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Association Between Exaggerated Blood Pressure Response to Exercise with Masked Hypertension in Persons with Normal Blood Pressure

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Original Article

Summary

The masked hypertension is common health problem facing physicians due to difficulty in detection and its future co-morbidities. Early detection of masked hypertension is helpful in preventing cardiovascular complications and decreasing the death rates. We aimed to evaluate the incidence of masked hypertension in normotensive population with exaggerated blood pressure response to exercise. Hence, a clinical prospective follow up study carried out in Cardiology department of Surgical Specialty Hospital in Erbil city, Kurdistan region/Iraq during one year period included 120 normotensive persons, 60 persons (cases) with positive, and 60 persons with negative (as controls), exaggerated blood pressure response to exercise, respectively. Diagnosis of normal blood pressure, exaggerated blood pressure response to exercise levels, ambulatory blood pressure levels and masked hypertension according to European Society of Hypertension guidelines. Findings revealed significantly higher prevalence of masked hypertension and positive exaggerated blood pressure response to exercise ($p<0.001$). The means of day time, night time and mean 24 hour ambulatory blood pressure were significantly higher in cases than controls ($P<0.05$, in all comparisons). Physical inactivity and smoking history are the common risk factors of exaggerated blood pressure response to exercise. In conclusion, The exaggerated blood pressure response to exercise in normotensive persons is associated with masked hypertension.

Keywords: *Masked hypertension, exaggerated blood pressure response to exercise, Ambulatory blood pressure monitoring.*

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1. INTRODUCTION

Despite the worldwide use of antihypertensive agents, the blood pressure mean in all over the world remains stable or reduced slightly in last 40 years and hypertension prevalence was increased especially in developing countries with wide increase of risk factors prevalence such as high salts intake, obesity, physical inactivity and sedentary lifestyles. Although these recorded changes in hypertension prevalence; the population awareness, prevention and self-control of blood pressure were low mainly in developing countries (1). The hypertension is the most prevalent etiology of cardiovascular diseases and early death globally. The uncontrolled hypertension is responsible for many complications like coronary heart diseases, myocardial infarction, cerebrovascular accident, hypertensive encephalopathy, renal failure, peripheral arterial diseases, aortic aneurysm and high mortality rates (2,3). Many screening tools were developed to help in identification of hypertension at earlier stages like exaggerated blood pressure response during the exercise treadmill test (4). The exaggerated blood pressure response to exercise is regarded as a common risk factor for development of hypertension and cardiovascular diseases. It was found that chance of hypertension among normotensive persons with positive exaggerated blood pressure response to exercise is about four to five times greater than normotensive persons with normal blood pressure by exaggerated blood pressure response to exercise (5). However, other authors found no association between exaggerated blood pressure response to exercise and development of hypertension (6). The masked hypertension is diagnosed technically when office blood pressure measures are within normal range, while the out-of office-blood pressure measures by ambulatory blood pressure measurement are high (7-9). For known hypertensive cases on treatment, high blood pressure reading by ambulatory assessment after normal blood pressure measurement by office assessment is called masked uncontrolled hypertension (7). The masked hypertension (MH) is accompanied by high rates of organs damage, cardiovascular diseases and death (10). The clinic or office blood pressure assessment depends mainly on three blood pressure readings in the office. Since few years ago, the true blood pressure was described after assessing the ambulatory blood pressure (11), which defined as the mean blood pressure level, through time, during natural environment. Many authors reported that clinic blood pressure had low validity in diagnosis of true blood pressure and the ambulatory blood pressure monitoring that measuring the out-

of-clinic blood pressure during the whole day environment had higher validity in diagnosis of true blood pressure (12). Masked hypertension is directly related to high rates of cardiovascular co-morbidity and all-cause mortality in addition to great burden on national health institutes. Recently, many guidelines encouraged the physicians to select the out-of-office blood pressure monitoring to diagnose the masked hypertension in some situations. Many challenges in screening of masked hypertension were recorded especially in inclusion criteria and the best screening tool. Nowadays, the ambulatory or home blood pressure monitoring for blood pressure are widely used. However, the screening of masked hypertension requires more valid, easy applicable and cost-effective tools than routine applicable tools (13). Positive exaggerated BP response to exercise test is mainly related to endothelial dysfunction, low proximal aortic compliance and higher exercise-related neurohormonal activation that all related to cardiovascular risk factors (14). The left ventricular hypertrophy, close family history of hypertension, obesity and cardiovascular risk factors are considered as the main risk factors for masked hypertension . The prevalence of masked hypertension was found to occur in about 10-30% of population (7) and the masked hypertension is detected by ambulatory blood pressure assessment in 14% of persons, while the home blood pressure assessment detected 11% of masked hypertension (15). Nowadays, it is recommended screening of masked hypertension by ambulatory blood pressure monitoring when office blood pressure is between 120/75 to 129/79 mmHg (15-18). In Iraq, the hypertension prevalence among adults is shown to reach about 44% of population (19). In fact, literatures discussing hypertension prevalence and control among Iraqi population are scarce. In previous study, it was shown that blood pressure control was observed among 48.2% of hypertensive patients with diabetes mellitus (20). Blood pressure control represented a problem for health policy makers in Iraq and the uncontrolled hypertension is a major public health problem that needs strategic planning and modernized health polices in changing the guidelines of blood pressure assessment and identifying masked hypertension and white coated hypertension (21). Recent study revealed that blood pressure control in Iraq was suboptimal (22). The hypertension prevalence in Erbil city is relatively high with high prevalence of undiagnosed hypertension (23). For all of these reasons, this study aimed to evaluate the relationship between exaggerated blood pressure response to exercise and masked hypertension in normotensive population.

2. PATIENTS and METHODS

The current study was a clinical prospective follow up study carried out in Cardiology department of Surgical Specialty Hospital in Erbil city, Kurdistan region/Iraq. The duration of the study was one year through the period from 1st of August, 2020 to 31st of July, 2021. The study population was persons with normal blood pressure referred to exercise Electrocardiography (ECG) Stress Unit of Surgical Specialty Hospital. The exclusion criteria were patients with confirmed diagnosis of hypertension, patients taking anti-hypertensive medications, pregnant women and contraindications of exercise test like unstable angina, severe symptomatic atrial stenosis. The ethical considerations were implemented according Helsinki Declaration regarding ethical approval of Health authorities, an ethical approval was taken from Kurdistan Board Ethical Committee, confidentiality of data, an oral informed consent was taken from each selected person and management of hypertensive patients accordingly. A convenient sample of 60 normotensive persons with exaggerated blood pressure response to exercise was selected. Another sample of 60 normotensive persons with negative exaggerated blood pressure response to exercise test was selected as controls.

The data were collected by the researcher from selected persons directly and fulfilling a prepared questionnaire. The researchers designed the questionnaire. The questionnaire included the followings: general characteristics of normotensive persons (age, gender, weight, history of diabetes mellitus, hyperlipidemia, family history of hypertension, physical activity (regular exercise for at least one hour daily and 3 days per week), smoking history (current or ex-smoking as positive and negative if no smoking history) and investigational findings of selected normotensive persons (HbA1c test, total cholesterol level, HDL cholesterol level, LDL cholesterol level and serum creatinine level). Diagnosis of normal was done by the researcher according to European Society of Hypertension guidelines with systolic blood pressure of 120-139 mmHg and diastolic blood pressure of 75-89 mmHg (7).

The exaggerated blood pressure response to exercise with Treadmill test was done by specialized nurse under supervision of researcher. The Treadmill equipment used was (MORTARA-Philips-Germany). Positive exaggerated blood pressure response to exercise was defined by systolic blood pressure more than 200 mmHg in men and systolic blood pressure more than 180 mmHg in women.

The ambulatory blood pressure monitoring was done for both groups by specialized nurse under supervision of researcher by (Philips ambulatory BP monitor device-Germany) and the interpretation of results was according to European Society of Cardiology and European Society of Hypertension guidelines. High ambulatory blood pressure is defined according to European Society of Cardiology and European Society of Hypertension guidelines (7).

Daytime mean BP= systolic BP≥135 mmHg and or diastolic BP≥85 mmHg.

Night time mean BP= systolic BP≥120 mmHg and or diastolic BP≥70 mmHg.

24-hour mean BP= systolic BP≥130 mmHg and or diastolic BP≥80 mmHg.

The masked hypertension was defined if 24-hour mean BP was ≥130/80 mmHg, daytime mean BP≥135/85and or mean nighttime blood pressure was ≥120/70 mmHg7.

The data collected were analyzed statistically by Statistical Package of Social Sciences software version 22. The Chi square and Fischer's exact tests were applied for analyzing the data as suitable. Independent sample t-test was used to compare between two means. Level of significance (p. value) was regarded statistically significant if it was 0.05 or less.

3. RESULTS

We selected 60 persons with positive exaggerated blood pressure (BP) response to exercise and 60 persons with negative exaggerated BP response to exercise. No significant differences were observed between normotensive persons with positive exaggerated BP response to exercise and normotensive persons with negative exaggerated BP response to exercise regarding age (p=0.55), gender (p=0.6), weight (p=0.2), history of diabetes mellitus (p=0.2), history of hyperlipidemia (p=0.8) and family history of hypertension (p=0.5). The positive exaggerated BP response to exercise was significantly higher among those with negative physical activity (p=0.04), and positive smoking (p=0.007). (Table 1). No significant differences were observed between normotensive persons with positive exaggerated BP response to exercise and normotensive persons with negative exaggerated BP response to exercise regarding HbA1c level (p=0.3), total cholesterol level (p=0.3), HDL cholesterol level (p=0.08) and LDL cholesterol level (p=0.08). The serum creatinin level was normal for all of studied persons. (Table 2). Although the findings of daytime ambulatory blood pressure measurement is not significant between normotensive persons with positive exaggerated BP response to exercise and normotensive persons with negative

exaggerated BP response to exercise (p=0.4), the mean daytime blood pressure of normotensive persons with positive exaggerated BP response to exercise was significantly higher than mean daytime blood pressure of normotensive persons with negative exaggerated BP response to exercise (p=0.01). There was a significant association between positive night time BP measurement and of normotensive persons with positive exaggerated BP response to exercise (p=0.003). Although the findings of 24-hours ambulatory blood pressure measurement is not significant between normotensive persons with positive exaggerated BP response to exercise and normotensive persons with negative exaggerated BP response to exercise (p=0.1), the mean 24-hours blood pressure of normotensive persons with positive exaggerated BP response to exercise was significantly higher than 24-hours mean blood pressure of normotensive persons with negative exaggerated BP response to exercise (p<0.001). A highly significant association was observed between high prevalence of masked hypertension among normotensive persons with positive exaggerated BP response to exercise (p<0.001), sixty percent of normotensive persons with positive exaggerated BP response to exercise had masked hypertension, while 6.7% of normotensive persons with negative exaggerated BP response to exercise had masked hypertension. (Table 3 & 4).

Table 1. Distribution of normotensive persons' general characteristics according to exaggerated BP response to exercise.

Variable		Response				P
		Positive		Negative		
		No.	%	No.	%	
Age (year)	<40	12	20.0	21	35.0	0.055 NS
	40-49	28	46.7	16	26.7	
	50-59	8	13.3	14	23.3	
	≥60	12	20.0	9	15.0	
Gender	Male	44	73.3	42	70.0	0.6 NS
	Female	16	26.7	18	30.0	
Weight	<80 Kg	24	40.0	31	51.7	0.2 NS
	≥80 Kg	36	60.0	29	48.3	
Diabetes mellitus		20	33.3	14	23.3	0.2 NS
Family history of hypertension		48	80.0	45	75.0	0.5 NS
Physical activity		56	93.3	60	100.0	**0.040** S
Smoking		28	46.7	14	23.3	**0.007** S

S=Significant, NS=Not significant.

Table 2. Distribution of normotensive persons' investigations findings according to exaggerated BP response to exercise.

Variable		Response				P
		Positive		Negative		
		No.	%	No.	%	
HbA1c level (%)	<6.5	36	60.0	41	68.3	0.3 NS
	≥6.5	24	40.0	19	31.7	
Total cholesterol level	Normal	40	66.7	45	75.0	0.3 NS
	High	20	33.3	15	25.0	
HDL cholesterol level	Normal	28	46.7	27	45.0	08 NS
	High	32	53.3	33	55.0	
LDL cholesterol level	Normal	40	66.7	45	75.0	0.3 NS
	High	20	33.3	15	25.0	
Serum creatinine level	Normal	60	100.0	60	100.0	-
	High	0	-	0	-	

NS=Not significant.

Table 3. Distribution of normotensive persons' ambulatory blood measurement findings according to exaggerated BP response to exercise.

Variable		Response				**P**
		Positive		Negative		
		No.	**%**	**No.**	**%**	
Daytime BP	Positive	12	20	9	15.0	0.4 NS
	Negative	48	80	51	85.0	
Night time BP	Positive	39	65	23	38.3	**<0.001 S**
	Negative	21	35	37	61.7	
24-hrs mean BP	Positive	23	38.3	15	25.0	**0.1** NS
	Negative	37	61.7	45	75.0	
Masked hypertension	Positive	36	60	4	6.7	**<0.001** S
	Negative	24	40	56	93.3	

S=Significant, NS=Not significant.

Table 4. Comparison of mean values of BP of normotensive persons' ambulatory blood measurement according to exaggerated BP response to exercise.

Variable		Response				P
		Positive		Negative		
		Mean	SD	Mean	SD	
Daytime BP (mmHg)	SBP	125.6	15.6	119.1	11.5	**0.01** S
	DBP	78.9	8.9	68.7	6.8	
Night time BP (mmHg)	SBP	120.2	14.8	106.9	10	**<0.001** S
	DBP	70.8	9.3	68.7	9.3	
24-hrs mean BP (mmHg)	SBP	122.6	14.5	112.2	8.2	**<0.001** S
	DBP	75.5	8.4	75.0	4.6	

SD: standard deviation; S=Significant, NS=Not significant.

4. DISCUSSION

Present study showed a highly significant association between high prevalence of masked hypertension detected by ambulatory blood pressure monitoring and normotensive persons with positive exaggerated BP response to exercise ($p<0.001$). This finding is consistent with results of many literatures such as Kayrak et al. (24) study in Turkey and Peacock et al. (25) study in USA which documented that normotensive persons with positive exaggerated BP response during exercise of treadmill test are more likely to develop masked hypertension than normotensive persons with negative exaggerated BP response during exercise of treadmill test. However, our study findings are inconsistent with results of Grossman et al. (26) study on 277 patients with high-normal blood pressure undergone exaggerated BP response to exercise test and ambulatory blood pressure monitoring test and found that masked hypertension was not associated with exaggerated BP response to exercise. This inconsistency might be attributed to differences in blood pressure cutoff values adopted by different guidelines in addition to differences in sample size and design of different studies. A study conducted in Greece by Dipla et al. (27) on 16 patients with masked hypertension and 26 normotensive persons found that using brief low intensity handgrip exercise test is useful in screening of masked hypertension. Another study carried out in Brazil by Dutra-Marques et al 28 reported that reported that exaggerated blood pressure exercise test is a significant marker of hypertension, sympathetic hyperactivation, low baroreflex sensitivity

and future cardiovascular complications.

The current study revealed that (60%) of normotensive persons with positive exaggerated BP response to exercise developed masked hypertension, while only (6.7%) of normotensive persons with negative exaggerated BP response to exercise developed masked hypertension. These findings are close to results of Miyai et al.(29) study in Japan which revealed that more than 50% of study sample with positive exaggerated BP response to exercise had developed masked hypertension. In our study, means of blood pressure at day time, night time and 24-hour mean blood pressure were significantly higher among normotensive persons with positive exaggerated BP response to exercise. These findings are in agreement with reports of Kim et al. (30) study in South Korea which stated that increased means of blood pressure recoded by ambulatory blood pressure monitoring in normotensive persons with positive exaggerated BP response to exercise is diagnostic of masked hypertension.

In the present study, there was a significant association between normotensive persons with positive exaggerated BP response to exercise and physical inactivity (p=0.04). This finding coincides with results of Bond et al. (31) study in USA which stated that changes in total peripheral vascular resistance accompanying regular physical activity affected the results of exaggerated BP response to exercise treadmill test. Our study found also a significant association between normotensive persons with positive exaggerated BP response to exercise and positive smoking (p=0.007). This finding is similar to results of Thanassoulis et al. (32) study in USA which documented that smoking is a common risk factor for positive exaggerated BP response to exercise among normotensive persons.

5. CONCLUSIONS

Exaggerated blood pressure response to exercise in normotensive persons is associated with masked hypertension. Physical inactivity and smoking history are the common risk factors of exaggerated blood pressure response to exercise. This study recommended physicians to select the exaggerated blood pressure response to exercise test in screening of masked hypertension. Further longitudinal researches on validity of exaggerated blood pressure response to exercise test must be supported.

Ethical Clearance: Ethical clearance and approval of the study are ascertained by the authors. All ethical issues and data collection were in accordance with the World Medical Association Declaration of Helsinki 2013 for ethical principles for medical research involving human subjects, informed consent obtained from all patients. Data and privacy of patients were kept confidentially.

Conflict of interest: Authors declared none

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