

## Adherence to Antihypertensive Medications: Rate and Predictors

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### Abstract:

**Background:** Hypertension is a prevalent health problem with serious complications. Adherence to antihypertensive medications (AHMs) is a key in control of hypertension and prevention of complications. **Objectives:** This study aimed to estimate the rate of adherence to AHMs, and to predict factors that are likely affect adherence to these medications. **Methods:** A cross-sectional study was conducted from July to December 2018 including 473 hypertensive patients attending the outpatient clinics of two primary health care centers in Gharbia and Menoufia governorates, Egypt. The Hill-Bone questionnaire was used to assess adherence level. Factors related to adherence were evaluated through questionnaire items. **Results:** The rate of good adherence was only 40.2%. Significant predictors of good adherence were older age ( $p < 0.001$ ; OR=0.335, 95% CI= (1.232-1.585), higher level of education ( $p < 0.001$ ; OR=2.538, 95% CI= (3.476-46.082), duration of hypertension  $> 10$  years ( $p < 0.001$ ; OR=0.34, 95% CI= (0.184-0.628), using one medication ( $p < 0.002$ ; OR=1.553, 95% CI= (1.783-12.522), and once per day dosing ( $p < 0.001$ ; OR=3.364, 95% CI= (11.637-71.781). Self-payers ( $p < 0.001$ ; OR=-3.141, 95% CI= (0.02-0.096), and patients reporting poor physician relationship ( $p < 0.001$ ; OR=-1.731, 95% CI= (0.540-0.578) were predictors of poor adherence. **Conclusion:** A low rate of adherence to AHMs was recognized. The study highlights the importance to simplify the dosing and frequency of medications, to improve the patient-physician relationship, and the need for policies to extend the umbrella of health insurance in Egypt to overcome the economic barrier of adherence.

**Keywords:** Adherence, Antihypertensive medications, Predictors, Rate.

### Introduction:

Hypertension (HTN) is a global health problem affecting nearly one billion population worldwide. It is a major, yet modifiable cardiovascular risk factor with significantly related morbidities and mortalities.<sup>(1)</sup>

Hypertension is a prevalent diagnosis in Egypt. Hasan et al, 2014<sup>(2)</sup> in their systematic review of hypertension studies in Egypt revealed that the highest prevalence of HTN in Egypt was estimated at 26.3% as reported by the study conducted by Ibrahim and his colleagues.<sup>(3)</sup>

A goal of blood pressure (BP) below 140/90 mmHg is recommended to control HTN, and to decrease the cardiovascular risk complications.<sup>(4)</sup>

Antihypertensive medications (AHMs) are key components to control BP levels. The effectiveness of AHMs is well recognized and has been counted in terms of reduction in the risk of stroke and other cardiovascular disease events.<sup>(5)</sup>

Patients with difficult-to-control hypertension should be assessed particularly for adherence to the prescribed management plan including adherence to antihypertensive medications

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(AHMs) and the recommended lifestyle modifications.<sup>(6)</sup>

Patients frequently do not continue in taking their AHMs persistently. The most accurate response about adherence could be obtained by a nonjudgmental approach of asking. For example, a health professional might ask, “Many patients intermittently miss a dose or more of their medication(s). How often is this for you?” Patients may encounter difficulty adhering to AHMs for financial reasons, or they may not understand the regimen because of its complexity, health illiteracy, or barriers like cultural, or language barriers.<sup>(7)</sup>

A once-daily regimen is suggested to improve adherence to AHMs. Because most patients need more than one class of AHMs (e.g., a diuretic with an Angiotensin Converting Enzyme inhibitor), fixed-dose combination pills may also improve adherence, although sometimes at an increased cost to the patient, creating another obstacle to adherence. An additional once-daily agent (e.g. a long-acting Calcium Channel Blocker) may be needed for patients with difficult to control HTN.<sup>(8)</sup>

A relationship between sodium chloride intake and BP have been recognized. A moderate reduction in the daily intake of sodium chloride can produce a small reduction in blood pressure. The average daily

consumption of sodium chloride not exceed 6 g, as recommended by the American Heart, this may lower BP by 2-8 mm Hg.<sup>(9)</sup>

To the knowledge of the workers of this study, very few studies have addressed factors and predictors of adherence to AHMs in Egypt.

The aim of this work was to study the rate of medications’ adherence and its predictors among hypertensive patients attending the outpatient clinics of two primary health care centers in 2 primary health care centers in Gharbia and Menoufia Governorates, Egypt.

### **Methods**

This was a cross-sectional study conducted during five months period from 1<sup>st</sup> of July to end of December 2018 in two primary health care centers of Beltag village, Gharbia governorate, and Al-Rahib village, Menoufia governorate, Egypt.

A total of 473 hypertensive patients were interviewed face-to-face by trained interviewers during their existence in the waiting area of the outpatient clinics of the health care centers. The interviewers explained the aims of the study and those who consented to participate were asked to complete a self-administered questionnaire. Interviewers were available to respond to any potential queries. For those participants who

could not read or write, the interviewers helped them by reading the questionnaire questions, and recording their responses.

A sample size of 382 was calculated using the statistical formula  $(n = Z^2pq/d^2)^{(10)}$ , where  $n$  = sample size,  $Z$  = confidence interval (CI),  $p$  = prevalence rate (in %),  $q=1-p$ ,  $d$  = degree of precision. A confidence interval of 95%, and degree of precision (margin of error) set at 5% was used. Prevalence rate of 26.3% for hypertension among Egyptians was used<sup>(2, 3)</sup> and the total population size is above 10000 population. However, 473 participants were studied.

**Criteria of inclusion:** Those hypertensive patients who are 18 years or older, have been diagnosed with hypertensive and are on antihypertensive medications for more than 6 months have been included in the study. Pregnant hypertensives, and those individuals who have been diagnosed within the previous 6 months were excluded from the study as they were likely to require frequent monitoring for medication adjustment to achieve a controlled blood pressure.

**Study Instrument:** To measure adherence level, an Arabic version of the Hill-Bone questionnaire was used. <sup>(11, 12)</sup> The Arabic version was validated in a study reporting a Cronbach's alpha of 0.76. <sup>(13)</sup>

Each question in this Medication Adherence Scale had a four-point Likert-type response format. Each response coded a score: none of the time = 4, some of the time = 3, most of the time = 2, and all the time = 1. Adherence level was categorized into good adherence and poor adherence by scoring as follows: the total scores of the 8-item likert scale of the questionnaire were calculated for every individual patient as described above. Accordingly, the total score for each patient could range from 8 (minimum) and 32 (maximum). Lower scores would reflect poorer adherence to medication therapy. A decision was taken to make a score of 25 and more as good adherence, and 24 or less as poor adherence.

Review of the current literature revealed a number of factors related to antihypertensive medications adherence which were also included in the questionnaire. These factors include duration of hypertension, frequency of medication use, dosing and regimen, self-payment for medication, and physician-patient relationship. <sup>(14)</sup> All these items used five-point Likert scale responses (1= very bad to 5 = very good). <sup>(15)</sup>

Similar to the Hill-Bone questionnaire, a four-point Likert-type response format was done for salt questions; three questions. So, a total

score for each patient could range from 3 (minimum) and 12 (maximum). A score of 11 and more was categorized as good adherence, 9 -10 as moderate adherence and 8 or less as poor adherence.

### **Statistical Analysis:**

SPSS version 20 (SPSS IBM Statistics) was used to conduct statistical analyses. Descriptive statistics were used to describe the socio-demographic, health-related and adherence-related variables. Bivariate analyses using the Pearson's Chi-square test were used to assess the association between the outcome measure (level of adherence) and each of the socio-demographic, health-related, and adherence-related factors. Binary logistic regression analysis using the backward stepwise likelihood-ratio method was used to assess the predictors of adherence controlling for the socio-demographic factors (age, gender, level of education, smoking, self-payment, and comorbidities) which were fixed into the model. Finally, the binary logistic regression includes the socio-demographic factors and the predictors of adherence. The level of significance for all statistics was set at  $p \leq 0.05$ .

### **Results:**

The socio-demographic characteristics of the 473 participants who responded to all questionnaire items are shown in table 2. The majority of participants were females (60.7%), mean age ( $59.008 \pm 11.803$ ), with university level education (26.3%), and smokers (39.3%).

Regarding health and adherence-related factors, almost two thirds of participants had a diagnosis of hypertension between 5 to 10 years, while one third of them had hypertension diagnosed for less than 5 years, almost half are diabetic (45.9%), one fourth of them had comorbidities other than hypertension and diabetes mellitus, two thirds are using one form of medications, in once per day frequency, 39% of them are paying for their medications, and more than half (57.5%) reported poor patient-physician relationship (Table 2).

**Adherence rate:** Only 40.2% of participants were classified as good adherent to AHMs, and the majority (61.1%) were poorly adherent to salt reduction advice (Table 1).

**Bivariate analysis** (Table 2), revealed significant association between adherence to AHMs and patients' age being older, female gender, with higher level of education, diabetic rather than hypertensive only, with

longer duration of hypertension, using one medication, in once per day frequency. Poor adherence was reported by participants who pay for their medications (self-payment), and those reported poor patient-physician relationship.

**Logestic regression analysis** revealed the predictors of adherence to AHMs (Table 3). Patients' older age, female gender, higher level of education, longer duration of hypertension, using one medication, and once per day regimen were predictors of good adherence. Predictors of poor adherence were attributed to self-payment for medications, and poor patient-physician relationship.

### **Discussion**

This study aimed at testing adherence of patients with hypertension to AHMs. It revealed that only 40.2% of patients are adherent to AHMs at a good level. This low rate of adherence is consistent with results of many previous studies. <sup>(16, 17, 18)</sup> However, some other studies reported higher prevalence of medication adherence among hypertensive patients. <sup>(19-21)</sup> (This could be explained by the fact that adherence to medications is a patient personal behavior and attitude that varies between different communities and cultures.

Moreover, some other studies have used different method to assess adherence using questionnaires assessing responses with yes/no category. The current study used the Hill-bone questionnaire with 4-likert responses, which revealed high validity and reliability in testing adherence to AHMs. <sup>(10-12)</sup>

In Egypt, a rate of 25.9% of poor adherence to AHMs was described by Youssef and Moubarak. <sup>(23)</sup> They assessed adherence by a single direct question on the number of times the patient uses AHMs per month, and considered using medications 90% of times or more as perfect adherence; a method different from the current study.

There are many factors in the literature that affect adherence to AHMs and when studied could predict adherence. The current study recognized positive relation between the patient's age and the improved adherence, where the older the age the more likely the adherence. Though, there was no relation between age and medication adherence in the study performed by Hacıhasanoglu, <sup>(20)</sup> other researchers found inverse relation between patient's age and adherence where younger age affected adherence positively. <sup>(18, 22, 24)</sup> Discrepancies in results of the studies could be attributed to the variations in the disease problems that urge patients to use medications

more regular varies by age. Since patients accept diagnosis of chronic diseases by increasing age, at least as part of the aging process, subsequently, adherence to regular daily use of medications improves. It is thought that the difficulty in accepting the diagnosis of hypertension in younger people and the fact that they are not aware of the importance of regular medication use may have affected the result of the current study.<sup>(22)</sup> Moreover, it has been found that increasing patients' cardiovascular risk, which could accompany older age, improves adherence to medications.<sup>(19)</sup>

According to the current study, patients with HTN duration  $\geq 10$  years were more likely to be adherent to AHMs. Although some studies did not find relation between medications adherence and duration of HTN, other studies observed that the longer the duration of HTN, the increased the medication adherence,<sup>(18, 22, 25)</sup> similar to the current study. It is observed that newly diagnosed hypertensive patients often show less commitment in taking medications regularly, as they are less likely to adapt the behavior of adopting diagnosis of HTN.<sup>(19)</sup>

Greater level of formal education was found by the current study to be a predictor of adherence to AHMs, in line with previous

studies,<sup>(18, 26, 27)</sup> where patients with formal education reported a higher level of medication adherence compared to those with non-formal education. Patients with greater levels of formal education may have a better understanding of the goal of controlling their blood pressure, the consequences of poor adherence and the potential side effects associated with antihypertensive treatment.<sup>(16, 25)</sup> However, a study by Boratas et al 2018<sup>(19)</sup> did not recognize difference in adherence related to education and patient knowledge on medications

Females were observed by the current study as being more likely to be adherent to AHMs, similar to a study by Li et al, 2016, and Ramli et al, 2012.<sup>(18, 24)</sup> Other studies did not recognize such a relation between gender and medication adherence.<sup>(18, 19, 24)</sup> This could be owed to different individual behavior among different communities.

Patients with diabetes mellitus showed significantly better adherence compared to non-diabetic patients, (p 0.001, table 2) comparable to results of other researchers.<sup>(16, 24)</sup> However, bivariate analysis failed to reveal diabetes as a predictor of good adherence. Apparently, according to the current study, presence of comorbidities was not a predictor of improved adherence, in line with study by

Li et al, 2016, and Alsolami et al, 2015.<sup>(18, 24)</sup> However, previous studies in the U.S. found that patients with both hypertension and diabetes were more likely to adhere to multiple medications.<sup>(28, 29)</sup> This is because of their experience with wider range of symptoms from hypertension and the other co-morbid conditions which urges them to adhere to their medications to alleviate these symptoms.<sup>(24)</sup>

Medications number and frequency of intake inversely affected adherence as indicated by the current study. Although Boratas et al, 2018 described insignificant relation,<sup>(19)</sup> other studies demonstrated findings similar to the current study.<sup>(18, 21, 30)</sup> This recognized the importance of keeping the number of medications prescribed and the frequencies of the daily dose to a minimum. Keeping the medication regime simple will support better adherence by hypertensive patients.

The cost of medication is another factor that can affect adherence to prescribed medications.<sup>(31, 32)</sup> Self-payers were found to show lower level of adherence to medications. Li et al, 2016 in China recognized similar findings among patients with lower economic level.<sup>(18)</sup> Alsolami et al, 2015 in Saudi Arabia did not recognize income as predictor of adherence to medications.<sup>(16)</sup> Poverty and

economic burden in Egypt and China could explain the finding.

The findings of the current study revealed significant association between poor patient-physician relationship and poor adherence to AHMs, whilst good patient-physician relationship is associated with good AHMs adherence. These findings are consistent with that of previous studies.<sup>(16, 31, 33)</sup> It is noted that health care in Egypt is fragmented and patients seek care from multiple levels at private clinics, and governmental health care facilities. Primary care physicians at primary health care centers, other than centers known as “ideal family health care centers”, spend short time early in their career in services at a given primary care center, then shift to training at secondary or tertiary care facilities. Lack of continuity of care prevents the development of quality long-term patient-physician relationship. Development of patient-physician trust is reinforced by communicating to patient’s clear information and the expectation of a long-term relationship.<sup>(34)</sup>

### **Conclusion:**

It has revealed that lower level of education, complexity of dosing and frequency of medications, self-payment of medications, and poor patient-physician relationship are

predictors of poor adherence to antihypertensive medications. Subsequently, the study highlighted the importance for interventions to improve education, to simplify the dosing and frequency of medications, the need for policies to overcome the economic barrier of adherence, and to improve the patient-physician relationship to improve adherence and subsequent hypertension control.

**Limitations of the study:**

This study acknowledges a number of limitations including the small number participants, non-random sampling. So, its results could not be generalized to the whole population of Egypt. Also, the high level of participants with education below university level which probably affected their understanding of the survey items. Moreover, the results have depended on participants reporting, therefore could be inaccurate and a higher level of poor adherence is possible, although a high level is already reported. Therefore, a large studies are needed, and utilization of other means of testing adherence, e.g. review medical records, counting medications, and estimating regularity of follow up, is suggested.

**Authors' contribution:**

Both authors have contributed equally in formulating the idea and objectives of the study, the study design and its instrument, training of interviewers for data collection, statistical analysis of data, and editing the manuscript. However, most of data (~ 60%) were collected from the health center related to the principle author.

**Conflict of Interest:**

There is no conflict of interest.

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**Table (1): Results of the Hill-Bone adherence to antihypertensive medications, and adherence to salt advice.**

		N	%
<b>Medications' adherence</b>	Good adherence	190	40.2
	Poor adherence	283	59.8
<b>Sodium use</b>	Good adherence	75	15.9
	Moderate adherence	109	23.0
	Poor adherence	289	61.1

**Table (2): Socio-demographic characteristics of participants and factors affecting adherence to antihypertensive medications.**

	All subjects		Medications' adherence		P-value
			Good adherence	Poor adherence	
Age*			Mean 62.27±SD 9.70 190(40.2%)	Mean 56.8 ±SD12.57 283(59.8%)	0.037**
Gender	Male	186(39.3%)	52(28%)	134(72%)	0.001
	Female	287(60.7%)	138(48.1%)	149(51.9%)	
Education status	University	77(26.3%)	42(54.5%)	35(45.5%)	0.001
	Secondary	129(27.3%)	67(51.9%)	62(48.1%)	
	Primary	147(31%)	48(32.7%)	99(67.3%)	
	No formal education	73(15.4%)	18(24.7%)	55(75.3%)	
Diabetic	Yes	217(45.9%)	111(51.2%)	106(48.8%)	0.001
	No	256(54.1%)	79(30.9%)	177(69.1%)	
Associated co-morbidities (other than diabetes)	Yes	120(25.4%)	53(44.2%)	67(55.8%)	0.301
	No	353(74.6%)	137(88.8%)	216(61.2%)	
Smoker	Yes	186(39.3%)	81(43.5%)	105(56.5)	0.227
	No	287(60.7%)	109(38%)	178(62%)	
Duration of hypertension	< 5 years	167(35.3%)	35(21%)	132(79%)	0.001
	5-10 years	306(64.7%)	65(38%)	106(62%)	
	> 10 years	135(28.5%)	90(66.7%)	45(33.3%)	
Number of medications	One medication	313(66.2%)	164(52.4%)	149(47.6%)	0.001
	> one medication	160(33.8%)	26(16.2%)	134(83.8%)	
Frequency of medications	once\day	296(62.6%)	177(59.8%)	119(40.2%)	0.001
	Twice \day	177(37.4%)	13(7.3%)	164(92.7%)	
Self-payment	Yes	185(39.1%)	20(10.8%)	165(89.2%)	0.001
	No	288(60.9%)	170(59%)	118(41%)	
Physician-patient relationship	Good	272(57.5%)	143(52.6%)	129(47.4%)	0.001
	poor	201(42.5%)	47(43.4%)	154(76.6%)	

\*Age has been calculated by mean and standard deviation (SD), \*\*t-test was used to examine the p-value

**Table (3): Logistic regression analysis of predictors of adherence to anti-hypertensive medications.**

Predictors	B	Odds Ratio	95% C.I. limit		P-value
			Lower	Upper	
Age	0.335	1.397	1.232	1.585	0.001
Gender (male)	-.391	0.677	0.256	1.785	0.430
<b>Education status:</b>					
- University	2.538	12.657	3.476	46.082	0.001
- Secondary school	2.352	10.507	3.601	30.662	0.001
- Non-formal	-.844	0.430	0.146	1.265	0.125
Smoking ( Non-smoker)	-0.054	0.947	0.357	2.513	0.913
Diabetic	0.674	1.963	0.987	3.905	0.055
Co-morbidities (associated)	-0.176	0.839	0.370	1.899	0.673
<b>Duration of hypertension:</b>					
- 5-10 years	-1.843	0.158	0.830	0.300	0.001
- More than 10 years	-1.078	0.340	0.184	0.628	0.001
Number of medications (one medication)	1.553	4.725	1.783	12.522	0.002
Frequency of medications (Once per day)	3.364	28.902	11.637	71.781	0.001
Payment (Self-payment)	-3.141	0.043	0.020	0.096	0.001
Patient-physician relationship (poor relationship)	-1.731	0.177	0.540	0.578	0.004

\*Poor adherence is the response category and good adherence is the reference category

## الملخص العربي الإلتزام بالأدوية المضادة لإرتفاع الضغط: المعدل و التنبؤات

رضا عبدالمعطي جويده ، مختار محفوظ شنتلة

**الخلفية:** إرتفاع ضغط الدم يعتبر مشكلة صحية سائدة بمضاعفاته الخطيرة و الإلتزام بالأدوية المضادة للضغط هو مفتاح السيطرة على إرتفاع ضغط الدم والوقاية من المضاعفات. **الأهداف:** تهدف هذه الدراسة إلى تقييم معدل الإلتزام بالأدوية المضادة لإرتفاع الضغط ، والتنبؤ بالعوامل التي من المحتمل أن تؤثر على الإلتزام بهذه الأدوية. **المنهجية وطرق البحث:** أجريت دراسة مقطعية من يوليو إلى ديسمبر 2018 شملت 473 مريض يعانون من إرتفاع ضغط الدم في العيادات الخارجية في إثنين من مراكز الرعاية الصحية الأولية في محافظتي الغربية والمنوفية بمصر. تم استخدام إستبيان هيل-بون لتقييم مستوى الإلتزام بالأدوية و تم تقييم العوامل المتعلقة بالإلتزام بالأدوية المضادة لإرتفاع الضغط من خلال بنود الإستبيان. **النتائج:** أظهرت النتائج أن 40.2% فقط من المرضى ملتزمون إلتزاما جيدا بهذه الأدوية. كما أظهرت نتائج الإنحدار اللوجستي للتنبؤ بالعوامل التي قد تؤثر على الإلتزام بهذه الأدوية على النحو التالي : الإلتزام الجيد من المرضى كبار السن، وذوى مستوى أعلى من التعليم ، و مدة ارتفاع ضغط الدم < 10 سنوات ، و مستخدمى دواء واحد ، و مرة واحدة لكل الجرعات اليومية. أما من يتكفلون بمصاريف العلاج بأنفسهم، والمرضى الذين يبلغون عن علاقة بالطبيب الضعيفة كانت تنبئ بضعف الإلتزام. **الخلاصة:** فقد وجد ان عدم الإلتزام بأدوية الضغط هو الغالب. تسلط الدراسة الضوء على أهمية تبسيط الجرعات وعدد مرات اخذ الأدوية باليوم ، وتحسين العلاقة بين المريض والطبيب ، والحاجة إلى وضع سياسات لتمديد مظلة التأمين الصحي في مصر للتغلب على العائق المالى لدى المرضى غير الملتزمين بأخذ أدوية الضغط.