Research Paper
Relationship Between Medication Adherence and Ankle-Brachial Index Value in Patients With Hypertension

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ABSTRACT

Background: Hypertension is one of the leading causes of death and physical disabilities. The ankle-brachial index (ABI) is one of the useful indicators of blood pressure with the ability to show the risk of peripheral artery disease. This study aims to investigate the relationship between medication adherence and the ABI lavue in patients with hypertension.

Methods: In this descriptive cross-sectional study, 250 patients with hypertension referred to medical health centers in Karaj, Iran were enrolled using a convenience sampling method. To collect data, a demographic form and the 8-item morisky medication adherence scale (MMAS-8) were used. Also, the ABI was measured manually using an acoustic Doppler probe. Data were analyzed in SPSS software, v. 25.

Findings: The Mean±SD of the right and left ABI were 1.055±0.134 and 1.036±0.113, respectively. The Mean±SD of MMAS-8 score was 5.88±1.74. It was found that 127 patients (50.8%) had low adherence level, 68 (27.2%) had moderate adherence level, and only 55 (22%) had high adherence level. There was a positive significant correlation between patients' medication adherence and the ABI value. Moreover, a statistically significant difference was observed in the mean scores of the ABI in patients with three different levels of medication adherence.

Conclusion: The medication adherence is poor among hypertensive patients in Karaj. It is related to the ABI such that with the decrease of medication adherence, the ABI value decreases. Therefore, adherence to medication regimen in patients with hypertension can be effective in preventing arterial complications.

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1. Introduction

Hypertension, affecting more than 1.2 billion people worldwide, has become the most prominent and costly public health problem. It is a multifactorial disease, involving environmental and genetic factors along with risky behaviors. The cause of this disease is identified in 10% of cases (secondary hypertension), but in 90% of cases, no cause is found (primary hypertension). For this reason, many researchers seek to properly understand the mechanisms of blood pressure control in patients with normal and high blood pressure [1]. Hypertension is the most important modifiable risk factor for cardiovascular disease [2]. High salt intake may predispose children to hypertension [3]. Reducing the average salt intake can lead to the promotion of public health [4]. Targeted weight-loss interventions may be more effective than a general approach to prevent hypertension [5]. A diet rich in fruits and vegetables with high potassium, especially fresh foodstuffs, is strongly recommended; the canning or freezing of foods can reduce the natural content of potassium [6]. Calcium supplementation lowers blood pressure in people with hypertension by chronic inhibition of nitric oxide synthesis, but a high-calcium diet raises blood pressure due to causing nitric oxide deficiency. Proper magnesium intake should be considered by anyone seeking to prevent or treat hypertension [7]. For having proper blood pressure, there is a need for a healthy diet, adequate exercise, stress reduction, and adequate amounts of potassium and magnesium intake. However, more research is needed for definitive recommendation of magnesium. It seems that stress management should be used as an intervention for patients with hypertension [2].

Numerous complications of hypertension have emphasized the need for a variety of methods for its control and treatment. One of the methods is the administration of antihypertensive drugs such as beta-blockers, diuretics, angiotensin system inhibitors, alpha-receptor antagonists, and calcium channel blockers [8]. In a study by Kannel et al. on 79 men and 46 women, the relationship between hypertension and cardiovascular problems and subsequent cardiovascular and cerebrovascular diseases was reported, indicating the need for vascular examination of patients with hypertension [9]. Emdin et al. in a cohort study in the United Kingdom examined 4,222,459 people aged 30-90 years. They stated that hypertension was a risk factor for peripheral arterial disease in many participants. In their opinion, physicians should be aware that patients with the peripheral arterial disease are at risk for a wide range of other cardiovascular diseases, including chronic kidney disease, ischemic heart disease, heart failure, atrial fibrillation, and stroke [10]. There are various methods for diagnosing cardiovascular diseases, one of the simple and fast methods is the Ankle-Brachial Index (ABI) [11]. Myslinski conducted a study on 51 patients with hypertension, which showed that the ABI was the most valuable indicator for predicting and diagnosing cardiovascular diseases [12].

The best way to prevent cardiovascular diseases is to treat hypertension where medication therapy is one of the most important treatment options. Sadeghian in a study on 80 patients with mental disorders showed that mediation education had a significant effect on increasing medication adherence [13]. Zare conducted a cross-sectional study on 282 heart disease patients referred to Imam Reza Clinic in Shiraz, Iran who were taking the antihypertensive drugs, using the 8-item morisky medication adherence scale (MMAS-8). The results revealed that adherence to antihypertensive drugs was low in 76% of patients [14]. The current study aims to examine the cardiovascular status of patients with hypertension by using the ABI, assess its relationship with patients' medication adherence, and evaluate the effect of demographic factors on medication adherence and the risk of cardiovascular complications.

2. Materials and Methods

This is a descriptive cross-sectional study. To assess the sample size using the following equation, the patients' medication adherence was considered moderate (P=0.58) according to Dianati et al.'s study [15], the first type error α=0.05 at 95% confidence level, the second type error β=0.2 (80% power), and d=0.087. The sample size was estimated to be 250 (Equation 1).

1. $n=((z_{1-\alpha/2}+z_{1-\beta})^2$

$p\times(1-p))/d^2=([(1.96+0.84)]^2$

$0.58\times0.42)/[0.087]^2=(1.905)/(0.0075)=250$

Therefore, 250 patients with hypertension, referred to three medical centers in Karaj city (Shahid Kalantari clinic, Valiasr clinic, and the clinic of Shahid Rajai Hospital) were selected using a convenience sampling method and based on the inclusion criteria which were age 45-65 years, having hypertension for at least 6 months, and taking antihypertensive drugs. The exclusion criteria were the unwillingness to continue participation, having a drug addiction, exercising profession-

ally, participation in other educational and therapeutic programs in the last 6 months, and having any physical or mental disorder affecting the results.

A demographic form and the MMAS-8 were used to collect data. The demographic form surveys information such as age, gender, education, and marital status. The MMAS-8 consists of 8 items; 7 are answered by Yes with zero point or No with one point. The item 5 has reversed scoring and the item 8 is rated on a five-point Likert scale (0=never, 0.25= "once in a while, 0.5=sometimes, 0.75=usually, and 1=always) [16]. A score of 8 indicates high adherence, score 6-7 shows moderate adherence, and score <6 shows low adherence [17]. This questionnaire has been originally designed to measure the medication adherence of patients with hypertension. However, in various studies, it has been used on other patients with cancer [18], and cardiovascular diseases [15]. In the study by Morisky et al. [16], a Cronbach's alpha coefficient of 0.83 was reported for this questionnaire. For its Persian version, Mehrtak et al., reported a Cronbach's alpha coefficient of 0.68 indicating its acceptable reliability [19].

After providing a complete explanation of the study objectives to the participants and obtaining their written informed consent, they completed the questionnaires. For the participants with the inability to read and write, the researcher completed the questionnaires through an interview. Then, their systolic pressure was measured with Richter digital sphygmomanometer. The Bistos Doppler probe was used to calculate the ABI. The ABI value was obtained by dividing the systolic pressure at the ankle by the systolic pressure at the arm, which was calculated separately for the both sides of the body [11]. In this study, all measurements were performed by the researcher (Master's student, Simin Heidari).

Mean±SD, frequency, and percentage were used to describe the data. Pearson correlation test and one-way analysis of variance (ANOVA) were used to investigate the relationship between medication adherence and patients' ABI at the right and left sides, and the relationship between patients' ABI at the right and left sides and their demographic characteristics. Moreover, chi-square test was used to compare qualitative variables.

3. Results

The Mean±SD age of participants was 57.56±6.73 years. Of 250 participants, 86 (34.4%) were male and 164 (65.6%) were female; 38 (15.2%) were single, divorced, or widow/widower, and 212 (84.8%) were married; 37 (14.8%) were illiterate, 112 (44.8%) had a high school education, 71 (28.4%) had a diploma, and 30 (12%) had a bachelor's degree; 123 (49.2%) were housekeeper and 30 (12%) were retired. Moreover, 26 (10.4%) were smokers.

The results showed that 127 patients (50.8%) were had low medication adherence, 68 (27.2%) had moderate medication adherence, and only 55 (22%) had high medication adherence. The Mean±SD score of medication adherence was 5.88±1.74. The Mean±SD of the right and left ABI values was 1.055±0.134 and 1.036±0.113, respectively (Table 1).

According to the results in Table 2, the patients' medication adherence had a direct and positive correlation with the right ABI (r=0.143, P=0.04) (P<0.05), but had no significant correlation with the left ABI (r=0.117, P=0.065 >0.05). The Mean±SD of the right ABI in those with low level of medication adherence was 1.054±0.146; in those with moderate adherence level, it was 1.059±0.124, and in patients with high adherence level, it was 1.074±0.115. The Mean±SD of the left ABI for the low level of medication adherence was 1.023±0.115; for the moderate

Table 1. Mean scores of the study variables

Variables		Mean±SD/No. (%)
Right ABI		1.055±0.134
Left ABI		1.036±0.113
MMAS-8		5.88±1.74
Medication adherence	Low	127(50.8)
	Moderate	68(27.2)
	High	55(22.0)

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Table 2. Results of ANOVA for assessing the relationship between medication adherence and right and left ABI among patients

Variables		Mean±SD	
		Right ABI	Left ABI
Medication adherence	Low	1.054±0.146	1.023±0.115
	Moderate	1.059±0.124	1.032±0.11
	High	1.074±0.115	1.072±0.107
ANOVA test		F=0.904 df=2.247, P=0.406	F=3.663 df=2.247, P=0.027

Table 3. Evaluation of the relationship between right and left sides ABI with demographic variables of patients

Variables		Right ABI Mean±SD	P	Left ABI Mean±SD	P
Educational level	Illiterate	1.041±0.143		0.998±0.104	
	High school	1.036±0.027	0.027	1.033±0.105	0.002
	Diploma	1.067±0.152		1.033±0.133	
	University degree	1.11±0.077		1.10±0.064	
	Test results*	F=3.112, df=3.246, P=0.027		F=5.243, df=3.246, P=0.002	
Occupation	Housekeeper	1.040±0.142		1.026±0.115	
	Employed	1.090±0.085	0.115	1.091±0.078	0.01
	Unemployed	1.027±0.163		1.040±0.070	
	Retired	1.07±0.131		1.022±0.125	
	Test results*	F=1.99, df=3.246, P=0.115		F=3.85, df=3.246, P=0.01	
Marital status	Single/Divorced	1.042±0.147	0.505	1.019±0.128	0.306
	Married	1.019±0.128		1.04±0.110	
	Test results**	t=0.668, df=248, P=0.505		t=-1.026, df=248, P=0.306	
Gender	Male	1.077±0.136	0.067	1.052±0.120	0.118
	Female	1.044±0.132		1.028±0.109	
	Test results**	t=1.841, df=248, P=0.067		t=1.568, df=248, P=0.118	
Smoking	Yes	0.969±0.190	>0.001	0.991±0.085	0.030
	No	1.065±0.123		1.042±0.115	
	Test results**	t=-3.532, df=248, P<0.001		t=-2.188, df=248, P=0.030	

* Independent t-test; ** One-way ANOVA.

level, 1.032±0.11, and for the high level, 1.072±0.107. It was reported that 98.2% of patients with high level of medication adherence had a normal left ABI (0.1 to 9.4) and 96.4% had a normal right ABI.

The relationship between demographic variables and the right and left ABI values was assessed using the one-way ANOVA. According to the results, the Mean±SD of the right ABI was 1.041±0.143 for the illiterate patients, 1.036±0.027 for those with high school education, 1.067±0.152 for those with diploma, and 1.11±0.077 for those with a university degree. A statistically significant difference was observed in the mean right ABI scores in terms of educational level (P<0.05). The Mean±SD of the left ABI was 0.998±0.104 for the illiterate patients, 1.033±0.105 for those with high school education, 1.033±0.133 for those with diploma, and 1.10±0.064 for those with a university degree. A statistically significant difference was observed in the mean left ABI scores in terms of educational level (P<0.05) (Table 3). There was no statistically significant difference between the left and right ABI scores.

In terms of occupation, the Mean±SD of the left ABI was obtained 1.026±0.115 for housekeeper patients, 1.091±0.078 for employees, 1.043±0.070 for unemployed patients, and 1.022±0.125 for retirees. A statistically significant difference was observed in the mean scores of left ABI in terms of occupation (P<0.05) (Table 3).

In terms of smoking, the Mean±SD of the right ABI was 0.969±0.190 in smokers and 1.065±0.123 in non-smokers. The Mean±SD of the left ABI was 0.991±0.085 in smokers and 1.042±0.115 in non-smokers. The results of independent t-test indicated that the differences were statistically significant (P<0.05) (Table 3).

The relationship between medication adherence and demographic variables was also investigated using the chi-square test. According to the results, a statistically significant relationship was observed only between marital status and medication adherence (P<0.05). The medication adherence status of single patients was higher than that of married patients. The relationship between patients' age and the right and left ABI values was examined and an indirect relationship was observed between age and the right ABI (r=-0.227), and between age and the left ABI (r=-0.988), both were statistically significant (P<0.05).

4. Discussion

The present study investigated the relationship between medication adherence and the ABI in patients with hypertension. In the current study, 78% of patients had low to moderate medication adherence and their Mean±SD medication adherence was 5.88±1.74. Zare also conducted a study on 282 patients with heart diseases taking antihypertensive drugs by using MMAS-8 questionnaire. The results revealed that adherence to the antihypertensive medication regimen was low in 76.95% of patients [14]. In a study by Fakhri et al. in Qazvin, only 7.8% of patients had high medication adherence [20]. In the present study, medication adherence was low in 50.8% of patients. They also indicated that less than half of patients (30%-39%) used their medications correctly and 65% did not use their medications correctly; they reduced or stopped taking them. In a study on Chinese hypertensive patients, Shen et al. stated that more than half of patients with hypertension adhered to anti-hypertensive medication regimen [21]. This discrepancy can be due to patients' sensitivity to the correct use of medications and lack of awareness of the positive effects of medications on lowering blood pressure. Physicians and other health care providers should increase patients' awareness of the benefits of taking the medications in a timely manner and in accordance with prescribing instructions.

In the current study, the Mean±SD of the right and left ABI were 1.055±0.134 and 1.036±0.113, respectively. Regarding the right ABI, 90.4% of patients had a normal ABI, 9.2% had ABI<0.9 (indicating the presence of peripheral arterial disease), and 0.4% had ABI>1.4 (indicating that the blood vessels in lower limbs are stiff). In terms of the left ABI, 90.4% had a normal ABI, 8.8% had ABI<0.9, and 0.8% had ABI>1.4. In a prospective study in Spain on 5679 patients, 5517 (97.1%) had a normal ABI, while 162 (2.9%) had ABI≥1.4 [22], which is consistent with the results of the present study. A study by Królczyk in Poland on the different effects of ABI on mortality in older patients, 118 participants had a low ABI (13.9%), 662 had a normal ABI (77.7%), and 72 had a high ABI (8.4%) [23].

The results of the present study regarding the prevalence of abnormal ABI, are consistent with the previous studies. The reported prevalence is normal compared to epidemiological data from the general population (3%-10%) [20], but for specific patient populations, such as patients with hypertension (40.9% and 67.3%) [24, 25], with cardiovascular disease (31.6%) [26], elderly people with hypertension (25.5% and 26.8%)

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[27, 28], and arterial hypertension (29.7%) [29] it is likely to be abnormal. Furthermore, in other studies on patients with hypertension, the prevalence of abnormal ABI was reported 17.5% [30] and 19% [31]. It should be noted that although the study population in our study were people with hypertension, all participants were asymptomatic and had no history of the disease.

In the current study, the ABI had a negative significant relationship with age which is consistent with the results of Velescu [22]. In our study, with decrease of educational level, the ABI value decreased and, hence, the risk of vascular stenosis increased. In a study by de Bulhões, no association was found between abnormal ABI and level of education [31]. The relationship between the ABI and smoking was statistically significant in our study, such that abnormal ABI was higher in smokers (19.2%) than in non-smokers (8%). In the study by Velescu, there was no association between smoking and abnormal ABI [22], which is not consistent with the present study. Epidemiological studies should be performed in different parts of the world to collect data on the incidence and prevalence of abnormal ABI.

According to the results of the present study, there was a significant relationship between patients' medication adherence and the ABI such that the high medication adherence reduced the prevalence of abnormal ABI. In this regard, no similar study was found to compare the results. The results of Hemmati Maslakpak indicated that educating and following up the patients using reminder cards improved their adherence to treatment [32]. Pérez-Idárraga et al. reported that a proper diet education along with an exercise program could reduce the cardiovascular risk factors [33]. In a study by Zakipour et al., the intervention led to an increase in medication adherence of patients with ischemic heart disease [34].

Overall, the present study revealed the importance of medication adherence in the prevention of cardiovascular diseases. There is a need to increase the medication adherence of patients with hypertension by teaching the proper method of taking medications and self-care skills and awareness. One of the most important limitations of this study was the lack of access to the Doppler device in Iran, which was borrowed from a physician. Also, considering the age of the participants, not all patients had reading and writing literacy; hence, the questionnaires were completed by interviewing them.

5. Conclusion

The medication adherence is poor in most hypertensive patients in Karaj, Iran. Their medication adherence is directly related to the ABI value, such that by the decrease of medication adherence, their ABI decreases. Adherence to medication regimen in patients with hypertension can be effective in preventing cardiovascular complications. In patients with hypertension, medication adherence decreases with ageing. The role of adherence to medication regimens in preventing disease recurrence, reducing future disabilities, and maintaining independence requires designing and implementing programs to enhance the patients' willingness and ability to adhere to medications.

Ethical Considerations

Compliance with ethical guidelines

Prior to the study, the consent form was signed by all participants. They were assured that their information would be kept confidential. This study was approved by the ethics committee of Qazvin University of Medical Sciences (Code: IR.QUMS.REC.1399.459).

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