Epidemiological insights of hypertension incidence; findings from the ATTICA Prospective Study, 2002-2022

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ABSTRACT

Aims: The aim of the present work was to evaluate the 20-year hypertension incidence in Greece. **Methods:** In 2002, 3,042 men and women (>18 years) without any clinical evidence of cardiovascular disease, living in greater Athens area, in Greece, were enrolled. In 2022, the 20-year follow-up was performed. Hypertension was defined according to WHO-ICD-10 criteria. To study the hypertension incidence, participants who had been identified as hypertensive at baseline examination (912 individuals) were excluded; thus, and considering those who were lost to the follow-up, data from 1,415 non-hypertensive Greek adults (44% men, age: 41±13 years) were analysed. **Results:** The 20-year hypertension incidence was 22.2% (n=314). The profile of participants who developed hypertension during the 20-year period was mainly characterised by older, men with low educational and socio-economic level. Hypertension incidence was significantly associated with obesity (p<0.001), diabetes (p<0.001), hypercholesterolemia status (p<0.001) and increased triglycerides levels (p=0.005). **Conclusion:** The 20-year incidence of hypertension was particularly high. For this reason, continuous actions to raise awareness of the population and a personalized approach that will help to prevent hypertension are necessary.

🔑 **Key-words:** hypertension, risk, incidence, epidemiology, prevention

INTRODUCTION

Hypertension is one of the leading causes of cardiovascular disease (CVD) incidence and premature death, worldwide. Based on estimates, in 2010, 31.1% of adults (1.39 billion) worldwide had high blood pressure. Specifically, the prevalence of hypertension among adults was higher in low- and middle-income countries (31.5%, 1.04 billion people) than in high-income countries (28.5%, 349 million people). In 2015, an estimated 8.5 million deaths were attributable to high systolic blood pressure, 88% of which were in Asian and African countries[1].

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In line with these figures, the World Health Organization (WHO) reports that an estimated 1.28 billion individuals aged 30-79 years have hypertension, worldwide, and most of them (i.e., 2 out of 3) are living in low- and middle-income countries. An estimated 46% of adults with hypertension are unaware that they have the condition. Less than half of adults (i.e., 42%) who have hypertension are diagnosed and treated, whereas only 1 in 5 adults (i.e., 21%) with hypertension have it under control. One of the global targets of WHO for non communicable diseases is to reduce the prevalence of hypertension by 33% between 2010 and 2030[2].

One way to control or reduce the prevalence of hypertension is the pharmacological treatment. The World Health Organization recommends initiation of pharmacological treatment in adults with a confirmed diagnosis of hypertension, when systolic blood pressure is ≥140 mmHg or diastolic blood pressure is ≥90 mmHg. Those with existing cardiovascular disease and systolic blood pressure of 130-139 mmHg or without any cardiovascular disease but at high risk, such as diabetic patients and systolic blood pressure of 130-139 mmHg should also start a pharmacological treatment. First line treatment includes: thiazide and thiazide-like agents, angiotensin enzyme inhibitors (ACE) and long acting dihydropyridine calcium channel blockers (CCBs). The target blood pressure goal is <140/90 mmHg in all patients with hypertension and <130 mmHg in patients with hypertension and cardiovascular disease or other comorbidities[3].

However, due to the widespread use of effective antihypertensive medications, it has been suggested that the mean blood pressure levels of individuals around the world have remained constant or decreased slightly over the past four decades[4]. Nevertheless, management of hypertension remains a global challenge, as even a combination of antihypertensive medications is not enough to control blood pressure levels and decrease CVD risk. Lifestyle modifications include stopping smoking, being physically active for at least 150 minutes per week, whereas dietary recommendations are mainly based on sodium and trans fatty acids restrictions; few studies have also shown that a Mediterranean type of diet can contribute to a relatively small but significant reduction of blood pressure levels[5,6].

Current epidemiologic data regarding the prevalence and incidence of hypertension in the Greek population are sparse in the literature. Thus, the aim of the present study was to present epidemiological insights of the 20-year hypertension incidence, in Greece, based on a representative sample of the adult Greek population from the ATTICA study (2002-2022).

METHODS

Study design

The ATTICA study is a prospective cohort study carried out in adult women and men, living in the greater Athens area in Greece. Baseline assessment was conducted during 2001-2002, and multiple follow-ups were conducted in 2006, 2012 and 2022[7,8,9,10].

Sampling procedure

Based on a stratified by age and sex, random sampling procedure, 3,042 individuals (1,514 men and 1,528 women), aged 18 years-old or older, were enrolled in the study, during 2001-2002, all living in the Athens metropolitan area (baseline examination). The main exclusion criterion at baseline examination was the absence of any cardiovascular disease. For the present epidemiological analysis participants who had been identified as hypertensive (see below for definition) at baseline examination (i.e., 610 individuals) were excluded; thus, considering those who were lost to the 20-year follow-up (i.e., 144 individualshad missing, incorrect or incomplete contact information or refused to be screened again), data from 1,415 participants (44% men, age: 41±13 years) were analysed in this work. No significant differences were observed between those who were lost to follow-up and the rest of the participants regarding sex (p=0.99) and age distribution (p=0.78), body mass (p=0.88), smoking habits (p=0.12), physical activity status (p=0.44), dietary habits (all p-values>0.20), education level in years of school (p=0.67), as well as history of hypertension (p=0.12), diabetes (p=0.27) and hypercholesterolemia (p=0.12).

Power analysis

The sample used in this analysis was adequate and representative to evaluate relative risks equal to 1.10, achieving >80% statistical power at the 5% level of statistical significance (two-sided hypotheses).

Measured characteristics

Participants' demographic characteristics, medical history, dietary and lifestyle habits were recorded following standard procedures, as it can be found in

detail in previous publications[8,10]. Cardiologists, internists, nurses, and dietitians performed face-to-face interviews and clinical examinations of the participants, both at baseline and follow-up examinations. Specifically, arterial blood pressure was measured at the end of the physical examination with individuals in sitting position, at least 30 minutes at rest; blood pressure measurements were taken three times, at the right arm relaxed and well supported by a table, with an angle of 45° from the trunk (ELKA aneroid man metric sphygmometer, Von Schlieben Co, West Germany). Systolic blood pressure was determined by the first perception of sound (of tapping quality) and diastolic blood pressure was determined by phase V when the repetitive sounds disappear. Following the International Coding of Diseases (ICD)-10, participants whose average systolic/diastolic blood pressure levels were greater or equal to 140/90 mmHg or were under antihypertensive medication or had been diagnosed by a physician, were classified as hypertensive. Moreover, hypertensive patients were asked about the reception and type of medication; those who answered no to any medication were classified as untreated; those who answered yes, but their blood pressure levels were not controlled (i.e., >140/90 mmHg) were classified as treated-uncontrolled; the rest of them were classified as controlled. Body mass index (BMI) was measured as weight (in kilograms) divided by standing height (in meters squared). Obesity was defined as body mass index (BMI)>29.9 Kg/m². Central obesity was defined according to the WHO criteria as waist circumference ≥102 cm for men and ≥88 cm for women. For the other clinical characteristics, hypercholesterolemia was defined as total cholesterol levels more than 220 mg/dl or the use of hypolipidemic medication, hypertriglyceridemia as triglycerides levels more than 150 mg/dl, diabetes mellitus as a fasting blood sugar >125 mg/dl or the use of antidiabetic medication. Dietary habits were evaluated through a validated food frequency questionnaire[11], whereas adherence to the Mediterranean diet was assessed using the MedDietScore[12] i.e., a validated diet index that incorporates all main characteristics of the traditional Mediterranean diet and has a theoretical range of 0-55, where higher values indicate greater adherence. MedDietScore was also divided into two groups (low adherence if score was <27, suggesting being away from the traditional dietary pattern, moderate-to-high adherence if score was >=27, suggesting being close to the traditional pat-

tern). Pack-years of cigarette smoking were calculated for each participant by multiplying smoking duration (in years) with the number of packs/day (assuming 20 cigarettes in a pack). Physical activity was divided into four groups based on the type and intensity of physical exercise (minimally active, aerobic moderate, aerobic health-enhancing physical activity, aerobic and resistance).

Bioethics

The approval of the study was obtained from the Institutional Ethics Committee of Athens Medical School (#017/1.5.2001) and was carried out in accordance with the principles of the Declaration of Helsinki (1989) of the World Medical Association. All participants were informed about the purpose and procedures of the study, and they agreed to participate providing their written consent.

Statistical Analyses

Continuous variables are presented as mean and standard deviation (SD), while categorical variables are presented as absolute and relative frequencies (percentages). To evaluate the relationship between categorical variables, the Pearson's chi-square test was applied. Differences in mean values of continuous variables, after tested for normality through P-P plots, where assessed using Student's t-test or the Mann-Whitney test. Crude non-fatal and fatal incidence rates of hypertension were calculated as the ratio of new cases to the number of people that participated in each of the three follow-up examinations. All reported p-values were based on two-tailed hypotheses. STATA version 17 (STATA Corp, College Station, Texas, USA) was used for the statistical analyses.

RESULTS

In total, during the 20-year follow-up period 152 men (48,4%) and 152 women (48,4%) of the 1,415 who participated in the follow-up, were newly diagnosed as hypertensive. Of them, 85% of hypertensive men and 75% of hypertensive women were on special pharmaceutical and/or dietary treatment; 34% of hypertensive men and 32% of hypertensive women were found to be uncontrolled. In *Table 1* the baseline prevalence, as well as the 5-year, 10-year and 20-year incidence of hypertension is presented, in men and women. A strong linear trend was observed across all age groups, in both men and women. The

Table 1. Baseline prevalence and 5-, 10- and 20-year incidence of hypertension in the aging cohort of the ATTICA Study.

	Baseline examination, 2002	5-year follow-up, 2002-2006	10-year follow-up, 2002-2012	20-year follow-up, 2002-2022
No. of participants	3,042	2,104	1,154	1,415
Mean age(SD)	45.2 (13.8)	50.7 (13.8)	56.0 (14.1)	60.7 (12.5)
Men	382/1,000[*]	143/1,000	292/1,000	114/1,000
Women	239/1,000[*]	134/1,000	264/1,000	107/1,000

[*]hypertension prevalence rates at baseline; these patients were excluded from the follow-up examinations.

Table 2. Baseline socio-demographic and lifestyle characteristics (in 2002) of the ATTICA study's participants according to the 20-year incidence of hypertension (2002-2022).

	Status at 20-year follow-up		
	Normotensive	Developed hypertension	P
No. of participants	1,101	314	
Socio-demographic characteristics			
Age (years), mean (SD)	38(11)	50(14)	0.001
Years of school, mean (SD)	13(3)	11(4)	0.001
Marital status, % married	61%	78%	0.001
Socio-economic status, % low	9%	22%	0.001
Lifestyle factors			
Pack-years of smoking, mean (SD)	366(375)	545(538)	0.001
MedDietScore (0-55), mean (SD)	28(6)	24(6)	<0.001
Physical activity, % minimally active	61%	65%	0.045

Continuous variables are presented as mean and standard deviation (SD). Categorical variables are presented as absolute and relative frequencies (percentages).

sex-adjusted risk of hypertension increased by 11% per 10-year increase in age during the first 10 years of follow-up (95%CI 9% to 12%), and by 48% per 10-year increase in age during the second follow-up period, i.e., 2012-2022 (95%CI: 21% to 97%).

The distribution of baseline demographic, clinical and lifestyle characteristics, into those who were diagnosed as hypertensive during the 20-year follow-up and the rest of the participants, is presented in *Table 2*. It was observed that hypertensive individuals were older (p<0.001), had higher BMI (p<0.05), blood glucose, total cholesterol and triglycerides levels, as well as higher prevalence of hypercholesterolemia and diabetes and lower level of education and Mediterranean diet adherence (p<0.001), as compared to those who were not diagnosed.

DISCUSSION

The aim of our present study was to evaluate the 20-year (2002-2022) incidence of hypertension in Greece based on current data from the ATTICA epidemiological cohort study. We observed that the 20-year incidence of hypertension was 22.2% and was strongly dominated by age of the participants. Moreover, during the second follow-up period (i.e., 2012-2022), the risk of hypertension quadrupled for every 10-year increase in age compared to the first decade (i.e., 2002-2012). In addition, many hypertensive individuals were not adequately treated or were untreated, and had several other co-morbidities, mainly obesity, hypercholesterolemia, and diabetes.

One of the first large-scale epidemiologic studies in Greece, that was conducted in late 1990s, the Greek European Prevention In Cancer (EPIC) study, a large population-based study with approximate-

Table 3. Baseline clinical, anthropometric and biochemical characteristics (in 2002) of the ATTICA study's participants according to the 20-year incidence of hypertension (2002-2022).

| | Status at 20-year follow-up | | |
	Normotensive	Developed hypertension	P
	1,101	314	
Clinical and biochemical characteristics			
Obesity, %	8%	21%	0.001
Central obesity, %	39%	59%	0.001
Hypercholesterolemia %	31%	45%	0.001
Total cholesterol, mg/dl, mean(SD)	185(40)	197(44)	0.018
Triglycerides, mg/dl, mean(SD)	101(85)	125(75)	0.005
Diabetes, %	2%	9%	0.001
Glucose levels, mg/dl, mean(SD)	88(14)	95(26)	0.001
Anthropometric characteristics			
Body mass index, kg/m^2, mean(SD)	24(4)	27±4	0.022
Waist, cm, mean(SD)	84(14)	93(13)	0.136

Continuous variables are presented as mean and standard deviation (SD). Categorical variables are presented as absolute and relative frequencies (percentages).

ly 27,000 men and women participants from all over Greece reported that the prevalence of hypertension was 40.2% for men and 38.9% for women (age-adjusted to the adult Greek population of 2001). Moreover, awareness among hypertensives was 54.4%, use of pharmaceutical treatment among those aware was 83.9%, and effective control among hypertensives was only in 15.2%. In addition, and similarly to our findings, the prevalence of hypertension increased with age and was higher in rural areas and among individuals of lower education[13]. Epidemiology of hypertension in Greece has also been studied by the Hypertenshell Study. The study was conducted in early 2000s, with the collaboration of physicians from 98 Health Centers across Greece. A total of 11,950 individuals participated in the study. The prevalence of hypertension was 31.1% (i.e., men 33.6%, women 28.4%), whereas, among older individuals (i.e., >65 years) the prevalence was much higher (65.4%). Of the hypertensive individuals, 39.8% were unaware that had hypertension and only 12.4% were aware but not treated (men 13.1%, women 11.8%). Overall, according to the Hypertenshell Study investigators, 51.2% of hypertensive participants were treated; 67.2% were treated but not controlled and 32.8% were treated and controlled[14]. More recently, the National Survey of Morbidity and Risk Factors (EMENO) cross-sectional study, which was carried out during 2013-2016, presented similar results with our study; in particular, based on the 4,822 stud-

ied participants (51.5% women, median age: 47.9 years), the prevalence of hypertension was 39.2%, and it was higher in men (42.4%) than in women (36.1%)[15,16]. Moreover, in the EMENO study, 31.8% of hypertensive participants were unaware of the condition, 2.7% were aware but untreated, 35.1% treated but uncontrolled and 30.5% treated and controlled. These figures are also in line with our findings, and highlight the emerging need for public health actions to reduce hypertension risk[15].

Regarding the CVD risk factors' profile of participants in our cohort, it was revealed that those who developed hypertension during the 20-year follow-up, had a higher prevalence of obesity and specifically central obesity, diabetes, hypercholesterolemia and high triglycerides. In addition, they had a lower adherence to the Mediterranean type diet (i.e., recorded a lower MedDietScore). According to the European and International guidelines of hypertension[17], hypertensive patients are recommended to consume a balanced diet that includes a variety of fruits and vegetables, whole products, unsaturated fats (mainly olive oil), fish and dairy products weekly and a limited intake of saturated lipids. Furthermore, better dietary habits should be accompanied with physical exercise and weight loss. Hypertensive patients should be advised to participate in at least 30 min of moderate intensity dynamic aerobic exercise on 5-7 days per week and performance of resistance exercises on 2-3 days per week. However, as it was observed here, 2 out of

3 (65%) with hypertension were minimally active. Regular aerobic physical activity may be particularly beneficial for both the prevention and treatment of hypertension. Moreover, the majority (59%) of our hypertensive participants had central obesity and 21% were obese. Excessive weight gain has been significantly associated with the risk of hypertension[18]. The goal in this case is the reduction or the stabilization of body weight in order to prevent or treat high blood pressure levels[17,18]. In our study, smoking was considered as one of the most important lifestyle-related risk factors for hypertension. Hypertensive individuals had almost double pack-years of cigarette smoking compared to normotensive individuals. According to the guidelines of hypertension[17,18], recommendations include smoking cessation, supportive care and the referral to smoking cessation programs. Nevertheless, public health actions should focus on helping individuals, especially young ones, to never start smoking[17].

Strengths and Limitations

The present study is the first prospective cohort study on hypertension epidemiology of this magnitude in Greece, and of the few globally, with a long follow-up period (i.e., 20 years), and multiple waves (baseline examination, 5-, 10- and 20-year follow-ups). The sample was representative in terms of age-sex distribution of the urban Greek population (which reflects about 70% of total Greek population), and different determinants were studied and presented here. However, some limitations exist and should be considered before generalizations can be made. Measurement error is a common limitation of epidemiological studies, and especially for the identification of hypertensive individuals (i.e., white-coat effect). However, the applied methodology of the current study was like other prospective studies, thus comparisons can be made. Participants lived in the greater Athens metropolitan area, a mainly urban region; therefore, this sample cannot represent the total Greek population, especially those living in non-urban, rural regions.

CONCLUSIONS

Hypertension affects a large percentage of the Greek population. Health information and awareness is deemed necessary for proper prevention and effective treatment. A life-course personalized approach that is cost-effective and long-term sustained is needed to prevent hypertension burden at population level.

Conflict of interest: None declared.

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