COMMON RISK FACTORS OF NON-ADHERENCE ANTIHYPERTENSIVE MEDICATION AND ITS DETERMINANTS AMONG PATIENTS

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ARTICLE INFO	ABSTRACT	ORIGINAL RESEARCH ARTICLE

Background: Adherence to pharmacological treatment for hypertension is considered a key factor in guaranteeing successful therapy outcomes. Non-adherence to antihypertensive therapy can be determined by demographic, drug related, disease related and setting related factors. **Objective:** To assess the common risk factors of non-adherence antihypertensive medication and its determinants among patients. **Methods:** A prospective cross-sectional study was conducted at Cardiology Dept. Islami Bank Community Hospital Faridpur and 250 Bedded General Hospital, Gopalgonj, Bangladesh July to December 2021. A total of 120 patients were interviewed with a structured standard questionnaire and patient medication charts were reviewed. The questionnaire contained of demographic questions and characteristics of hypertension and its therapy. The data collected were cleaned, entered and analyzed using Statistical Package for Social Science (SPSS) version 19 for windows with 95% confidence interval and P value <0.05. **Results:** Total 120 study participants were interviewed of which 74 (61.7%) were female and 46 (38.3%) were males. The mean age of respondents was 54.7±12.7 years. Forty-five (37.5%) of the participants were at the age of above 60 years and 81 (67.5%) were illiterate. A large proportion of the subjects, 85 (70.8%), were married and 40 (33.3%) of the total study population were unemployed while 30 (25%) were housewives. Around one fourth (25%) of the study participants were found to be non-adherent to their treatment. Family support on adherence (AOR = 0.170, 95%CI = 0.030-0.905), spot blood pressure (AOR = 0.052, 95%, CI =0.003-0.242), place of patient residence (AOR=0.184, 95%CI =0.024-0.597) and hypertension related complications (AOR= 21.737, 95%CI =1.568-418.428) were found significantly and strongly associated with treatment non-adherence. **Conclusions:** In conclusion, this study were

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completely non-adherent and only around half of them were adherent to their medications. The absences of family support, being at the prehypertension class of blood pressure, hypertensive heart disease were shown to decrease adherence to antihypertensive medications. Therefore, health care professionals should be adequately trained and resourced to offer proper counseling to hypertensive patients on their medication and disease conditions.

INTRODUCTION

Hypertension is an overwhelming global challenge which ranks third as a cause of disability-adjusted life-years. It affects close to one billion individuals worldwide. The number is continuously growing due to the progressive aging of the population [1]. Untreated or sub optimally treated hypertension could lead to increased risk of morbidity and mortality due to cardiovascular, cerebrovascular, or renal diseases. The WHO reported that suboptimal blood pressure (>115 mmHg systolic blood pressure) was the cause of 62% of cerebrovascular diseases and 49% of ischemic heart diseases [2]. It is well known that high blood pressure increases the risk of ischemic heart disease 3- to 4-fold and of overall cardiovascular risk by 2- to 3-fold. The incidence of stroke increases approximately 3-fold in patients with borderline hypertension and approximately 8-fold in those with definite hypertension. It has been estimated that 40% of cases of acute myocardial infarction or stroke were attributable to hypertension [3]. Adherence is a term that is often inappropriately used interchangeably with compliance. However, the term adherence is preferred over compliance because it implies an interactive, collaborative relationship between the patient and the care-giver [4]. Compliance is defined as the extent to which a person's medication-taking behavior coincides with the healthcare providers' medical advice [5]. The word compliance originated from a practitioner - cantered paradigm and implies an authoritarian model that places the patient in a passive role

[6]. Non-adherence can take many different forms. Patients can fail to fill or refill a prescription, take an incorrect dose, take a medication at the wrong time, forget to take doses, or stop therapy too soon. Non-adherence can also involve taking foods or other medications that alter bioavailability or alter metabolism rates [7]. From the available research in the field of hypertension treatment, factors influencing hypertensive patients' adherence behavior to antihypertensive medication include patient related factors (e.g., socio-demographic factors and the individual's knowledge and skills), health system-related factors (such as treatment cost and patients' resources), and provider-related factors (such as patient-provider relationships and communication) [8, 9]. Medication non-adherence is an enormous burden to the world's health care system. For example, half of the 3.2 billion annual prescriptions dispensed in the United States were not taken as prescribed and numerous studies have shown that patients with chronic conditions adhere only to 50-60 percent of medications as prescribed, despite evidence that medication therapy improves life expectancy and quality of life. Unfortunately, poor adherence to medications is widespread especially in the treatment of chronic conditions such as hypertension leading to poor health outcomes and huge medical spending on drug-related morbidity. Only 20 to 80% of patients receiving treatment for hypertension in real life situations are considered to be "good compliers". The situation is reported to be worse in developing countries due to poor

accessibility to medications and health care services. The asymptomatic nature of the condition intensifies the problem of non-adherence in hypertension. Studies also have shown that patients' attitude about hypertension, their reliance on their medications and whether or not their lifestyle has been modified greatly affect their adherence to antihypertensive therapy. Hence, in view of the consequences of non-adherence to anti-hypertensive medicines and high cost of standard hypertension medication non-adherence and its determinants among patients on follow up.

MATERIALS AND METHODS

A prospective cross-sectional study was conducted at Cardiology Dept. Islami Bank Community Hospital Faridpur and 250 Bedded General Hospital, Gopalgonj, Bangladesh July to December 2021. One hundred twenty (120) patients were included. All people who were diagnosed with hypertension and were on follow up were considered as source population and all adult hypertensive patients attending the facility on out-patient basis and on medication for not less than six months were used for the study as a study population. All hypertensive patients who had follow up and fulfilling the inclusion/exclusion criteria were included in the study.

Hypertensive patients who were on follow up as outpatients, were at age of 18 or greater, and had been on medication for at least 6 months were included in the study. Hypertensive patients who were admitted to inpatient wards, pregnancy related hypertensive patients, or patients diagnosed hypertensive but not on antihypertensive were excluded from this study.

Demographic variables (age, sex, marital status, educational status, financial support, social support, occupation, residence, family history), disease related variables (stage of hypertension, complications), drug related variables (duration of therapy, number of antihypertensive drugs) and setup related variables (distance from house of patient, frequency of follow up visits) were considered as independent variables & non-adherence to antihypertensive was considered as dependent variable.

A structured questionnaire which contains questions descriptive of demographic status of patient and questions assessing the characteristics of hypertension and antihypertensive treatment were used as a data collection instrument. The self-reported measure of medication taking was developed from a previously validated four item scale and supplemented with additional items addressing the circumstances surrounding adherence behavior. The theory underlying this measure was that failure to adhere to a medication regimen could occur due to several factors such as "do you sometimes have problems remembering to take your medication", "do you sometimes forget to take your medication," and problems with the complexity of the medical regimen such as, "do you ever feel hassled about sticking to your treatment plan". The questions were phrased to avoid the "yes saying" bias by reversing the wording of the questions about the way patients might experience failure in following their medication regimen since there is a tendency for patients to give their physicians or other health care provider's positive answers. Each item is measuring a specific medication-taking behavior and not a determinant of adherence behavior. Response categories were yes/no for each item with a dichotomous response and a 5-point Likert response for the last item. The questionnaire was presented to each patient as an interview with proper explanation. Patient medication charts were also reviewed carefully for assessing the characteristics of hypertension and antihypertensive treatment. Data collection was conducted with appropriate training of the data collectors and continuous advices to keep the quality of the data. Close

supervision was made by the investigators and the collected data were checked for completeness every day.

Data analysis: The data were entered and analyzed using SPSS version 16 statistical package. Data cleaning was performed to check for accuracy, consistency and if there were no missed values during entry. Frequencies, proportions and summary statistics were used to describe the study

population in relation to relevant variables. Chi-square and multivariate logistic regression analyses were carried out to see the putative associations of each independent variable with the dependent variable. Odds ratio and 95% confidence interval were also used to identify the presence and strength of association. P value <0.05 was considered as significant for all of the analyses.

RESULTS

Table-1: Socio-demographic characteristic of the study participants (N=120)

Variables	Frequency	Percent (%)
Age		
<40	13	10.8%
40-49	21	17.5%
50-59	41	34.7%
>60	45	37.5%
Sex		
Female	74	61.7%
Male	46	38.3%
Education status		
Illiterate	81	67.5%
Primary or bellow	22	18.3%
Intermediate and secondary	12	10%
Graduate n above	5	4.2%
Marital status		
Single	8	6.7%
Married	85	70.8%
Divorced or widowed	27	22.5%
Family support or adherence		
Absent	78	65%
Present	42	35%
Occupation of the patients		
Retired	9	7.5%
Unemployed	40	33.3%
Housewife	30	25%
Teacher	2	1.7%
Farmer	15	12.5%
Employed	16	13.3%
Others	8	6.7%
Residence		
Urban	95	79.2%
Rural	25	20.8%
Medication payment		

Self	40	33.3%
Family	29	24.2%
Welfare/charity	41	34.2%
Employer	10	8.3%

A total of 120 study participants were interviewed of which 74 (61.7%) were female and 46 (38.3%) were males. The mean age of respondents was 54.7±12.7 years. Forty-five (37.5%) of the participants were at the age of above 60 years and 81 (67.5%) were illiterate. A large proportion of the subjects, 85 (70.8%), were married and 40 (33.3%) of the total study population were unemployed while 30 (25%) were housewives. Ninety-five (79.2%) of the study participants were from urban area. Seventy-eight (65%) of the subjects lack family support on adherence and 40 (33.3%) pay their medication expenses by themselves (Table 1).

Table-2: Clinical characteristics of the study participants (N=120)

Clinical characteristics		Frequency	Percent (%)
SBP	<120/80	4	3.3%
	120180 to 139/89	35	29.2%
	140/90 to 159/99	48	40%
	>160/100	33	27.5%
Hypertension Related complication	Hypertensive Heart Disease	10	8.3%
	End stage Renal Disease	3	2.5%
	Peripheral Arterial Disease	3	2.5%
	Stroke	9	7.4%
	None	95	79.2%
Frequent Depressed Mood	Absent	97	80.8%
	Present	23	19.2%
Family History of Hypertension	Absent	98	81.7%
	Present	22	18.3%

The clinical characters studied were Spot Blood Pressure (SBP), hypertension Related Complications, frequent depressed mood, and family history of hypertension. A greater portion of the subjects 48 (40%) had SBP of 140/90 to 159/99 which is of stage I hypertension. Among the 25 (20.8%) patients who developed hypertension related complications, 10 (8.3%) developed hypertensive heart disease. Twenty-three (19.2%) of the study participants had frequent mood of depression and 22 (18.3%) of them had a family history of hypertension (Table-2).

Table-3: Medication and follow up characteristics of the study participants (N=120)

Medication and follow up		**Frequency**	**Percent (%)**
Last follow-up visit	< 1months	52	43.3%
	2 months	47	39.2%
	3 months	17	14.7%
	>4 months	4	3.3%
No. of Anti-	1 drugs	40	33.3%

hypertensive Drug	2 drugs	69	57.5%
	≥3 drugs	11	9.2%
Duration of Therapy	<1 years	20	16.7%
	1 to 3 years	53	44.2%
	> 3years	47	39.2%
Initial Diagnosis as hypertensive	Regular check-up	2	1.7%
	Check-up for Hypertension	60	50%
	Check-up for Other Causes	58	48.3%

More than half of the study subjects, 69 (57.5%), had an antihypertensive regimen containing 2 drugs. The last follow up visit of 52 (43.3%) patients were before 1 month or less, followed by 47 (39.2%) patients with last follow up visit 2 months ago. Greater portion of patients, 53 (44.2%), had been on antihypertensive medication for 1 to 3 years, followed by 47 (39.2%) patients who had been on medication for ≥3 years. Sixty (50%) of the study subjects were initially diagnosed as hypertensive through checkup for hypertension related symptoms and only 2 (1.7%) of the patients were diagnosed via regular checkup (Table-3).

Table-4: Adherence characteristics of the study participants (N=120)

Adherence characteristics	Frequency	Percent (%)
Adherent	64	53.3%
Non-adherent	31	25.8%
Moderately adherent	25	20.8%

Of the 120 study subjects, 64 (53.3%) were adherent, 25 (20.8%) were moderately adherent while 31 (25.8%) were non-adherent to their anti-hypertensive medication (table-4).

Table-5: Association between demographic characteristics and adherence to antihypertensive medication of the study participants (N=120)

Variables	P Value
Range of age among patients	
<40	0.562
40-49	
50-59	
>60	
Sex of the patients	
Female	0.702
Male	
Education status	
Illiterate	0.818
Primary or bellow	
Intermediate and secondary	
Graduate and above	

Marital status		
Single	0.50	
Married		
Divorced or widowed		
Family support or adherence		
Absent	0.000	
Present		
Occupation of the patients		
Retired	0.231	
Unemployed		
Housewife		
Teacher		
Farmer		
Employed		
Others		
Residence		
Urban	0.008	
Rural		
Medication payment		
Self	0.008	
Family		
Welfare/charity		
Employer		

Among the demographic characteristics, the setting in which patients had their follow up (P value = 0.000), presence of family support (P value = 0.000), their residence (P value = 0.008), and who pay their medication expenses (P value = 0.008) were significantly related with adherence (Table-5).

Table-6: Association between clinical and medication related characteristics and adherence to anti-hypertensive medication of the study participants (N=120)

Variable	N (%)	P value
<120/80	3(2.5%)	0.000
120/80 to 139/89	35(29.2%)	
140/90 to 159/99	48(40%)	
>160/100	34(28.3%)	
Hypertension related complication		
Hypertensive Heart disease	11(9.2%)	0.000
End stage renal disease	3(2.5%)	
Peripheral arterial disease	3(2.5%)	
Stroke	8(6.7%)	
None	95(79.2%)	
Depressed Mood		
Absent	96(80%)	0.008
Present	27(22.5%)	

Family history of hypertension		
Absent	98(81.7%)	0.008
Present	22(18.3%)	
Last follow up visit		
<1 month	52(43.3%)	0.074
2 month	46(38.3%)	
3 month	17(14.2%)	
> 4 month	5(4.2%)	
No. of anti-hypertensive drugs		
1 drug	40(33.3%)	0.289
2 drugs	70(58.3%)	
>3 drugs	10(8.3%)	
Initial diagnosis as hypertensive		
Regular check up	2(1.7%)	0.909
Checkup for hypertensive related symptoms	60(50%)	
Checkup for other causes	58(48.3%)	
Duration of therapy		
<1 year	21(17.5%)	0.612
1 to 3years	52(43.3%)	
>3 years	47(39.2%)	

From the clinical and medication related factors, the spot blood pressure of the patients (P value = 0.000), hypertension related complications (P value = 0.000), family history of hypertension (P value =0.008), frequent mood of depression (P value = 0.008) were found to have association with adherence (Table-6).

Table-7: Association of factors with moderate adherence in reference to adherence of the study participants (N=120)

Variable	Adherence to antihypertensive		AOR (95% CI)
	Adherent	Moderately adherent	
SBP			
<120/80	6	0	
120/80-159/99	30	12	0.660(0.042-1.434)
140/90/100	35	15	0.733(0.130-2.557)
>160/100	14	8	1.00
Depressed mood			
Absent	69	31	0.266(0.0054-1467)
Present	11	9	1.00
Family history of HTN			
Absent	68	32	0.327(0.052-4253)

Present	12	8	1.00
Family support on adherence			
Absent	67	15	0.170(0.030-0.905)
Present	16	22	1.00
Residence			
Urban	68	37	0.750(0.038-2.270)
Rural	9	6	1.00
Hypertension related complication			
Hypertensive heart disease	2	4	9.833(0.438-83.948)
End stage renal disease	0	5	
Peripheral arterial disease	0	4	
Stroke	4	0	
None	75	26	1.00
Expense			
Self	48	3	0.389(0.022-2.367)
Family	8	12	4.375(0.157-19.824)
Wale fare/ charity	28	10	1.590(0.153-7.695)
Employer	9	2	1.00
Setting			
MGH	75	26	0.245(0.202-17.163)
ARH	9	10	1.00

Table-8: Strength of the association of factors with non-adherence in reference to adherence of the study participants (N=120)

Variable	Adherence to antihypertensive		AOR (95% CI)
	Adherent	**Moderately adherent**	
SBP			
<120/80	6	0	
120/80-159/99	30	12	0.660(0.042-1.434)
140/90/100	35	15	0.733(0.130-2.557)
>160/100	14	8	1.00
Depressed mood			
Absent	69	31	0.266(0.0054-1467)
Present	11	9	1.00
Family history of HTN			
Absent	68	32	0.327(0.052-4253)

Present	12	8	1.00
Family support on adherence			
Absent	67	15	0.170(0.030-0.905)
Present	16	22	1.00
Residence			
Urban	68	37	0.750(0.038-2.270)
Rural	9	6	1.00
Hypertension related complication			
Hypertensive heart disease	2	4	9.833(0.438-83.948)
End stage renal disease	0	5	
Peripheral arterial disease	0	4	
Stroke	4	0	
None	75	26	1.00
Expense			
Self	48	3	0.389(0.022-2.367)
Family	8	12	4.375(0.157-19.824)
Wale fare/ charity	28	10	1.590(0.153-7.695)
Employer	9	2	1.00

Upon multinomial logistic regression analysis, the absence of family support (AOR = 0.170, 95%, CI = 0.030-0.905) decreased adherence (Table-7), being at the prehypertension class of blood pressure (AOR=0.052, 95%, CI = 0.003-0.242) was also showed to decrease adherence to antihypertensive medications. Living in urban area (AOR = 0.184, 95%CI =0.024-0.597) had an inverse relation with adherence. People who developed hypertensive heart disease (AOR=21.737, 95%, CI=1.568-418.428) were 21 times more non-adherent to their antihypertensive therapy than the other population (Table-8).

DISCUSSION

Adherence to pharmacological treatment for hypertension is considered a key factor in guaranteeing successful therapy outcomes. A total of 120 study participants were interviewed of which 74 (61.7%) were female and 46 (38.3%) were males. This goes in line with studies done in Malaysia[10] in which females were 62.8% of the sample population. The mean age of respondents in this study was 54.6 while 71.2% of the study subjects were of age ≥50. Similarly, in the study done in Malaysia, [10] mean age was 57.8 and 69.2% of the study subjects were at age of ≥50 years. With regard to educational status, 67.5% of the populations in this study were illiterate which goes in line with the study. In the contrary, 85.5% of the study subjects in the study conducted in Malaysia[10] had attended some sort of formal education to at least primary level. A large proportion of the subjects, 85 (70.8%), were married and 40 (33.3%) of the total study population were unemployed while 30 (25%) were housewives. Ninety-five (79.2%) of the study participants were from Urban area. Seventy-eight (65%) of the subjects lack family support on adherence and 40 (33.3%) pay their medication expenses by themselves. A large proportion of the subjects 70.8% were married. This was higher than that in a study conducted in Gondar, Ethiopia[11] in which 60.7% were married. Availability of Support System in a study done in Pakistan[12] was 54% which was greater support for adherence than that in this study. A greater portion of the subjects in this study (40%) had SBP of 140/90 to 159/99 which is

higher than a study done in Brazil[13] in which 30.4% of the uncontrolled hypertensive patients were in the same blood pressure (BP) range and lower than that reported from a study done on Military Healthcare Providers of the northeast United States[14] in which 43% of the patients had a blood pressure in the range 140-159 mm Hg systolic or 90-99 mm Hg diastolic. Similarly, in a study done in Gondar, Ethiopia[11], more than half (53.4%) of the study subjects had uncontrolled blood pressure. More than half of the subjects (58.3%) had an antihypertensive regimen containing 2 drugs while a study done in Brazil[13] revealed that 33.3% of the subjects had an anti-hypertensive regimen of only 1 drug. Greater portion of patients (43.3%) in this study had been on antihypertensive medication for 1 to 3 years. Similarly, in the study conducted in Ghana, in more than half of the patients (52%), disease conditions were between one and three years old. In this study the prevalence of short duration of therapy was attributed to the fact that most hypertensive patients do not live long with their disease condition, most probably due to development of disease complications resulting from non-adherence to medications. It was also reasoned that the hypertensive patients could have been retired and have relocated or changed a health facility.[8] Almost half (50%) of the study subjects were initially diagnosed as hypertensive through checkup for hypertension related symptoms and only 2 (1.7%) of the patients were diagnosed via regular checkup. This might be an indication that patients start anti-hypertensive therapy after the disease reaches its symptomatic stage. This makes it harder to control BP or prevent complications. This is even more exaggerated in the study done in Pakistan[12] in which majority of the patients (70.8%) discovered their disease during medical checkup for symptoms related to hypertension and/or its complications. Only 52.9% were adherent while 20.7% were moderately adherent and

26.4% were non adherent. This was similar to the study conducted in Malaysia[10] in which 53.4% were adherents. It was however reported that from the study done in Gondar, 12 (64.6%) were adherent and from the study done in Nigeria, which was based on patients' self-report adherence rating, (67.7%) of the patients adhered strictly to their medications while only (32.3%) were poor adherents. It should be noted that not only patients who were completely non-adherent were in problem. Patients who were partially or moderately adherence need to be focused on. This level of adherence is even more dangerous as it might lead the patient not to think the medications are working. In this study, presence of hypertension related complications was shown to decrease adherence. People who developed hypertensive heart disease were 21 times more non-adherent to their antihypertensive therapy than the other population. In the contrary, in the study from Pakistan,[12] a greater proportion of the cases suffering from hypertension related complications were adherent. Other studies also show the relationships between adherence to antihypertensive therapy and cardiovascular complications of hypertension.[15] Absence of family support (AOR=0.170, 95% CI = 0.030- 0.905) was reported in this study to have a strong negative effect on adherence. Similarly, the study from Pakistan stated that increasing self-reliance in old age has been shown to decrease adherence. In the Pakistani population, a better social support structure ensured by the common extended family system, reduces self-reliance and could be the reason for better adherence in this age group. It is usual for other family members to take full responsibility of the medication routine of the families' patients. [12] In the study conducted in Gondar[11] the multivariate logistic regression showed that as the distance from the hospital decreased, the adherence to treatment of hypertension got improved (AOR = 2.02, 95% CI = 1.19- 3.43).

Although medication related factors like number of antihypertensive drugs were reported not to associated with adherence in this study, it is reported to affect adherence in the study done in Brazil in which, patients with higher adherence were taking 3 or more antihypertensive medications daily (70.6%) and 7 or more anti-hypertensive pills daily (54.6%).[16] However it is usually generalized that increasing complexity of medication regimen results in lower treatment adherence. The SBP of the patients was found to have strong association with adherence to antihypertensive therapy. Specifically, patients at the prehypertension class of blood pressure (AOR = 0.026, 95% CI = 0.003-0.242) were less adherent to their medications. This can be because their state will make them less symptomatic and makes them feel like they don't even need medication. On the contrary, it is reported from the study done in Gondar[11] that those who have controlled hypertension had a significantly higher chance of being adherent to their treatment (AOR = 2.93, 95% CI = 1.73-4.96). On its top, only 2.5% of the patients in our study had SBP in the normal range (<120/80) all of which were adherent to their medication.

CONCLUSION

In conclusion, this study was completely non-adherent and only around half of them were adherent to their medications. The absences of family support, being at the prehypertension class of blood pressure, hypertensive heart disease were shown to decrease adherence to antihypertensive medications. Therefore, health care professionals should be adequately trained and resourced to offer proper counseling to hypertensive patients on their medication and disease conditions.

Conflict of interest: None.

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