FACTORS AFFECTING ADHERENCE TO MEDICATIONS IN HYPERTENSIVE PATIENTS VISITING A TEACHING HOSPITAL IN KHYBER PAKHTUNKHWA

Yasmin Akhtar, Muhammad Abdur Rahman Afridi✉, Zafar Ali, Atta Muhammad Khan

Department of Medicine, Lady Reading Hospital Peshawar- Pakistan

Address for correspondence:
Muhammad Abdur Rahman Afridi
Department of Medicine, Lady Reading Hospital Peshawar- Pakistan

E-mail:
rahmanafridi@hotmail.com

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ABSTRACT

Objective: To determine various factors affecting adherence to antihypertensive medications.

Methodology: An observational descriptive study conducted in Medical Out-Patient Department of Lady Reading Hospital Peshawar from June 2019 to October 2019. A total of 250 adult hypertensive patients of both genders were included. Adherence to medication was assessed using 'proportion of days covered' method. A score of ≥ 80% was considered as 'good adherence'. Four factors affecting adherence, were specifically studied: 'Asymptomatic state' of the patient; 'Affordability of medications; influence of the 'Local GP'; and 'Adverse effects' of the drugs. SPSS version 21 used for data analysis; correlation carried out; chi square (χ^2) p≤0.05 considered statistically significant.

Results: Out of 250 patients, 67(26.8%) were males and 183(73.2%) females. Mean age was 56.13 years ±10.30 SD. Overall, 108(43.2%) patients had good adherence and 142(56.8%) had poor adherence ($\chi^2(4)=250.0$, r(4)=0.89, p=0.001). The most common factor affecting adherence was the 'asymptomatic' state (56.3%, p=0.001); followed by 'non-affordability' (21.1%, p=0.001); 'Local GP' influence (14.8%, p=0.001); and drugs' adverse effects (7.8%, p=0.003). Patients taking 'combination' of drugs, ARBs and BBs had 60%, 58% and 18% adherence, respectively ($\chi^2(4)=35.41$, r(4)=0.50, p=0.018).

Conclusion: Factors associated with poor adherence to medications include 'asymptomatic state' of the patient, 'non-affordability' of drugs, 'influence of local practitioner' and 'adverse effects' of drugs; all significantly inversely correlated with adherence. Economic status, duration of hypertension and drug groups also significantly correlated with adherence.

Keywords: Hypertension; Drug Adherence; Factors; Antihypertensive Medications.

INTRODUCTION

Hypertension is a major public health problem worldwide, affecting 31.1% (1.39 billion) people.[1] A meta-analysis[2] revealed its prevalence between 4% to 78%, which increases with advancing age. It is a silent killer; most of the patients remain asymptomatic. Another systematic review revealed that a 10 mm Hg reduction in Blood Pressure (BP) leads to a 13% reduction in all-cause mortality and significantly reduce the risk of cerebrovascular/cardiovascular syndromes.[3] 'Adherence' to medication is defined as the extent to which a patient takes medications by prescription and expressed as the percentage of the prescribed treatment taken.[4] Poor adherence to antihypertensive medications is a major contributor to uncontrolled hypertension, resulting in increased morbidity and mortality.[5] Choi et al reported around 20% non-adherence in Korea.[6] Recently published meta-analysis reported comparatively higher adherence of 83.87% in western countries including Europe and US than elsewhere (54.30%).[7] Similarly, wide variations in adherence were reported around the globe; in Russia[8], adherence varied from 11 to 44%, whereas a large Italian study[9] reported 19.3% adherence. An adherence of 46% reported in Egypt[10], 49.3% in Iran[11], and 55.9% in the Middle-East.[12] In China, 36.4% adherence by Shi et al[13] and 28% by Pan et al[14] reported in their studies. In Pakistan, Saqlain et al[15] reported adherence of 39%, Ali et al 50% from Karachi[16] and Mahmood et al 38.3% from Islamabad.[17] The 'Asymptomatic' factor associated with poor adherence was reported in 25% non-adherent patients from Islamabad[17], Indonesia[18] and India.[19] Similarly drugs adverse effects leading to poor adherence were reported in 11% patients in Isalamabad[17] and 19% in an Indian study.[20]

Adherence to medications is affected by a variety of

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different factors, including personal, behavioral, cultural, ethnic, socio-economical and drug related factors. Hence there are wide variations in adherence to medications in our community. Proper attention and correction of these barriers is of paramount importance in improving drug adherence.

We conducted a study in 2018 regarding adherence of our local population to anti-hypertensive medications and found that most of our patients were non-adherent.[21] This led us to further investigate the factors predicting non-adherence in our patients. The aim was to assess different factors affecting adherence in hypertensive patients in a teaching hospital in Khyber Pakhtunkhwa, having different cultural and ethnic norms. It may further help in the awareness of the problem at the patient level and in devising better management plan by the policy makers. The objective of this study was, therefore, to determine various factors affecting adherence to antihypertensive drugs. This study will provide an opportunity to address the underlying barriers to medication adherence and will highlight the need for the development of interventions and policies which will improve health education and patients' quality of life.

METHODOLOGY

This descriptive observational study was conducted in the Medical Outpatient Department of Lady Reading Hospital, Medical Teaching Institution Peshawar, from June 2019 to October 2019. A total of 250 adult patients of essential hypertension, 20 years old and above, of both genders, consenting for the study, were included. Sample size was calculated using 95% Confidence level, 20% anticipated population proportion[6] and 5% margin of error. Patients were recruited through consecutive sampling technique. Exclusion criteria: unstable patients with heart failure, encephalopathy/confusion, acute coronary syndrome, those with secondary hypertension and those who declined consent were excluded to control the confounders.

A patient was considered hypertensive if his/her resting blood pressure in comfortable environment was more than 140/90; or taking antihypertensive medications for at least 3 months. 'Adherence' to medication was defined as the extent to which the patients act in accordance with the prescribed dose and frequency of medications. Adherence was calculated as the 'proportion of days covered' (PDC) by the patient taking medications. The number of days patient took his/her medications in the last thirty days were determined and divided by the total period of 30 days and expressed as percentage of adherence. A score of ≥80% was considered as "good adherence" and score <80% as "poor adherence".

We specifically studied four different factors inversely correlated with drug adherence: the 'asymptomatic' state, when the patient has no symptoms and does not feel the need to consult a physician; the 'non-affordability' when the patient cannot continue regular purchase of antihypertensive drugs; the 'local GP' is a local doctor or any unqualified general practitioner who influences the patient to stop/change his medication without indications; and the 'adverse effects' of drugs that compel the patient to stop the medications, like dizziness, dyspnea, cough, pedal edema, and palpitations etc.

The study was conducted after the approval of Institutional Ethical Review Board. Written informed consent was taken from the participants of the study. Patients' history was obtained regarding antihypertensive medications; dose, cost, adherence and side effects. Any reason(s) of the non-adherence were asked and recorded as 'factors'. Economically, patients were divided into 'Satisfactory' group having own house with adjusted monthly income of 100,000 or above; and 'Poor' living in rented house with adjusted monthly income of <100,000.

After a 10 minutes rest, BP recorded in sitting position with standard sphygmomanometer having appropriate adult size brachial cuff and Littmann® stethoscope. Three readings of BP were obtained and the last one recorded. Physical examination of patients carried out by the consultant physician and findings recorded. Relevant investigations were done; including ECG, FBC, serum sugar, renal profile, lipid profile and urinalysis. Abdominal ultrasound, Chest X-Ray and Echocardiography also advised.

Data analyzed using IBM® SPSS® Statistics version 21. Mean ± standard deviations (SD) calculated for numerical variables like age; frequency and percentages for categorical variables like gender, adherence and factors affecting adherence. Chi square (χ^2) test was applied for association of factors with adherence; Pearson's correlation (r) determined for the strength of correlation. A p value ≤0.05 was considered statistically significant. Results of the study presented in tables and compared with local, regional and international studies.

RESULTS

A total of 250 patients were included in the study; age of the patients ranged from 20 to 80 years (mean 56.13 years ±10.30 SD). Out of 250 patients, 67(26.8%) were males and 183(73.2%) females. Among the females, 77(42%) had good adherence and 31(46%) men had good adherence ($\chi^2(1)=0.35$, $r(1)=0.037$, $p=0.56$). Overall, 108(43.2%) patients had good adherence and 142(56.8%) had poor adherence, as shown in Table 1. More than half (n=129, 51.6%) were in middle age group; however, the difference was not significant ($\chi^2(2)=2.98$, $r(2)=0.079$, $p=0.23$), as shown in Table 2. Among the 211 economically 'satisfactory' patients, 49% were adherent and 51% non-adherent. Among

Table 1: Gender-wise adherence to medications (n=250)

Gender	Adherence to medications		Total	Chi-Square P Value
	Good adherence	Poor Adherence		
Male	31 (46.3%)	36 (53.7%)	67 (26.8%)	χ^2(df1)=0.35, p=0.56
Female	77 (42.1%)	106 (57.9)	183 (73.2%)	
Total	108 (43.2%)	142 (56.8%)	250 (100%)	

Table 2: Descriptive statistics of hypertensive patients (n=250)

Characteristics		No. of Patients (%)	P Value
Gender	Female	183 (73.2%)	P=0.56
	Male	67 (26.8%)	
Adherence to Medication	Good Adherence	108 (43.2%)	P=0.001**
	Poor Adherence	142 (56.8%)	
Age groups	Less than 40 years	20 (8.0%)	P=0.23
	41 to 60 years	129 (51.6%)	
	61 & above	101 (40.4%)	
Economic Status	Poor	39 (15.6%)	P=0.001**
	Satisfactory	211 (84.4%)	
Education of Patients	Nil to Primary	195 (78.0%)	P=0.108
	Matric	48 (19.2%)	
	Graduate	7 (2.8%)	
Duration of Hypertension	Less than 5 years	74 (29.6%)	P=0.035**
	5 to 10 years	156 (62.4%)	
	More than 10 years	20 (8.0%)	
Drug Groups	ARBs*	36 (14.4%)	P=0.018**
	ACEIs*	5 (2.0%)	
	Beta Blockers	77 (30.8%)	
	CCBs*	40 (16.0%)	
	Combinations of Drugs	92 (36.8%)	

*ARBs Angiotensin II Receptor Blockers
*ACEIs Angiotensin Converting Enzyme Inhibitors
*CCBs Calcium Channel Blockers
**Statistically Significant Correlation

Table 3: Factors associated with poor adherence to medications (n=142).

Factors	Frequency (%)	Correlation coefficient	Chi-square (χ^2) value	df	P value
Asymptomatic state	80/142 (56.3%)	-0.598**	89.48	1	p=0.001
Non Affordability	30/142 (21.1%)	-0.322**	25.93	1	p=0.001
Local GP* influence	21/142 (14.8%)	-0.264**	17.45	1	p=0.001
Side effects of drugs	11/142 (7.8%)	-0.187**	8.75	1	p=0.003

Note **Correlation is significant at the 0.01 level (2-tailed).
*GP General practitioner
*df Degree of freedom

the 39 'poor' patients, 10% were adherent and 90% had poor adherence (χ^2(1)=20.44, r(1)=0.286, p=0.001). Majority of the patients (n=195, 78%) were uneducated (χ^2(2)=5.38, r(2)=0.102, p=0.108). Among 250 patients, 157(63%) had comorbidity with hypertension; dyslipidemia was the most frequent comorbidity in 59(23.6%) patients, Diabetes Mellitus in 13.6% patients (χ^2 (9)=2.25, r(9)=0.018, p=0.99). Majority (62.4%) of patients had hypertension for 5-10 years (χ^2(2)=6.72, r(2)=0.159, p=0.035). Patients used different classes of antihypertensive drugs and had different rates of adherence; those on 'combination' of drugs had 60%, ARBs 58%, CCBs 40% and Beta Blockers had 18% good adherence (χ^2(4)=35.41, r(4)=0.50, p=0.018).

Among the poorly adherent 142 patients, the most common factor affecting adherence was the 'asymptomatic' state of hypertension in 80(56.3%) patients (χ^2(1)=89.48, r(1)=-0.598, p=0.001), followed by 'non-affordability' in 21.1% patients (χ^2 (1)=25.93, r(1)=-0.322, p=0.001), as shown in Table 3.

DISCUSSION

Factors associated with non-adherence vary from country to country and society to society.[4,6,7,18,22] Patients in our region of the country have distinct characteristics which determine their views, understanding and response to the disease and its management options. Illiteracy, poverty, lack of proper facility, abundance of quackery and alternate treatment options are some of the predictors of poor adherence to medications in our region.[15-17] Non-affordability, influence of the local practitioner and adverse effects of drugs[18] also contribute to poor adherence.

The present study revealed that around 57% patients were non-adherent. Three quarters of the study population were women; however the difference in adherence between genders was not significant (p=0.56). Similarly, most of the patients were middle aged and elderly but there was no statistical difference of adherence in different age groups (p=0.23). Our study results are similar to some other studies done in Pakistan; as Saqlain et al[15] reported non-adherence of 61%, no correlation of adherence with gender, age and education level, similar to our study

results; also 50% by Ali et al[16] from Karachi and 61.7% by Mahmood et al[17] from Islamabad. Similar findings of 50.7% poor adherence reported in Iranian patients.[11] In Egypt, 46% were adherent; young age and less number of pills predicted good adherence.[10] Different studies from China corroborated our results; poor adherence in 63.6% by Shi et al[13] and in 72% by Pan et al.[14] Conversely, in a middle-eastern study[12] from Jordan and Lebanon, 55.9% were adherent, where most of the patients were elderly and newly diagnosed. In Korea[6], 81.7% adherence reported where increasing age predicted adherence. Around 83% adherence reported in Taiwan[22] and 65% in China[23]; where old age positively correlated with adherence. In contrast to our findings, however, a US meta-analysis[7] reported 69% adherence where older age, mono-therapy or single pill poly-therapy were associated with good adherence. In Russia[8], adherence varied from 11 to 44%. Extremely lower adherence of 11% reported from Indonesia[18], where 'asymptomatic' state and preference of using alternative traditional medicines predicted adherence. Conflicting results have been reported from Italy; in a large study[9] of 140537 patients, 19.3% had good adherence; old age, female gender and poly-pharmacy associated with poor adherence. In another Italian study[24], men had better adherence. However, in an Italian systematic review of 82 studies, no significant gender difference in adherence was observed.[25]

Although most of our patients were not educated but there was no significant difference in adherence and levels of education (p=0.108). Similarly, presence of comorbidity did not affect adherence significantly (p=0.99). Conversely, Mahmood et al[17] found significant correlation between adherence, education level and comorbidity, as also seen in Iranian patients[11]; whereas absence of comorbidity, higher education and income predicted good adherence in Egyptian study[10] as well as in Russian patients.[8] However, in contrast, comorbidity predicted good adherence in Korea.[6] Reasons for variability of findings in these studies may be attributed to the differences in sample sizes, different tools of adherence measurements, data collection techniques, levels of health care systems, literacy rates, culture and ethnicity etc.

We studied four different factors which inversely correlated with drug adherence: the 'asymptomatic' state of hypertensive patient; the 'non-affordability' of antihypertensive drugs; the influence of 'local practitioner'; and the 'adverse effects' of drugs. The 'Asymptomatic' patient, not feeling the need of taking medications, has also been reported in 25% non-adherent patients from Islamabad[17], Indonesia[18] and India.[19] Hypertension is a silent killer; the patient usually remains asymptomatic. Such patients do not realize the need to consult a physician because of the absence of symptoms. Even if they are informed about their hypertension on routine checkup, they would give baseless explanations and lame excuses. They usually end up in emergency room with acute cerebrovascular/cardiovascular events. Around 56% of the non-adherent patients in present study belonged to this 'asymptomatic' group, which significantly correlated with poor adherence (p=0.001).

The 'non-affordability' of drugs was another significantly correlated factor, observed in 21% of non-adherent patients (p=0.001). Poor economic status of the patients inversely correlated with adherence. This is in conformity with other studies from Pakistan (59%)[17] and Egypt (69%).[10] Influence of the 'local practitioner' also inversely correlated with adherence. This is also in conformity with another study from Indonesia with low adherence of 11% only[18]; however, this factor has not been reported much. The local practitioner, mostly in rural and occasionally in urban areas, is usually an unqualified person who even cannot check BP properly. He, often, misguides the patient about medications or even stops it altogether. The patient strictly follows his advice and becomes non-adherent. Around 15% of the poorly adherent patients in our study belonged to this group of negatively influenced by the local GP. The correlation was statistically significant (p=0.001). Around 8% of the poorly adherent patients reported 'adverse effects' of drugs as a cause of non-adherence (p=0.003). These included dizziness, dyspnea, cough, ankles swelling, frequent micturition, etc. Similar findings reported in 11% patients in Isalamabad[17] and in 19% Indian patients.[20]

Patients with prolong duration of hypertension had good adherence to their medication with significant correlation (p=0.035). This is consistent with findings in Korean[6], Chinese studies (59%)[13], (51%)[14], (52%)[23]; and US meta-analysis[7], where duration of disease was associated with good adherence. Patients on ARBs and Combinations had good adherence while those on BBs and CCBs had poor adherence. The difference was statistically significant (p=0.018). This is corroborated by findings of other studies from Korea[6], US[7] and Russia.[8]

The difference may be attributed to the differences in sample size of the studies, the tools and methods used for assessment of adherence, health education, support from the health system and other factors. The recent guidelines of the American college of Cardiology/American Heart Association and European Society of Cardiology emphasize the importance of adherence to medications in cardiovascular disorders.[4]

The results of this study can be implicated both for health care providers and policy makers. The need to devise and implement various interventions to improve medication adherence is obvious. Factors affecting adherence to medications have been identified; some of which can be modified to achieve

the goal of better adherence and thus reduce the morbidity and mortality. Effective strategies include patient and family education; awareness about the disease and its complications; importance of regular intake of medications; clarifying misconception of patients; educating the local practitioner, discouraging/regulating quackery and self-medication; simplifying prescription/dosage regimen; and de-prescribing poly-pharmacy etc. Improved adherence resulting in better clinical outcome would ultimately result in reduced health care costs.

Study conducted in outpatient department of single tertiary care hospital where the results may not be generalizable to other areas. Preferably, a large scale community or multicenter study is advised and appropriate for generalization of the study findings.

CONCLUSION

Adherence to antihypertensive medication was poor in majority of patients in this study. Factors associated with non-adherence include 'asymptomatic' state of the patients, 'non-affordability' of drugs, influence of 'local practitioner' and 'adverse effects' of drugs; all significantly inversely correlated with adherence. Economic status, duration of hypertension and drug groups also significantly correlated with adherence. Gender, age, education level and presence of comorbidity did not affect medication adherence significantly.

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Author's Contribution

YA conceived the idea, designed the study, and contributed to the literature search. MARA, ZA and AMK contributed to the collection of data, statistical analysis and reviewed the overall manuscript, and gave their final approval.Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest

Authors declared no conflict of interest

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None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.