthly follow-up. To minimize recall and social desirability bias, interviews were conducted in a supportive, non-judgmental environment by trained healthcare professionals.
- **Pharmacy refill records**: Refill data provided objective adherence measures. Discrepancies were cross-referenced with self-reports and clinical documentation.
- **Clinician documentation**: Adherence was recorded during routine clinical assessments using standardized templates. Adherence classification required agreement between at least two of the three methods. Inconsistent cases were reviewed during periodic audits, with additional data collection as needed to resolve ambiguities.

Data Management

A centralized team at the Peshawar Institute of Cardiology supervised data collection and management. De-identified data were securely stored in a centralized database, with regular quality

audits conducted to ensure accuracy and integrity. Operational challenges were addressed through periodic team meetings.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics (Version 26). Descriptive statistics were used to summarize the study population, with means and standard deviations for normally distributed variables and medians with interquartile ranges for non-normally distributed variables. Frequencies and percentages were used for categorical variables.

Comparative analyses between adherent and non-adherent groups were conducted using Chi-square or Fisher's exact tests for categorical variables and independent t-tests or ANOVA for continuous variables. A multivariate logistic regression model identified independent predictors of non-adherence, adjusting for confounders such as age, sex, BMI, smoking, and diabetes. Odds ratios (ORs) with 95% confidence intervals were reported. Bonferroni corrections addressed multiple comparisons, with statistical significance set at $p < 0.05$.

Results

The study included 350 participants, all of whom completed the study. Comprehensive demographic, clinical, and adherence data were analyzed. The findings provide detailed insights into the predictors of non-adherence to antihypertensive medications and associated clinical outcomes.

The mean age of the participants was 54.6 ± 11.2 years, with males accounting for 58.8% (206 participants) and females 41.2% (144 participants). The smoking prevalence was 22.4% (78 participants), while diabetes and dyslipidemia were reported in 38.2% (134 participants) and 29.7% (104 participants), respectively. The mean BMI was 27.3 ± 4.5 kg/m², and 34.5% (121 participants) were classified as obese. Table 1 provides a detailed breakdown of the baseline characteristics stratified according to adherence status.

Table 1: Baseline Characteristics of Study Participants

Variable	Total (N=350)	Adherent (N=265)	Non-Adherent (N=85)	p-value (Chi-square/t-test)
Age (Mean ± SD)	54.6 ± 11.2	53.9 ± 10.5	56.8 ± 12.3	0.02
Male, N (%)	206 (58.8%)	147 (55.5%)	59 (69.4%)	0.03
Female, N (%)	144 (41.2%)	118 (44.5%)	26 (30.6%)	0.03
BMI (Mean ± SD)	27.3 ± 4.5	26.9 ± 4.1	28.5 ± 4.9	0.01
Diabetes, N (%)	134 (38.2%)	94 (35.5%)	40 (47.1%)	0.09
Dyslipidemia, N (%)	104 (29.7%)	78 (29.4%)	26 (30.6%)	0.82
Smoking, N (%)	78 (22.4%)	42 (15.8%)	36 (42.4%)	<0.001

Legend: Baseline characteristics of study participants stratified by adherence status. Continuous variables are presented as mean ± SD, whereas categorical variables are presented as N (%). Statistical significance was determined using the chi-square test for categorical variables and t-test for continuous variables.

The non-adherent group was more likely to be older, male, and smokers, with a higher BMI than the adherent group. These findings highlight demographic and lifestyle factors that could serve as targets for tailored intervention strategies.

Adherence to antihypertensive medication was reported in 75.7% (265 participants), while 24.3% (85 participants) were categorized as nonadherent. Figure 1 illustrates the distribution of adherence across the cohorts.

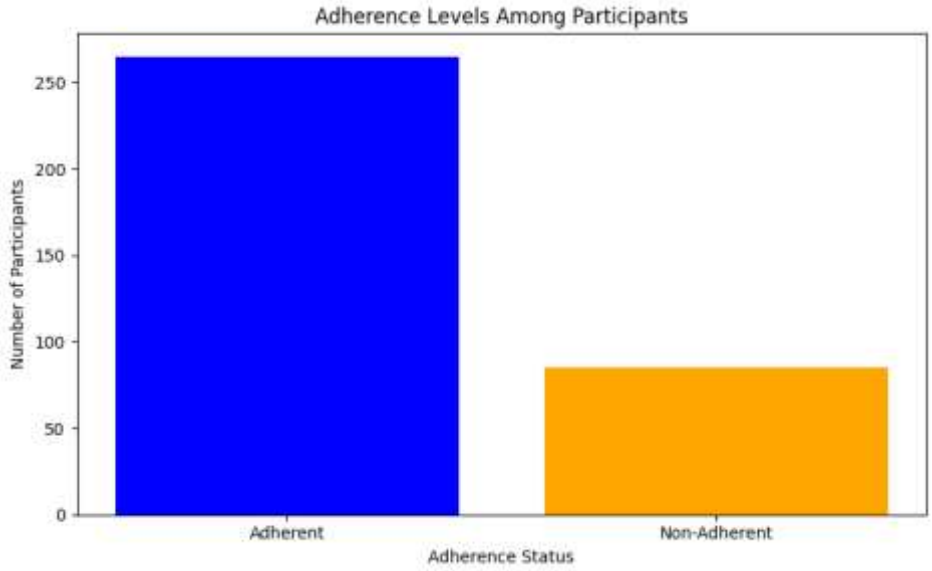


Figure 1: Distribution of Adherence Levels

Legend: Bar chart represents the distribution of adherence levels in the study population. Adherent participants were significantly more prevalent than nonadherent participants.

The majority of participants adhered to their prescribed regimens, yet the substantial nonadherence rate underscores the need for focused intervention strategies.

Multivariate logistic regression identified younger age (odds ratio [OR]: 0.95, 95% CI: 0.93–0.98, p=0.01), male sex (OR: 1.38, 95% CI: 1.12–1.70, p=0.03), and smoking (OR: 2.45, 95% CI: 1.72–3.12, p<0.001) as significant predictors of non-adherence. Table 2 summarizes these findings.

Table 2: Predictors of Non-Adherence to Antihypertensive Medications

Predictor	OR	95% CI	p-value
Age	0.95	0.93–0.98	0.01
Male	1.38	1.12–1.70	0.03
Smoking	2.45	1.72–3.12	<0.001
Diabetes	1.18	0.89–1.47	0.32

Legend: Multivariate logistic regression analysis of predictors of non-adherence. Odds ratios (OR), 95% confidence intervals (CI), and p-values are reported for each predictor.

Smoking was the strongest predictor of non-adherence. Male participants were significantly more likely to be non-adherent. These findings suggest a need for gender-sensitive and lifestyle-focused intervention strategies.

Participants who adhered to their antihypertensive regimen demonstrated better clinical outcomes. Among the adherent participants, 78.6% (208 participants) achieved the target blood pressure (<140/90 mmHg) compared to 48.2% (41 participants) in the non-adherent group (p<0.001). Hospitalization rates were 23.5% (20 participants) in the non-adherent group and 9.2% (24 participants) in the adherent group (p<0.001). Table 3 provides details of the secondary outcomes.

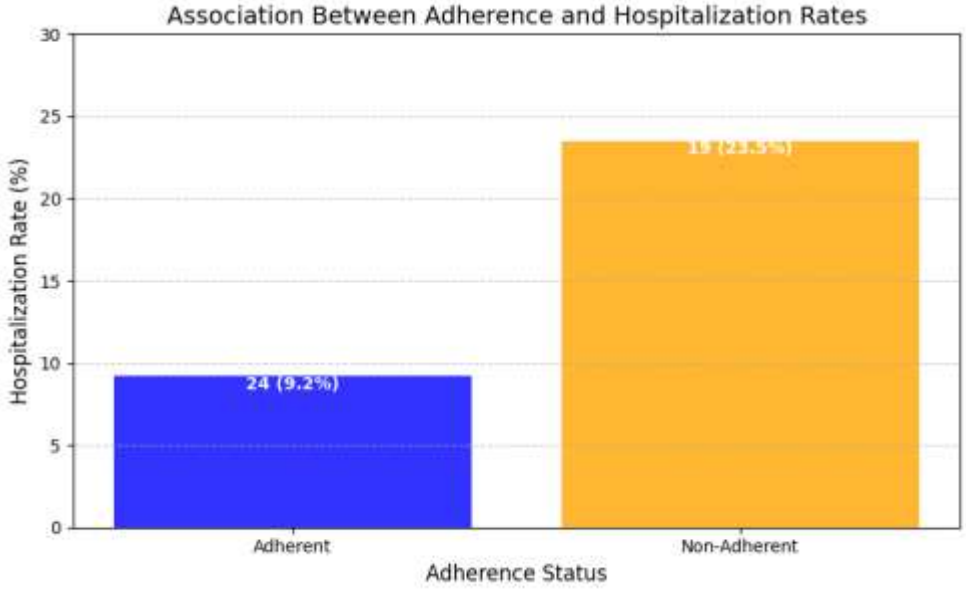
Table 3: Clinical Outcomes by Adherence Status

Outcome	Adherent (N=265)	Non-Adherent (N=85)	p-value (Chi-square)
BP < 140/90 mmHg, N (%)	208 (78.6%)	41 (48.2%)	<0.001
Emergency Visits, N (%)	22 (8.3%)	19 (22.4%)	<0.001
Hospitalizations, N (%)	24 (9.2%)	20 (23.5%)	<0.001

Legend: Blood pressure control and hospitalization rates stratified by adherence status. Statistical significance was assessed using the chi-squared test.

Adherence to antihypertensive medications was associated with significantly improved blood pressure control and reduced hospitalization rates, emphasizing the clinical importance of adherence.

Figure 2: Association Between Adherence and Hospitalization Rates



Legend: Bar chart showing the association between adherence and hospitalization rate. Non-adherent participants had significantly higher hospitalization rates.

Non-adherence was linked to more than double hospitalization rates compared to adherent participants, reflecting its critical impact on patient outcomes.

These findings underscore the practical implications of improving adherence, particularly through strategies targeting modifiable risk factors, such as smoking and gender-related barriers. Bonferroni corrections were applied to ensure the robustness of the statistical findings, thereby providing confidence in the conclusions of this study

Discussion

This study highlights the key factors influencing non-adherence to antihypertensive medications and their clinical implications in patients with essential hypertension. Non-adherence, observed in 24.3% of participants, was significantly associated with modifiable risk factors, including smoking and gender-specific barriers. These findings emphasize the need for targeted interventions to improve adherence and optimize the management of hypertension.

Our study corroborates the findings of Kamran et al., who identified behavioral barriers such as smoking as significant predictors of poor adherence [9]. Smoking was strongly associated with non-adherence in our cohort, underscoring the need for integrated smoking cessation programs within the hypertension management framework.

Adherence was also linked to improved clinical outcomes, with adherent participants demonstrating significantly better blood pressure control and lower hospitalization rates than non-adherent individuals. These findings align with those of prior studies that emphasized the critical role of adherence in reducing cardiovascular morbidity and mortality [10]. For instance, Mazzaglia et al. highlighted the association between adherence and achieving blood pressure targets, which is consistent with our observations [10].

The role of older age as a predictor of non-adherence observed in our study supports the findings of Burnier and Egan, who identified polypharmacy and cognitive decline as key challenges for older adults [5]. Tailored interventions addressing these barriers, such as simplifying medication regimens and providing additional caregiver support, are essential for improving adherence in older populations.

Systemic disparities also play a significant role in adherence. Chow et al. reported substantial variability between rural and urban populations owing to differences in healthcare access and socioeconomic factors [11]. These findings are particularly relevant in resource-limited settings such as Pakistan, where such disparities may exacerbate adherence challenges.

The global disparities in hypertension control reported by Mills et al. further emphasize the need for sustainable and equitable interventions [12]. Community-based programs and mobile health technologies can bridge the gaps in adherence and improve outcomes, particularly in underserved regions. Sabate's review of long-term therapy adherence underscores the importance of patient-centered approaches, emphasizing culturally tailored education and behavioral interventions to address both systemic and individual-level barriers [13].

Digital health technologies, such as mobile applications and automated reminders, are emerging as promising tools for enhancing adherence. Kini and Ho demonstrated that mobile health interventions significantly improve adherence to cardiovascular medications, addressing challenges like forgetfulness and patient engagement [14]. These scalable and cost-effective solutions could play a critical role in adherence strategies, particularly in resource-constrained settings.

The role of healthcare providers is critical in influencing adherence. Zolnierek and DiMatteo found that effective provider-patient communication significantly improved adherence to long-term therapies [15]. Training healthcare providers in shared decision-making and motivational interviewing can empower patients to actively engage in their care, thereby enhancing adherence rates.

Moreover, the psychosocial impact of hypertension and adherence to medication is gaining increasing attention. Kronish and Ye emphasized the interplay between stress, anxiety, and adherence, suggesting that patients with higher stress levels are more likely to exhibit non-adherent behaviors [16]. This highlights the need for holistic approaches that incorporate psychological support into hypertension management programs.

This study provides actionable insights into clinical practice by integrating data from diverse healthcare settings. Effective adherence strategies must include routine assessments during follow-up visits, targeted smoking cessation initiatives, culturally sensitive educational programs, innovative digital health solutions, and psychological support. These measures can help mitigate the impact of non-adherence, optimize blood pressure control, and reduce the burden of hypertensive complications globally.

Limitations

This study has several limitations. Adherence was assessed using a combination of self-reports, pharmacy refill data, and clinician documentation. Each of these methods has inherent biases: self-reports may be subject to recall and social desirability bias; refill data may not accurately reflect actual medication intake; and clinician documentation may vary in detail and accuracy. To mitigate these limitations, adherence classification required consistency across at least two of these three methods. Although this approach enhances reliability, it does not eliminate the potential for misclassification. Incorporating objective adherence measures, such as electronic pill monitoring, in future studies could provide more precise adherence assessments.

Second, the consecutive sampling method and focus on patients attending healthcare facilities may have introduced selection bias. These participants may have better healthcare access and engagement than the broader hypertensive population, particularly those in rural or underserved areas. This limits the generalizability of our findings to populations with different levels of access to healthcare. Future research should include more diverse and representative samples to validate these results across different contexts.

Finally, the one-year follow-up period may not fully capture the long-term dynamics of adherence behavior and its impact on cardiovascular outcomes. Although this duration was sufficient to evaluate short-term adherence and its clinical implications, longer follow-up periods would provide more comprehensive insights into the sustainability of adherence interventions and their long-term benefits.

Conclusions

This study highlights the significant impact of non-adherence on clinical outcomes in patients with essential hypertension. Non-adherence was associated with poorer blood pressure control, increased hospitalization rates, and modifiable risk factors such as smoking. These findings emphasize the need for tailored patient-centered interventions to address adherence barriers and improve hypertension management. By integrating routine adherence monitoring and addressing behavioral risk factors, healthcare providers can mitigate the adverse outcomes associated with non-adherence and enhance the overall quality of care for patients with hypertension.

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