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Original Research

Evaluation of Hypertension-Related Mortality in Turkey (2000-2014)

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ABSTRACT

Objective: Hypertension continues to be the leading risk factor for cardiovascular disease (CVD) and mortality worldwide. The purpose of the present study was to analyze the long-term trends of hypertension mortality in Turkey between 2000 and 2014 (for males and females).

Methods: Analyses were based on hypertension mortality data obtained from the Turkish Statistical Institute death database. Age-standardized mortality rates were calculated using direct standardization for each calendar year. We estimated the age-adjusted linear trend for annual percent change and average annual percent change (AAPC) with the corresponding 95% confidence interval (CI) using the joinpoint regression analysis. Furthermore, we conducted an age–period–cohort analysis to quantify recent time trends and to evaluate the significance of cohort and period effects.

Results: During the study period, a significant upward trend in the mortality of hypertension in Turkey is observed (AAPC=2.7%, 95% CI 1.9%–3.4%). The trend of hypertension mortality has increased in both males (AAPC=7.4%, 95% CI 3.0%–11.9%) and females (AAPC=8.7%, 95% CI 4.1%–13.5%). We found that the net drift rateswere 2.1% (95% CI 0.6%–3.6%) per year for males and 2.0% (95% CI 0.4%–3.7%) per year for females. According to longitudinal age curves, the mortality of hypertension increased with age in both males and females. The period and cohort effects are highly significant in both males and females.

Conclusion: Hypertension is one of the leading causes of mortality causing CVD. Knowing the risk factors and preventive methods could help to reduce hypertension-related mortalities.

Keywords: Age–period–cohort analysis, hypertension, join point regression analysis, mortality rate

INTRODUCTION

We live in a rapidly changing environment. Today, aging, rapid urbanization, and the globalization of unhealthy lifestyles are three important and powerful forces that shape human health globally. Hypertension is one of the major causes of disease burden worldwide. It is the leading CVD that causes at least 45% of deaths mostly owing to ischemic heart disease. In addition, it is responsible for 51% of deaths due to total stroke mortality (1). This cardiovascular major risk factor currently affects 1 billion people worldwide and causes heart attacks and stroke. Approximately 9 million people die annually due to hypertension (2).

Hypertension is more prevalent in low-income countries, but a large number of people are affected in high-income countries. As more people live in low-income countries and have weak health systems than other countries, the number of affected people is higher in those countries. People with undiagnosed, untreated, and uncontrolled hypertension are also higher in low-income countries than in high-income countries (3-5). The African region is the most prevalent region for hypertension (46% of adults, >25 years), whereas Americans have the lowest prevalence (35%) (6). Increased prevalence of hypertension, unhealthy diet, harmful use of alcohol, lack of physical activity, overweight, and permanent stress exposure are linked to population growth, aging, and behavioral risk factors. In 2008, approximately 40% of adults had hypertension in the 25 and over age group worldwide (6, 7).

Manyprevious studies have been conducted in Turkey on different perspectives of hypertension, define its prevalence and associated risk factors, but most of these studies are limited to specific areas (8, 9). There are limited data of large-scale surveys with nationally representative sample populations performed during 1991–2011 (10-13). All these studies were cross-sectional and did not evaluate the whole hypertension variation trends through a long period, and so the influence of changing demographics is unclear. Furthermore, there has been no wide analysis of the possible reasons underlying the temporal trends. To address these limitations, we aimed to investigate the long-term trends of hypertension mortality in Turkey between 2000 and

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2014, examining age-, period-, and cohort-specific effects by sex with the aid of the age–period–cohort (annual percent change, APC). Findings from our study could provide clues on thespecific etiologic inclusion on hypertension mortality in Turkey.

Demographers, sociologists, and epidemiologists attempt to distinguish age, period, and cohort effects. Owing to the disaggregation of this kind of data, it is likely to provide significant clues to the trends of different results, such as fertility, death, crime rates, and disease incidence. Age–period–cohort models are designed to predict the independent effects of age (A), period (P), and cohort (C) (14, 15).

The aim of an age–period–cohort analysis is intended to distinguish the contribution of age, period, and cohort effects on mortality. Although age, period, and cohort do not directly explain the variation in death rates, they are proxies for underlying biological, communal, and economical factors that affect mortality. Age effect reflects the biological and social processing of aging in a person and shows thedevelopmental changes throughout life. Period effect represents a complex set of historical cases and environmental effects, such as wars and economic crisis.Shifts in social, economic, healthier diet, or physical environments may in turn induce similar changes in the lives of individuals at a point in time. Cohort effect is the changes between groups of individuals experiencing a first event, such as birth or marriage in the same year (16).

METHODS

Analyses were based on hypertension mortality (ICD 10: I10–I15) data from the Turkish Statistical Institute death databasebetween 2000 and 2014 (17). The analysis was performed including central population of cities and villages between 2001 and 2008, but it was based on the total population number between 2009 and 2014.

Statistical Analysis

Age-standardized mortality rates per 100,000 people (using the World Health Organization (WHO) standard population)for each year were calculated using direct standardization. Changes in the age-standardized mortality rate were analyzed for hypertension (18). All analyses were performed separately for males and females as several aspects in hypertension differ between genders. First, these data were analyzed by joinpoint regression analysis(Joinpoint Trend Analysis, version 4.2.01; WA, USA) (19). This technique is generally used to module the time trends in mortality or incidence series in epidemiological studies. Joinpoint regression analysis was used to determine the significant change points in trends (i.e., "joinpoints").

The joinpoint regression model for observations, $(x_1, y_1),\ldots,(x_n,y_n)$, where $x_1 \leq \ldots \leq x_n$ without loss of generality, may be written as follows:

$$E(y|x)=\beta_0+\beta_1 x+\delta_1(x-\tau_1)^{+}+\ldots+\delta_k(x-\tau_k)+,$$

where the τ_k 's are the unknown joinpoints. β_0 shows constant coefficient in equation, and β_1 shows slope coefficient (20).

The analysis begins with aminimum number of joinpoints and tests whether one or more joinpoints are statistically significant and should be added to the model. The number of joinpoints is decided by performing permutation tests with the correct level of asymptotic significance. This level of significance is found using Monte Carlo methods and Bonferroni correction (20).

In this research, each of detected trends is calculated by fitting a regression line to the logarithm of the rates, using year as an independent variable [ln(rate)=$\alpha+bx$], where x is year; APC was estimated as [100*(e^b–1)]. The parameters are allowed with a maximum of four joinpoints to enter the final model while having a minimum of 4 years between two joinpoints.The latest model shows the best fitting joinpoints where the rate changes significantly. Each joinpoint reports of a statistically significant change, an estimated APC, and AAPC that are computed along with its 95% confidence interval (95%CI). The AAPC is the geometric mean of the annual changes of all sections. In addition, the AAPC considers trend transitions (20).

Age–period–cohort analysis is based on a log-linear model for expected rates with additive effects for age, period, and cohort as follows:

$$\rho_{p,\alpha} = \mu + \alpha_\alpha + \pi_p + Y_c,$$

where α_a represents the effect of age, π_p the effect of period, and γ_c the effect of the *c*th birth cohort.

The general additional effects in the above equation can be divided into linear and nonlinear components.The two most useful are the age–period form (cross-sectional form):

$$\rho_{p,\alpha} = \mu + \alpha_L - Y_L\,(\alpha-\bar{\alpha}) + (\pi_L + Y_L)\,(p-\bar{p}) + \acute{\alpha}_\alpha + \tilde{\pi}_{p+}\tilde{Y}_c,$$

and the age–cohort form(longitudinal form):

$$\rho_{c,\alpha} = \mu + \alpha_L - \pi_L\,(\alpha-\bar{\alpha}) + (\pi_L + Y_L)\,(c-\bar{c}) + \acute{\alpha}_\alpha + \tilde{\pi}_{p+}\tilde{Y}_c\,.$$

Some estimable parameters and functions in the APC model:
μ, grand mean;
$\acute{\alpha}_\alpha, \tilde{\pi}_p, \tilde{Y}_c$, age, period, and cohort deviations;
α_L, π_L, longitudinal age trend;
α_L, Y_L, cross-sectional age trend;
$\pi_L + Y_L$, net drift;
$\mu + (\alpha_L - \pi_L)\,(\alpha-\bar{\alpha}) + \acute{\alpha}_\alpha$, fitted longitudinal age-at-event curve;
$\mu + (\alpha_L - \pi_L)\,(\alpha-\bar{\alpha}) + \acute{\alpha}_\alpha$, fitted cross-sectional age-at-event curve;
$\mu + (\pi_L - Y_L)\,(p-\bar{p}) + \tilde{\pi}_p$, fitted temporal trends (21).

The referent age, period, and cohort are $\bar{\alpha}$=[(A+1)/2], $\bar{p}$=[(P+1)/2], and $\bar{c}=\bar{p}-\bar{\alpha}$+A, respectively, where P and A are the total numbers of the period and age groups.

Age–period–cohort analysis was performed for each gender to investigate age, period, and cohort effects onthe mortality rates of hypertension using a web tool, which was improved by the U.S. Department of Health and Human Services (Department of Biostatistics, Division of Cancer Epidemiology and Genetics, National Cancer Institutes, WA, USA) (22). The web tool fits the age–

Table 1. Time trends of age-standardized hypertension mortality rates in Turkey (2000-2014)

Joinpoints (years)	Time period	APC[1]	95%CI[2]	AAPC[3] 2000-2014	95%CI
Male					
1 joinpoint	2000-2005	−5.6	−15.3-5.3	7.4^	3.0-11.9
	2005-2014	15.3^	10.7-20.1		
Female					
1 joinpoint	2000-2005	−4.1	−14.4-7.6	8.7^	4.1-13.5
	2005-2014	16.6^		11.7-21.6	

[1]APC; [2]CI; [3]AAPC

^APC and AAPC are statistically significantly different from zero (two-sided p<0.05). CI: confidence interval: AAPC: average annual percent change: APC: annual percent change

period–cohort model and calculates parameters and predictable functions. The parameters are a combination of the observed hypertension rate and the functions that define the relationship between age, period, and cohort. The web tool also calculates a series of statistical hypothesis tests (Wald test) that determine whether the mortality due to hypertension is statistically significantly different from age, period, and cohort factors.

Net drift (annual percentage change of the expected age-adjusted rates over time) indicates the overall log-linear trend by period and cohort; the longitudinal age curve (expected age-specific rates in reference cohort$c_0$adjusted for period effects) in the mortality rates, which is the fitted longitudinal age-specific rates in reference cohort; cross-sectional age curve displays the fitted longitudinal age-specific rates in reference period (expected age-specific rates in reference period$p_0$adjusted for cohort effects); and local drifts (annual percentage change of the expected age-specific rates over time) can be generated from log-linear regressions. The web tool can also calculate the rate ratios. The period RR demonstrates the period relative risk adjusted for age and nonlinear cohort effects in a period versus reference period. Similarly, the cohort RR indicates the cohort relative risk adjusted for age and nonlinear period effects in a cohort versus reference period.In all APC analyses, the reference groups were the central age group, central period, and central cohort group (22). Ages included in the model were categorized into seven 5-year age groups (45–49, 50–54, 55–59, 60–64, 65–69, 70–74, and ≥75 years) since hypertension-related mortality had few cases under the age of 45 years. Years of mortality were divided into three 5-year calendar periods (2000–2004, 2005–2009, and 2010–2014). Finally, nine birth cohorts were obtained (1925, 1930, 1935, 1940, 1945, 1950, 1955, 1960, and 195). For all analysis in the present study, a bilateral p<0.05 was considered statistically significant.

RESULTS

A total of 109,615 people were involved in the research. Of the 109,615 individuals, 38% (n=41,751) were males, and 62% (n=67,864) were females. While the mortality rate of hypertension in females was 55% in 2000, it was increased to 63% in 2014. On the other hand, this ratio was reverse for males that was decreased from 45% to 37% in the same years. The average standardized or age-adjusted hypertension-related mortality rate in Turkey from 2000 to 2014 was found to be 9.20/100,000 people (8.60 for males and 9.80 for females). The hypertension-related mortality rate was female predominant, with the female-to-male rate ratio in age-standardized rate ranging from 0.89 to 1.23 across calendar years. The result of the joinpoint regression analysis, the APC for each trend, and the AAPC in both genders is shown in Table 1. For both genders, the hypertension-related mortality rates decreased during the period 2000–2005 (not statistically significant); however, there was a statistically significantdramatical increase throughout the period 2005–2014. With regard to gender, during the period 2000–2014, the AAPCs of the hypertension-related mortality rates were 7.4% in males and 8.7% in females (steadily increased).

During the study, local drift values showing APCs at mortality rates by gender for specific age groups are displayed in Figure 1. We saw local drift effects in similar patterns in both genders. The local drifts are highly significant in both males and females (male: χ^2:188.257, degrees of freedom (df): 6 and female: χ^2:227,289;df:6); local drift values increase by approximately 0%/year between males aged 55–59 years, approximately 6%/yearamong males aged 70–74 years, and approximately 18%/year among males aged ≥75 years; the local drift values increase from approximately 0%/year among females aged 60–64 years, approximately 6%/year among females aged 70–74 years, and approximately 18%/year among females aged ≥75 years.

Longitudinal age curves of hypertension-related mortality rates by gender are illustrated in Figure 2. As illustrated, the mortality of hypertension increased with age in both males and females. The risk of hypertension mortality increased monotonically in males until 62 yearsand then yielded significantly elevated increases for ≥65 years. The longitudinal age curves in females show similar overall patterns as males.

The estimated period and cohort effects by gender are shown in Figures 3 and 4, respectively. The period (male: χ^2:88.18, df:2 andfemale: χ^2:57.96, df:2) and cohort effects (male: χ^2:427.13, df:8 and female: χ^2:665.01, df:8) are highly significant in both males and females. We observed period effects in similar patterns for both genders, which shifted downwards since the period 2000–2007 and then turned upwards since the early 2008s with a significantly increased risk.

Figure 1. Local drift values for hypertension mortality rates. Age group-specific annual percent change (%) in the mortality rates of hypertension and corresponding 95% confidence intervals by gender

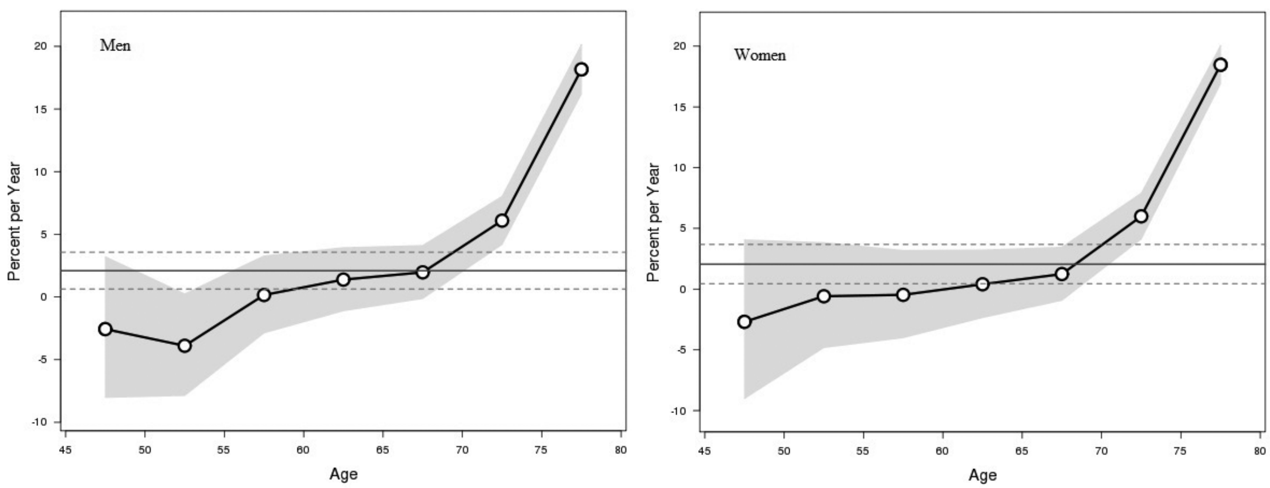
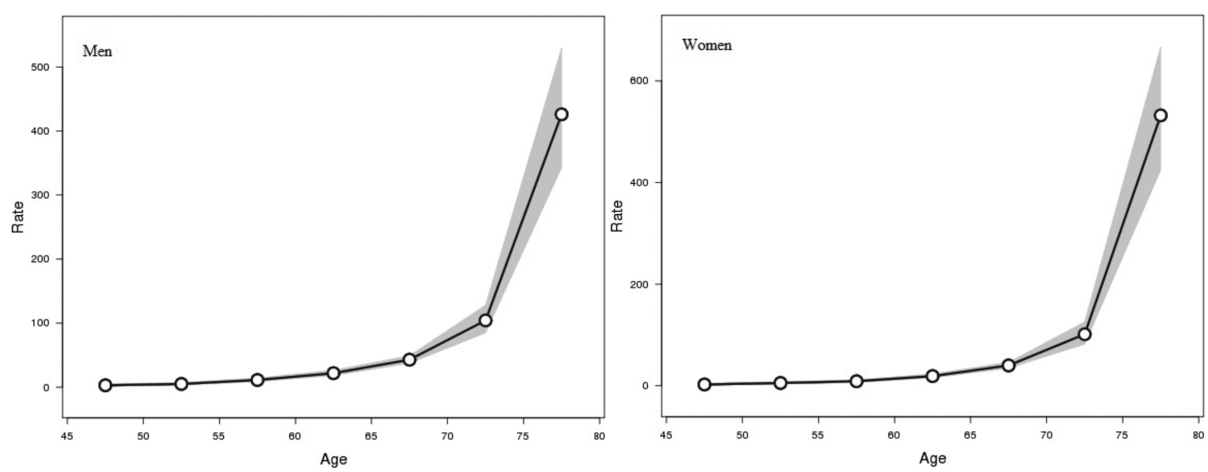


Figure 2. Longitudinal age curves of hypertension mortality rates. Longitudinal age curve of the mortality rates (1/100,000) of hypertension and corresponding 95% confidence intervals by gender



In general, the risk of hypertension increased with cohort in both genders. The cohort effects remained stable for the first several birth cohorts, followed by upwards inflation for males and females born after themid-1940s. Relative risk increased from 1925 to 1945, but then decreased.

DISCUSSION

The worldwide upward trend in mortality due to hypertension has been documented in the last decade. The present study included 109,615 cases of hypertension-related mortality recorded in the Turkish Statistical Institute death database between 2000 and 2014. To the best of our knowledge, this is the first study to investigate the trends of hypertension-related mortality in Turkey and to analyze age, period, and cohort effects by gender using the age–period–cohort analysis.

Our results indicated that there was a dramatic increase in age-standardized hypertension-related mortality rate (6.33–16.05) in Turkey. Using joinpoint regression analysis, a steady significant increase in both genders between 2000 and 2014, especially between 2005 and 2014, is observed. This significant increase may be related with the technology that made our lifestyles worse. More sedentary lifestyles, increase in the number of obese people, unhealthynutrition (e.g., fast food, frozen, salty, and fried foods), and increase in tobacco use would be the main factors that caused the increase in hypertension-related deaths. This increase alarmed the Ministry of Health, and in 2015, with a circular, sugar and salt were eliminated from the tables of cafes, restaurants, and dining halls, and so on (23).

Regarding the research by Kung and Xu (24), in the USA, the hypertension-related mortality rate for females is higher than

Figure 3. Period effects on hypertension mortality rates. Period effects obtained from age–period–cohort analysis for mortality rates of hypertension and corresponding 95% confidence intervals by gender

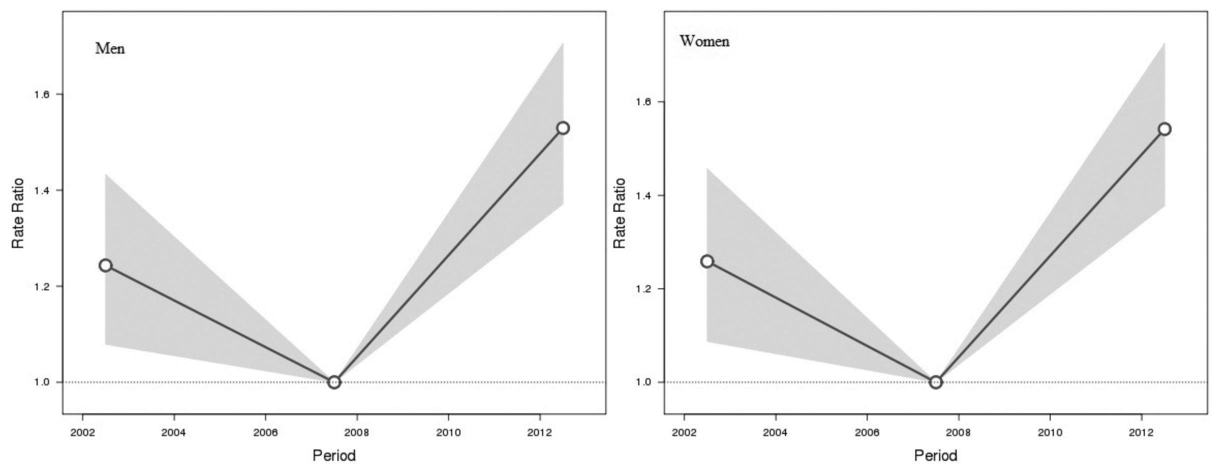
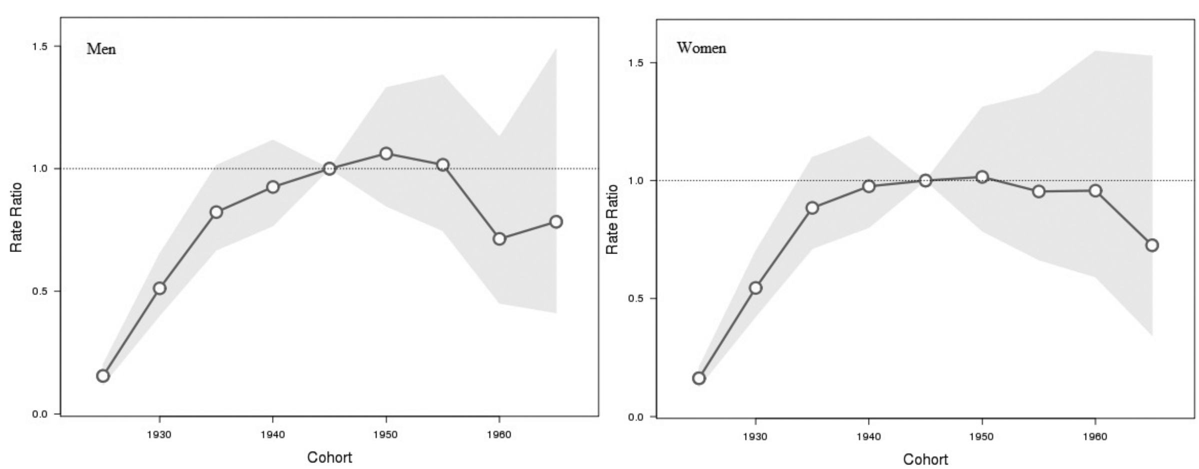


Figure 4. Cohort effects on hypertension mortality rates. Cohort effects obtained from age–period–cohort analysis for mortality rates of hypertension and corresponding 95% confidence intervals by gender



that for males aged ≥85 years, but more than that for females <84 years. Throughout the period 2000–2013, the rates for both females and males continued to increase until 2013, but progressed much more slowly (24). Similarly, the mortality rate was also higher in older females than in males in our study, especially after 2008. Through this period (especially in 2008), the mortality rates of hypertensive females were higher in the 75 and over age group, whereas there was a decrease in the other age groups. This similarity could probably be the result of higher prevalence of obesity and increasing CVD prevalence in females. In addition, the increase in sedentary lifestyle as females become oldercan be another risk factor. On the other hand, males are more active than femalesin Turkey, which makes the biggest difference in prevalence between the two gendersin older ages (6).

Aging is the unchanging risk factor for both genders. The results from age–period–cohort analysis showed that the curves of age and period effects increased, but generally decreased cohort effects.

Age is the most important risk factor for hypertension among a series of demographic factors. The risk of death from hypertension varies from different life stages.The present study and other studies (24, 25) showed that the rate of hypertension-related mortality increased with age. As the aging population increases, chronic diseases, especially hypertension, become more important and the most probable reason for mortality worldwide.Populations globally are rapidly aging, andthe prevalence of hypertension increases with age (25, 26). This condition reflected to cohort effects. In our study, the cohort effects (relative risk) increased upwards for both genders from 1925 to 1945 (especially those born after the mid-1940s). This indicated that currently, people born in this period are aged between 73 and 93 years, which is overthe expected life duration. Regarding WHO,72.0 years was the average life expectancy at birth of the global population in 2016 (27). In these ages, not only hypertension but also other coexisting diseases would be the reasons of this upward increase.

The study data of Trabzon on hypertension stated that hypertension is very common, and it is an important health problem in adult population in Trabzon (8). Hypertension rate is nearly 30% (similar with the previous study), and the difference between male and female and urban and rural disappears.There was an 11% decrease in the prevalence of age-standard hypertension from TURDEP-I to TURDEP-II. The smoking rate in Turkey increased to42% in 12 years (10). We can explain this by decreasing smoking rate and by strong legislative regulations on salt restriction. However, the decrease in hypertension prevalence did not affect the mortality rates; on the contrary, the mortality rate of hypertension increased.

Currently, media, especially the internet, is the main source of much knowledge including information about health. This makes many people aware of the risks of their hypertension, and they take care about preventive methods, for example, restricting salt, exercising, and paying attention to body mass index.

In the present study, time trend analysis on hypertension mortality rates was ecological descriptive analysis at population levels without deduction at individual levels.

The PatenT2 study showed that the prevalence of hypertension in Turkish adults was stable between 2003 and 2012, but showed a significant improvement in treatment and control rates in hypertension awareness (25). This would reflect a decrease in hypertension mortality rates in the future.

As an important public health problem, hypertension is still underlining the need for a specific national program to improve the detection and control of hypertension in this country. This national initiative should develop well-organized programs, guidelines, and policies to facilitate hypertension prevention, detection, awareness, and treatment.

These hypertension mortality rates showed us that hypertension is still an epidemic problem in our country. We are still not aware of this common problem and still cannot treat satisfactorily.As we know, there are many behavioral risk factors for development of hypertension includingfood consumption with too much salt and fat, not eating enough fruit and vegetables, and harmful alcohol levels; physical inactivity and lack of exercise; and poor stress management. In addition, there are a number of metabolic factors that increase the risk of heart disease, stroke, renal failure, and other hypertension complications, such as diabetes, high cholesterol, and excessively overweight or obese. Regarding these risk factors, we can argue the changes in hypertension mortality and morbidity rates.

Cohort effects reflectenvironmental factors, such as war, famine, inflation, and recession, that can affect the subject in their first years of life. The period effect refers to the impacts of environmental, nutritional, and sociological changes on the later years of an individual's life. These changes include lifestyle alternations, such as addiction, smoking, and diet changes during adolescence and adulthood. Among both male and female participants of the PatenT2 study, hypertension was associated with an increased frequency of well-known risk factors, as we mentioned above, such as self-reported parental hypertension, smoking, diabetes, obesity, and a sedentary lifestyle. During the past 10 years, the mean body mass index increased by 1.1 kg/m^2 in females and by 1.57 kg/m^2 in males in Turkey. The prevalence of obesity also increased from 20.5% to 28.7%. High salt consumption is also a major health problem in Turkey. Bread is an important component of meals in this country (28, 29).

Systolic blood pressure and salt intake were significantly correlated in normal weight subjects (r=0.257, p<0.01). The Turkish population consumes a large amount of salt, affecting blood pressure; there was a positive correlation between salt intake and blood pressure. In recent years, the Turkish Ministry of Health eliminatedsalt from the tables of restaurants. For this reason, efforts to restrict sodium are very important in the management of hypertension as part of national and global health policies (26, 28). Even a small decrease in sodium intake in the daily diet caused asignificant decline in blood pressure levels.

Our study has some limitations. One of the limitations of the study was the use of official published mortality data. Regarding this data, we could obtain village and urban data separatelyuntil 2008. However, after this year, as only the total numbers were provided, we could analyze the mortality rates for the whole population after that year. In addition, not obtaining the information about the comorbid diseases of the patients and other hypertension risk factors, such as nutrition, body mass index, medications, dyslipidemia, and smoking status, are the limitations of the present study.

CONCLUSION

Hypertension is one of the leading causes of mortality. Although hypertension-related mortality rates change, we know that age is the main risk factor for all periods. Knowing the risk factors and preventive methods could help to reduce hypertension-related mortalities. Screening for hypertension, especially in high-risk groups, such as elderly women, could help to reduce CVD. This will allow for early intervention and follow-up on populations atrisk, thus, contributing to improve strategies for reducing hypertension burden.

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