Original Article

Prevalence, awareness and risk factors of hypertension in a large cohort of Iranian adult population

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Background: There is considerable variation in hypertension prevalence and awareness, and their correlates, across different geographic locations and ethnic groups. We performed this cross-sectional analysis on data from the Golestan Cohort Study (GCS).

Methods: Enrollment in this study occurred in 2004–2008, and included 50 045 healthy individuals from Golestan Province in northeastern Iran. Hypertension was defined as a SBP at least 140 mmHg, a DBP at least 90 mmHg, a prior diagnosis of hypertension, or the use of antihypertensive drugs. Potential correlates of hypertension and its awareness were analyzed by logistic regression adjusted for sex, age, BMI, place of residence, literacy, ethnicity, physical activity, smoking, black and green tea consumption and wealth score.

Results: Of the total cohort participants, 21 350 (42.7%) were hypertensive. Age-standardized prevalence of hypertension, using the 2001 WHO standard world population, was 41.8% (95% confidence interval: 38.3–45.2%). Hypertension was directly associated with female sex, increased BMI, Turkmen ethnicity, and lack of physical activity, and inversely associated with drinking black tea and wealth score. Among hypertensive patients, 46.2% were aware of their disease, 17.6% were receiving antihypertensive medication, and 32.1% of the treated patients had controlled hypertension. Hypertension awareness was greater among women, the elderly, overweight and obese patients, and those with a higher wealth score.

Conclusion: Hypertension is highly prevalent in rural Iran, many of the affected individuals are unaware of their disease, and the rate of control by antihypertensive medications is low. Increasing hypertension awareness and access to health services, especially among less privileged residents are recommended.

Keywords: awareness, hypertension, obesity, smoking, socioeconomic status

Abbreviations: CVA, cerebrovascular accidents; CVD, cardiovascular disease; FFQ, food frequency questionnaire; GCS, Golestan Cohort Study; NHANES, National Health and Nutrition Examination Survey; NO, nitric oxide; SES, socioeconomic status

INTRODUCTION

The age-standardized prevalence of hypertension ranges between 5.5% in a rural part in India and 40% in Spain [1]. Although the average global prevalence of hypertension has declined slightly during the past two decades, there is an increasing trend in the middle and low income countries [2–4], and about two-thirds of patients with hypertension are now living in developing countries [1]. Iran is a Middle Eastern, middle-income country with diverse ethnicities and lifestyles across the country. A systematic review of published studies from Iran has estimated the prevalence of hypertension to be 22.1% [2]. There is considerable variation in the hypertension prevalence across different geographic locations, and ethnic groups [5]. A high proportion of hypertensive patients are unaware of their condition; for example, in the Iranian national household survey, only 34% of hypertensive patients knew they were hypertensive [6]. Studies from big cities like Tehran (50%) and Isfahan (43.8%) reported higher rates of awareness [7,8].

Polypill, a single-capsule combination of medications that lower blood pressure and serum cholesterol levels, is being evaluated for use in the primary and secondary prevention of cardiovascular disease (CVD) in those whose only risk factor is old age [9,10]. A number of trials have

supported the effectiveness of polypill, both in those who have risk factors for CVD and those who do not [11–16], but there is still a need for larger trials [17]. A pilot double-blind randomized controlled trial using polypill to control the main risk factors of CVD in Golestan Province, Iran has shown the safety, feasibility and effectiveness of this intervention [18], and a pragmatic main phase trial, POLYIRAN, conducted in the context of the Golestan Cohort Study (GCS), has already started [19,20]. GCS is a cohort of more than 50 000 adults from Golestan Province (2010 population approximately 1 700 000), a mainly rural area in northeastern Iran [21]. This cohort was primarily designed to study esophageal cancer in this high-risk area [22,23]. The first 5-year follow-up data of this cohort revealed that 50% of deaths were due to CVD and cerebrovascular accidents, and up to 33% of patients in a preliminary study were found to be hypertensive [24].

In the present study, we performed a cross-sectional analysis of the baseline data from GCS to report the crude and age-adjusted rates and correlates of hypertension and factors associated with awareness of hypertension in this population. These findings can be helpful in interpreting the results of the POLYIRAN trial, and provide a better perspective of hypertension, as an important CVD risk factor, in this mainly rural area.

METHODS

Study population

We performed this cross-sectional analysis on the data from the Golestan Cohort Study, which has been described before [22]. This study enrolled patients during 2004–2008, and included 50 045 healthy adults from 40 to 75 years old. About 20% of the participants were urban residents, randomly selected according to household numbers from five clustered areas of Gonbad, the second largest city in Golestan, and 80% were rural residents selected from all 326 villages in the planned area of the study. The study protocol was approved by the ethical committees of the Digestive Disease Research Center, the National Cancer Institute, and the International Agency for Research on Cancer.

Each interview was done by a trained general practitioner and a nutritionist. Two structured questionnaires, a lifestyle questionnaire and a food frequency questionnaire (FFQ), were given to each subject to collect information about age, sex, ethnicity, place of living, past medical history, drug use, household properties, education, and use of tobacco. After the interview, a short physical examination, including blood pressure measurement, was done, and blood, urine, hair and nail samples were collected.

The definitions of the covariate variables used in this analysis have been extensively explained before [25] and are briefly described here. Literacy was defined as more than 1 year of attendance in school. Physical activity was defined based on occupational activity; those having jobs involving heavy and intense physical activity were coded as active, and all others were coded as sedentary. Weight and height were measured wearing light clothes but no shoes, to calculate BMI. BMI was categorized according to the WHO classification: underweight (BMI $< 18.5\,\mathrm{kg/m^2}$), normal (BMI 18.5–$24.9\,\mathrm{kg/m^2}$), overweight (BMI 25–$29.9\,\mathrm{kg/m^2}$), and obese (BMI over $30\,\mathrm{kg/m^2}$) [26]. Our study included eight different ethnicities, which we combined into the two major groups, Turkmen and non-Turkmen.

Quartiles of black tea drinking were calculated among normotensive individuals and were used as the basis for classification of all individuals. As there were not many people who drank green tea regularly, individuals were classified only as drinkers or nondrinkers of green tea. The smoking history was recorded and divided into five categories: those who never smoked, those who smoked more than the median pack-years of the normotensive population (heavy smokers), those who smoked less than the median pack-years of the normotensive population (light smokers), those who had quit smoking (ex-smokers), and individuals who used other tobacco products (e.g. nass, hookah, or pipe).

Definition of hypertension

The blood pressure was measured twice in each arm in the sitting position. There was a 2-min rest between each two measurements. A person's blood pressure was calculated as the average of the two measurements in each arm. According to the JNC7 criteria [27], hypertension was defined as a SBP at least 140 mmHg, a DBP at least 90 mmHg, a prior clinical diagnosis of hypertension, or the use of antihypertensive drugs. Those hypertensives who self-reported having hypertension were considered aware of their disease, and those who took antihypertensive drugs were considered under treatment. Patients taking antihypertensive medication who had both SBP less than 140 mmHg and DBP less than 90 mmHg were defined as having controlled hypertension.

Statistical analysis

Age-standardization was calculated using the 2001 WHO standard world population [28], with the exact method for calculating confidence intervals. In order to classify the socioeconomic status, a wealth score was calculated as explained elsewhere [25], using multiple correspondence analysis. In calculating this composite wealth score, house ownership, house size, number of people living in the house and ownership of appliances such as car, TV, refrigerator, and so on were used.

Logistic regression was used, with hypertension as the outcome in every body, and awareness of hypertension only among hypertensive individuals. For crude associations, each variable (i.e., sex, age, BMI, place of residence, literacy, ethnicity, physical activity, smoking, black and green tea consumption and wealth score) was entered in the model alone. Two adjusted models were evaluated: in the first, we adjusted for age and sex only, and in the second, all of the variables were entered in the model. Most of these variables were selected based on their previously shown effect on cardiovascular disease risk, in general, and on hypertension and its awareness, in particular. Unlike coffee intake, there are only a few articles published about the association between tea intake and hypertension. As most people in this population drink tea frequently (median intake of 1035 ml per day), and such

data were available in detail, we used this opportunity to study both black and green tea consumption in the models. Two-tailed $P < 0.05$ were considered significant.

RESULT

Of the total cohort participants, 21 350 (42.7%) were hypertensive: 31.6% of those below the age of 50, 49.3% between 50 and 60 years old, and 61.8% above 60 (Table 1). The age-standardized prevalence of hypertension using the 2001 WHO standard world population was 41.8% [95% confidence interval (CI): 38.3–45.2%]. Hypertension was more prevalent in women (46.4 vs. 37.6%, $P < 0.0001$). The age-standardized prevalence in women was 44.1% (95% CI: 40.6–47.6%), and in men it was 33.1% (95% CI: 30.6–35.5%). In unadjusted models, hypertension was associated with increasing BMI, Turkmen ethnicity, lack of physical activity at work, and drinking green tea. There were fewer hypertensives among

underweight individuals, people living in towns, literate people, smokers, and those drinking more black tea. Hypertension was also inversely associated with the composite wealth score. Adjusting for age and sex attenuated the effects of smoking and drinking green tea. In the fully adjusted model, the associations between hypertension and age, BMI and place of residence were more pronounced than the crude model, and the inverse association among ex-smokers was no longer significant (Table 1). Table 2 shows the factors associated with hypertension separately for rural and urban residents. Place of residence showed significant interactions with sex, literacy, physical activity, and wealth score ($P < 0.001$). Sex and physical activity showed significant associations with hypertension only in rural villages, whereas markers of socioeconomic status (SES) (literacy and wealth score) had stronger associations in urban areas.

Nine thousand, eight hundred and seventy-one (46.2%) of the hypertensive patients were aware of their disease,

TABLE 1. Factors associated with hypertension in the Golestan Cohort Study

	Hypertensive, number (%)	Normotensive, number (%)	Crude OR (95% CI)	Model 1[a] OR (95% CI)	Model 2[b] OR (95% CI)
Total	21 350 (42.7)	28 695 (57.3)			
Sex					
Male	7985 (37.6)	13 249 (62.4)	1	NA	1
Female	13 365 (46.4)	15 446 (53.6)	1.44 (1.38–1.49)		1.11 (1.06–1.17)
Age					
Below 50	7991 (31.6)	17 323 (68.4)	1	NA	1
50–60 years	7559 (49.3)	7784 (50.7)	2.11 (2.02–2.19)		2.20 (2.11–2.30)
Above 60	5800 (61.8)	3588 (38.2)	3.51 (3.34–3.69)		4.29 (4.05–4.53)
BMI					
Underweight	597 (24.8)	1813 (75.2)	0.66 (0.60–0.73)	0.59 (0.53–0.65)	0.59 (0.53–0.65)
Normal	5939 (33.1)	11 990 (66.9)	1	1	1
Overweight	7678 (45.2)	9294 (54.8)	1.67 (1.60–1.74)	1.84 (1.75–1.92)	1.87 (1.79–1.96)
Obese	7130 (56.0)	5594 (44.0)	2.57 (2.46–2.70)	2.95 (2.81–3.11)	3.06 (2.90–3.22)
Place of residence					
Rural	17 173 (42.9)	22 839 (57.1)	1	1	1
Urban	4177 (41.6)	5856 (58.4)	0.95 (0.91–0.99)	0.90 (0.86–0.94)	0.85 (0.81–0.90)
Literacy					
Illiterate	16 382 (46.7)	18 736 (53.4)	1	1	1
Literate	4968 (33.3)	9959 (66.7)	0.57 (0.55–0.59)	0.88 (0.84–0.92)	0.84 (0.80–0.89)
Ethnicity					
Turkmen	16 247 (43.6)	21 006 (56.4)	1	1	1
Non-Turkmen	5103 (39.9)	7689 (60.1)	0.86 (0.82–0.89)	0.80 (0.77–0.84)	0.91 (0.87–0.95)
Physical activity					
No	19 599 (44.3)	24 629 (55.7)	1	1	1
Yes	1751 (30.1)	4064 (69.9)	0.54 (0.51–0.57)	0.74 (0.69–0.78)	0.82 (0.77–0.88)
Smoking					
Never	17 578 (44.8)	21 629 (55.2)	1	1	1
Light smoker	632 (28.0)	1621 (72.0)	0.48 (0.44–0.53)	0.62 (0.56–0.69)	0.75 (0.68–0.83)
Heavy smoker	949 (29.9)	2228 (70.1)	0.52 (0.48–0.57)	0.61 (0.56–0.66)	0.79 (0.73–0.87)
Ex-smoker	1277 (39.7)	1941 (60.3)	0.81 (0.75–0.87)	0.81 (0.75–0.88)	0.92 (0.85–1.00)
Others	914 (41.7)	1276 (58.3)	0.88 (0.81–0.96)	0.73 (0.67–0.80)	0.87 (0.79–0.96)
Black tea					
Q1 (<690 ml)	6919 (46.3)	8017 (53.7)	1	1	1
Q2 (691–1035 ml)	5103 (42.8)	6823 (57.2)	0.87 (0.83–0.91)	0.89 (0.85–0.94)	0.92 (0.88–0.97)
Q3 (1036–1500 ml)	4874 (41.5)	6884 (58.6)	0.82 (0.78–0.86)	0.85 (0.81–0.90)	0.90 (0.85–0.95)
Q4 (>1500 ml)	4454 (39.0)	6971 (61.0)	0.74 (0.70–0.78)	0.79 (0.75–0.83)	0.86 (0.81–0.91)
Green tea					
Nondrinker	17 623 (42.4)	23 915 (57.6)	1	1	1
Drinker	3727 (43.8)	4780 (56.2)	1.06 (1.01–1.11)	1.01 (0.96–1.06)	1.00 (0.98–1.02)
Wealth score					
1 unit increase	–	–	0.84 (0.77–0.92)	1.10 (1.00–1.21)	0.75 (0.67–0.83)

CI, confidence interval; NA, not applicable; OR, odds ratio.
[a]Model 1: adjusted for age and sex.
[b]Model 2: including all variables in the table.

TABLE 2. Factors associated with hypertension in rural and urban areas in the Golestan Cohort Study

	Rural areas OR (95% CI)	Urban areas OR (95% CI)
Sex		
Male	1	1
Female	1.17 (1.10–1.24)	0.94 (0.83–1.05)
Age		
Below 50	1	1
50–60 years	2.14 (2.04–2.25)	2.49 (2.26–2.75)
Above 60	4.13 (3.87–4.40)	4.87 (4.33–5.49)
BMI		
Underweight	0.59 (0.53–0.66)	0.57 (0.42–0.78)
Normal	1	1
Overweight	1.89 (1.79–1.99)	1.73 (1.55–1.93)
Obese	3.05 (2.88–3.24)	2.93 (2.61–3.30)
Literacy		
Illiterate	1	1
Literate	0.88 (0.83–0.94)	0.77 (0.69–0.85)
Ethnicity		
Turkmen	1	1
Non-Turkmen	0.90 (0.86–0.95)	1.00 (0.92–1.01)
Physical activity		
No	1	1
Yes	0.79 (0.73–0.85)	0.97 (0.80–1.17)
Smoking		
Never	1	1
Light smoker	0.75 (0.67–0.84)	0.73 (0.58–0.93)
Heavy smoker	0.80 (0.72–0.88)	0.76 (0.63–0.91)
Ex-smoker	0.90 (0.82–0.99)	0.96 (0.80–1.15)
Others	0.88 (0.79–0.98)	1.00 (0.76–1.32)
Black tea		
Q1 (<690 ml)	1	1
Q2 (691–1035 ml)	0.92 (0.86–0.97)	0.95 (0.84–1.06)
Q3 (1036–1500 ml)	0.91 (0.86–0.96)	0.86 (0.77–0.96)
Q4 (>1500 ml)	0.86 (0.81–0.92)	0.87 (0.77–0.98)
Green tea		
Nondrinker	1	1
drinker	0.99 (0.97–1.01)	1.04 (1.00–1.09)
Wealth score		
1 unit increase	0.86 (0.76–0.97)	0.54 (0.44–0.67)

3756 (38.1% of the aware patients, and 17.6% of everyone with high blood pressure) were receiving antihypertensive medication, and 1205 (32.1% of the treated patients, and 5.6% of all hypertensives) had controlled hypertension. Awareness of being hypertensive was significantly higher in women. It was also more common in older patients, overweight and obese patients, urban residents, illiterates, those with less physical activity and never-smokers (Table 3). Hypertension awareness was also directly associated with the composite wealth score. After adjusting for confounders, the associations with urban residence and current smoking were no longer significant, and hypertension awareness was significantly higher in ex-smokers. The composite wealth score also had a higher odds ratio in the adjusted models (Table 3).

DISCUSSION

In this study, the age-standardized prevalence of hypertension was 41.8%, and less than half of the hypertensives knew that they had this condition. Hypertension and its awareness were more prevalent among women, obese and less active people, and illiterates. Current (but not past) smoking was associated with a lower chance of having high

blood pressure, but hypertensive ex-smokers were more aware of their condition. The prevalence of hypertension showed an inverse relationship with the amount of black tea used. Higher wealth score was associated with lower chance of hypertension, and more awareness.

The overall 41.8% prevalence of hypertension in this study was higher than in many published reports from Iran and other countries, probably due to the higher age of our cohort population; the age-specific prevalences of hypertension by decades in our study (31.6, 49.3 and 61.8% in the 40–49, 50–59 and 60–69 year old age groups, respectively) were more similar to other reports. For example, Haghdoost et al. [2] estimated the national prevalence of hypertension in Iran to be 22.1% among adults and 49.5% among individuals older than 55 year old. Likewise, Esteghamati et al. [6] reported the overall prevalence of hypertension to be 25.2% in adults and 53.6% in the 55–64 year age group in an Iranian national household survey of risk factors for noncommunicable diseases. A worldwide study of hypertension reported that 26.1, 37.2, 46.6 and 51.7% of adults were hypertensive in the 40–49, 50–59, 60–69, and at least 70 year old age groups, respectively, in Middle Eastern countries, lower rates than we found in Golestan Province, and it reported hypertension rates of 32.4, 44.8, 60.3, and

TABLE 3. Factors associated with hypertension awareness among hypertensive individuals in the Golestan Cohort Study

	Aware, number (%)	Unaware, number (%)	Crude OR (95% CI)	Model 1[a] OR (95% CI)	Model 2[b] OR (95% CI)
Total	9871 (46.2)	11 479 (53.8)			
Sex					
Male	2549 (31.9)	5436 (68.1)	1	NA	1
Female	7322 (54.8)	6043 (45.2)	2.58 (2.44–2.74)		2.53 (2.34–2.74)
Age					
Below 50	3099 (38.8)	4891 (61.2)	1	NA	1
50–60 years	3707 (49.0)	3854 (51.0)	1.52 (1.42–1.62)		1.62 (1.52–1.74)
Above 60	3065 (52.9)	2734 (47.1)	1.77 (1.65–1.89)		2.28 (2.11–2.47)
BMI					
Underweight	225 (37.7)	372 (62.3)	0.99 (0.83–1.18)	0.88 (0.74–1.06)	0.88 (0.73–1.05)
Normal	2249 (37.9)	3690 (62.1)	1	1	1
Overweight	3516 (45.8)	4162 (54.2)	1.39 (1.29–1.49)	1.41 (1.31–1.52)	1.40 (1.30–1.50)
Obese	3881 (54.4)	3255 (45.6)	1.96 (1.82–2.10)	1.86 (1.72–2.00)	1.82 (1.68–1.96)
Place of residence					
Rural	7710 (45.6)	9203 (54.4)	1	1	1
Urban	2161 (48.7)	2276 (51.3)	1.13 (1.06–1.21)	1.06 (0.99–1.14)	0.93 (0.86–1.00)
Literacy					
Illiterate	8154 (49.8)	8228 (50.2)	1	1	1
Literate	1717 (34.6)	3251 (65.4)	0.53 (0.50–0.57)	0.97 (0.90–1.05)	0.84 (0.77–0.92)
Ethnicity					
Turkmen	7449 (45.8)	8798 (54.2)	1	1	1
Non-Turkmen	2422 (47.5)	2681 (52.5)	1.07 (1.00–1.14)	1.01 (0.95–1.08)	1.08 (1.00–1.15)
Physical activity					
No	9396 (47.9)	10 203 (52.1)	1	1	1
Yes	475 (27.1)	1276 (72.9)	0.40 (0.36–0.45)	0.67 (0.60–0.75)	0.70 (0.62–0.78)
Smoking					
Never	8501 (48.4)	9077 (51.6)	1	1	1
Light smoker	209 (33.1)	423 (66.9)	0.53 (0.45–0.62)	1.00 (0.84–1.20)	1.11 (0.93–1.33)
Heavy smoker	276 (29.1)	673 (70.9)	0.44 (0.38–0.51)	0.88 (0.75–1.02)	1.01 (0.86–1.18)
Ex-smoker	500 (39.2)	777 (60.8)	0.69 (0.61–0.77)	1.28 (1.12–1.45)	1.34 (1.18–1.53)
Others	385 (42.1)	529 (57.9)	0.78 (0.68–0.89)	1.04 (0.90–1.20)	1.16 (1.00–1.35)
Wealth score					
1 unit increase	–	–	1.36 (1.18–1.55)	1.77 (1.53–2.04)	1.55 (1.32–1.82)

CI, confidence interval; NA, not applicable; OR, odds ratio.
[a]Model 1: adjusted for age and sex.
[b]Model 2: including all variables in the table.

71.2% for these age groups in developed countries, figures closer to our own [1]. The National Health And Nutrition Examination Survey (NHANES) in the United States also had similar results among American adults between 1999 and 2004 [29].

Reports from NHANES show no significant relation between sex and hypertension in the United States. In Iran, most studies show a higher prevalence of cardiovascular risk factors, including hypertension [2] and the metabolic syndrome [30], in women. A countrywide study showed a slightly but not significantly higher prevalence of hypertension among younger men, whereas the prevalence of hypertension was significantly higher in older (45–64 year old) women [5]. Although higher BMI and lack of physical activity have been proposed as causes for this sex difference [30], in this study this difference was still significant after adjusting for these other variables.

We observed a reduced prevalence of hypertension in people reporting higher physical activity. Moderate regular physical activity can reduce SBP and DBP about 10 mmHg in 75% of hypertensive patients [31]. Moreover, it has been shown that physical fitness (as a consequence of regular physical activity) has protective effects on hypertension [32]. The underlying mechanisms by which physical activity acts are probably weight loss, increased metabolic rate and fat metabolism. Reduction in insulin resistance, plasma norepinephrine, plasma renin and vascular resistance can be other explaining mechanisms [33,34]. Physical activity can be used as a therapeutic choice for the treatment of hypertension and for prevention of its complications [35], and it improves cardiac autonomic modulation and reduces risk of coronary heart diseases [36].

Tea consists of different types of polyphenols (mostly flavonoid) that stimulate the release of nitric oxide (NO) – a strong vasodilator – from vascular endothelium and thereby can reduce blood pressure [37,38]. Animal studies consistently show that black tea consumption decreases hypertension, but the results of human studies are less consistent: some studies show that regular tea drinkers have lower blood pressures than nondrinkers [38–40], but others have failed to show a protective effect of short periods of tea consumption [41]. We also found a lower prevalence of hypertension in regular black tea users, and an inverse dose–response relationship between the amount of tea consumed and the risk of hypertension. Green tea drinkers, however, were not different from nondrinkers in our study. Although some studies on rats have showed a protective effect for green tea on hypertension [42,43], and green tea has more polyphenols and hence should have more antioxidant activity than black tea, there

is as yet no evidence that green tea lowers blood pressure in humans [38].

Talukder *et al.* observed that smoking leads to increased blood pressure in mice, and suggested that this effect was mediated by endothelial injury, increased reactive oxygen species and decreased NO release [44]. Other possible mechanisms are increased sympathetic activity induced by nicotine, increased blood viscosity due to production of more fibrinogen and augmented numbers of white blood cells, and changes in serum lipid levels caused by smoking [45–48]. Increased inflammatory mediators, such as C-reactive protein, in a smoker's blood may also be another reason explaining this effect [49,50]. Some studies had shown that smoking increases arterial stiffness [51,52], which secondarily can raise blood pressure. A prospective cohort study in Japan showed an independent and significant effect of smoking on hypertension [53]. Halperin *et al.* [54] also found both past and current smoking as risk factors for hypertension. The finding of an inverse association between hypertension and smoking in the present study is probably due to reverse causation, due to the fact that people with hypertension are more likely to be advised by their doctors to give up smoking. Our cross-sectional analysis is not able to prove this, but two pieces of evidence support it: we found that the inverse association disappeared in ex-smokers after adjusting for confounders and that ex-smokers were more aware of their hypertension compared to never-smokers (i.e. people who knew they were hypertensive were more likely to give up smoking). This pattern was also found in a study from Canada [55].

Higher SES and more education have been consistently reported to reduce the risk of hypertension [29,56]. Studies from Iran have also shown that people educated in second school or higher were less likely to be hypertensive [5,57]. Similarly, we found hypertension to be inversely associated with the composite wealth score and literacy. Possible mechanisms for these associations proposed by other investigators include lower birth weight, which has been shown to impact blood pressure, lower awareness of hypertension, resulting in less medical management and poorer control, bad job conditions and job strains among people with lower SES [58]. There are conflicting reports about the effects of residential area on the prevalence of hypertension; whereas most investigations have shown no difference between rural and urban areas [2,5,57], one national study in Iran reported higher rates in urban residents [59], and a WHO report has also shown that hypertension is more prevalent in urban areas in developing countries of Africa [60]. In contrast, we observed a lower prevalence of hypertension in urban areas of Golestan Province, although it is important to note that this province is mainly rural and even the towns are best described as extended villages. We observed an interaction between the place of residence and socioeconomic indicators, with a stronger association between these indicators and hypertension in urban areas. This may be due to more socioeconomic diversity in these urban areas, and more potential for a change in lifestyle as a result of this.

The rate of hypertension awareness was 46.2% in our study, which is much less than similar awareness in the United States [29]. A nationwide survey of noncommunicable diseases in Iran reported that 34% of people with high blood pressure knew about it [6], and another large study in the metropolitan area of Tehran found the awareness to be 49.6% [7]. Among our hypertensive patients, 17.6% were treated and 32.1% of those treated had controlled hypertension. Similar to awareness, control rates in this population were higher than the national average [6], and lower than control rates in the United States [29]. We saw a higher proportion of awareness in women, the elderly and people with other medical conditions such as obesity, results similar to previous studies [7,8,29,61,62]. Higher levels of awareness in older and more obese people may be due to the closer attention of the health system to these groups, and their more frequent contact with healthcare professionals [63–66]. We observed poorer knowledge of hypertension in lower wealth scores. Higher SES is probably related to better and easier contact with health workers and more availability of information technologies (e.g., TV, computer, etc.), which predictably lead to higher awareness. Van Rossum *et al.* [67] showed lower awareness among less-educated men and those men who lived without a partner. Living in rural areas was significantly associated with the knowledge of hypertension after adjusting for confounders. Existence of an efficient health network in villages, including the presence of local assistant health personnel (*Behvarz*) who are engaged in vaccination, family health and other primary healthcare functions and have good communication and rapport with villagers, may be one reason for this higher awareness. The cornerstone of primary healthcare (PHC) in Iran is the Health House, which is staffed with one or two Behvarzes. Golestan Province has 607 Health Houses and 1281 active Behvarzes. Each rural Health House is responsible for 1000–1500 individuals on average [68,69]. In urban areas, these Health Houses are replaced by Urban Health Centers, which are responsible for providing PHC for about 15 000 people. One review evaluating the weaknesses of the health system in Iran found that the flaws in the key functions of PHC occurred more frequently in urban than in rural areas [70].

The existence of a relatively good primary healthcare network on the one hand and the observed high prevalence, low awareness, and low treatment and control rates on the other hand suggest that some pragmatic measures may be able to control hypertension and its complications in Golestan Province. The use of polypill, a multidrug regimen for the prevention of hypertension and CVD in low-income and middle-income countries, is one potential strategy that has already shown promise in previous studies [13,71]. Moreover, a recent meta-analysis and mortality estimation in Iran found that using polypill in Iran could have prevented 28 500 deaths due to ischemic heart disease and 12 700 deaths due to stroke in 2006 [72,73]. Therefore, using polypill for primary and secondary prevention of hypertension and CVD in the general population seems to be a reasonable strategy to try in this region. The results of the ongoing POLYIRAN clinical trial will provide additional, stronger data to evaluate the wisdom of such a strategy [20].

Strengths of this study included the large sample size and the extensive collection of information on potentially associated demographic and lifestyle factors. A major limitation was the cross-sectional design of the analysis,

which made it difficult to rule out reverse causation, particularly for smoking and tea consumption. Another limitation was the fact that we measured blood pressure at only one session rather than two office visits, which may have led to some overestimation of the prevalence.

In conclusion, hypertension is a highly prevalent condition in adults in this rural area of Iran. Many of the affected individuals are unaware of their disease, and the rate of control of this disease by antihypertensive medications is very low. Possible ways to lower the prevalence of hypertension in this population include modifying risk factors such as high weight, eating habits and lack of physical activity, conducting a polypill intervention program for primary prevention, and improvement of secondary prevention by increasing hypertension awareness and access to health services, especially in urban areas and among less privileged residents.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet* 2005; 365:217–223.
2. Haghdoost AA, Sadeghirad B, Rezazadehkermani M. Epidemiology and heterogeneity of hypertension in Iran: a systematic review. *Arch Iran Med* 2008; 11:444–452.
3. World Health Organization. *The World Health Report 2002: Reducing risks, promoting healthy life.* Geneva: World Health Organization; 2002 .
4. Danaei G, Finucane MM, Lin JK, Singh GM, Paciorek CJ, Cowan MJ, *et al.* National, regional, and global trends in systolic blood pressure since 1980: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5.4 million participants. *Lancet* 2011; 377:568–577.
5. Ebrahimi M, Mansournia MA, Haghdoost AA, Abazari A, Alaeddini F, Mirzazadeh A, *et al.* Social disparities in prevalence, treatment and control of hypertension in Iran: second National Surveillance of Risk Factors of Noncommunicable Diseases, 2006. *J Hypertens* 2010; 28:1620–1629.
6. Esteghamati A, Abbasi M, Alikhani S, Gouya MM, Delavari A, Shishehbor MH, *et al.* Prevalence, awareness, treatment, and risk factors associated with hypertension in the Iranian population: the national survey of risk factors for noncommunicable diseases of Iran. *Am J Hypertens* 2008; 21:620–626.
7. Azizi F, Ghanbarian A, Madjid M, Rahmani M. Distribution of blood pressure and prevalence of hypertension in Tehran adult population: Tehran Lipid and Glucose Study (TLGS), 1999–2000. *J Hum Hypertens* 2002; 16:305–312.
8. Sarraf-Zadegan N, Boshtam M, Mostafavi S, Rafiei M. Prevalence of hypertension and associated risk factors in Isfahan, Islamic Republic of Iran. *East Mediterr Health J* 1999; 5:992–1001.
9. Wald NJ, Wald DS. The polypill concept. *Postgrad Med J* 2010; 86:257–260.
10. Lonn E, Bosch J, Teo KK, Pais P, Xavier D, Yusuf S. The polypill in the prevention of cardiovascular diseases: key concepts, current status, challenges, and future directions. *Circulation* 2010; 122:2078–2088.
11. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *BMJ* 2009; 338:b1665.
12. Wald NJ, Law MR. A strategy to reduce cardiovascular disease by more than 80%. *BMJ* 2003; 326:1419.
13. Gaziano TA, Opie LH, Weinstein MC. Cardiovascular disease prevention with a multidrug regimen in the developing world: a cost-effectiveness analysis. *Lancet* 2006; 368:679–686.
14. Yusuf S, Pais P, Afzal R, Xavier D, Teo K, Eikelboom J, *et al.* Effects of a polypill (Polycap) on risk factors in middle-aged individuals without cardiovascular disease (TIPS): a phase II, double-blind, randomised trial. *Lancet* 2009; 373:1341–1351.
15. Soliman EZ, Mendis S, Dissanayake WP, Somasundaram NP, Gunaratne PS, Jayasingne IK, *et al.* A Polypill for primary prevention of cardiovascular disease: a feasibility study of the World Health Organization. *Trials* 2011; 12:3.
16. Rodgers A, Patel A, Berwanger O, Bots M, Grimm R, Grobbee DE, *et al.* An international randomised placebo-controlled trial of a four-component combination pill ('polypill') in people with raised cardiovascular risk. *PLoS One* 2011; 6:e19857.
17. Nguyen C, Cheng-Lai A. The polypill: a proposed global solution to cardiovascular disease. *Cardiol Rev* 2013; 21:49–54.
18. Malekzadeh F, Marshall T, Pourshams A, Gharravi M, Aslani A, Nateghi A, *et al.* A pilot double-blind randomised placebo-controlled trial of the effects of fixed-dose combination therapy ('polypill') on cardiovascular risk factors. *Int J Clin Pract* 2010; 64:1220–1227.
19. Majed M, Moradmand Badie S. A pilot double-blind randomised placebo-controlled trial of the effects of fixed-dose combination therapy ('polypill') on cardiovascular risk factors. *Arch Iran Med* 2011; 14:78–80.
20. POLYIRAN in Primary and Secondary Prevention of Cardiovascular Disease in Middle-aged and Elderly Iranians. Available from: http://clinicaltrials.gov/ct2/show/NCT01271985. [Accessed 5 January 2013].
21. Khademi H, Malekzadeh R, Pourshams A, Jafari E, Salahi R, Semnani S, *et al.* Opium use and mortality in Golestan Cohort Study: prospective cohort study of 50 000 adults in Iran. *BMJ* 2012; 344:e2502.
22. Pourshams A, Khademi H, Malekshah AF, Islami F, Nouraei M, Sadjadi AR, *et al.* Cohort Profile: The Golestan Cohort Study: a prospective study of oesophageal cancer in northern Iran. *Int J Epidemiol* 2010; 39:52–59.
23. Malekzadeh R, Mohamadnejad M, Merat S, Pourshams A, Etemadi A. Obesity pandemic: an Iranian perspective. *Arch Iran Med [Review]* 2005; 8:1–7.
24. Bahrami H, Sadatsafavi M, Pourshams A, Kamangar F, Nouraei M, Semnani S, *et al.* Obesity and hypertension in an Iranian cohort study; Iranian women experience higher rates of obesity and hypertension than American women. *BMC Public Health* 2006; 6:158.
25. Golozar A, Khademi H, Kamangar F, Poutschi H, Islami F, Abnet CC, *et al.* Diabetes mellitus and its correlates in an Iranian adult population. *PLoS One* 2011; 6:e26725.
26. WHO.int. BMI classification. Geneva: World health organization; 2006 [updated 01/12/2012]; Available from: http://apps.who.int/bmi/index.jsp?introPage=intro_3.html2011. [Accessed 1 Dec 2012].
27. Aram V. Chobanian GLB, Henry R. Black, William C. Cushman, *et al.* The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003; 42:1206–1252.
28. Ahmad OB, Boschi-Pinto C, Lopez AD, Murray CJL, Lozano R, Inoue M. *Age standardization of rates: a new WHO standard.* Geneva: World Health Organization; 2001.
29. Ong KL, Cheung BM, Man YB, Lau CP, Lam KS. Prevalence, awareness, treatment, and control of hypertension among United States adults 1999–2004. *Hypertension* 2007; 49:69–75.
30. Azizi F, Salehi P, Etemadi A, Zahedi-Asl S. Prevalence of metabolic syndrome in an urban population: Tehran Lipid and Glucose Study. *Diabetes Res Clin Pract* 2003; 61:29–37.
31. Press V, Freestone I, George CF. Physical activity: the evidence of benefit in the prevention of coronary heart disease. *QJM* 2003; 96:245–251.
32. Carnethon MR, Evans NS, Church TS, Lewis CE, Schreiner PJ, Jacobs DR Jr, *et al.* Joint associations of physical activity and aerobic fitness on the development of incident hypertension: coronary artery risk development in young adults. *Hypertension* 2010; 56:49–55.
33. Frisoli TM, Schmieder RE, Grodzicki T, Messerli FH. Beyond salt: lifestyle modifications and blood pressure. *Eur Heart J* 2011; 32:3081–3087.

34. Reaven GM, Lithell H, Landsberg L. Hypertension and associated metabolic abnormalities–the role of insulin resistance and the sympathoadrenal system. *N Engl J Med* 1996; 334:374–381.

35. Palatini P, Visentin P, Dorigatti F, Guarnieri C, Santonastaso M, Cozzio S, *et al*. Regular physical activity prevents development of left ventricular hypertrophy in hypertension. *Eur Heart J* 2009; 30:225–232.

36. Cozza IC, Di Sacco TH, Mazon JH, Salgado MC, Dutra SG, Cesarino EJ, *et al*. Physical exercise improves cardiac autonomic modulation in hypertensive patients independently of angiotensin-converting enzyme inhibitor treatment. *Hypertens Res* 2012; 35:82–87.

37. Kawakami K, Aketa S, Sakai H, Watanabe Y, Nishida H, Hirayama M. Antihypertensive and vasorelaxant effects of water-soluble proanthocyanidins from persimmon leaf tea in spontaneously hypertensive rats. *Biosci Biotechnol Biochem* 2011; 75:1435–1439.

38. Stangl V, Lorenz M, Stangl K. The role of tea and tea flavonoids in cardiovascular health. *Mol Nutr Food Res* 2006; 50:218–228.

39. Kojima T, Ouchi Y. Epidemiology and prevention of elderly hypertension. *Nippon rinsho Japanese J Clin Med* 2005; 63:938–943.

40. Yang YC, Lu FH, Wu JS, Wu CH, Chang CJ. The protective effect of habitual tea consumption on hypertension. *Arch Intern Med* 2004; 164:1534–1540.

41. Yung LM, Leung FP, Wong WT, Tian XY, Yung LH, Chen ZY, *et al*. Tea polyphenols benefit vascular function. *Inflammopharmacology* 2008; 16:230–234.

42. Song L, Koo MWL, Lau CP, Cheung BMY. Effects of green tea on lipids, blood pressure and vasorelaxation in rats with hypercholesterolaemia-induced hypertension. *Int J Cardiol* 2008; 125 (suppl 1):S64.

43. Antonello M, Montemurro D, Bolognesi M, Di Pascoli M, Piva A, Grego F, *et al*. Prevention of hypertension, cardiovascular damage and endothelial dysfunction with green tea extracts. *Am J Hypertens* 2007; 20:1321–1328.

44. Talukder MA, Johnson WM, Varadharaj S, Lian J, Kearns PN, El-Mahdy MA, *et al*. Chronic cigarette smoking causes hypertension, increased oxidative stress, impaired NO bioavailability, endothelial dysfunction, and cardiac remodeling in mice. *Am J Physiol Heart Circ Physiol* 2011; 300:H388–H396.

45. Sleight P. Smoking and hypertension. *Clin Exp Hypertens* 1993; 15:1181–1192.

46. Gleerup G, Winther K. Smoking further increases platelet activity in patients with mild hypertension. *Eur J Clin Invest* 1996; 26:49–52.

47. Cryer PE, Haymond MW, Santiago JV, Shah SD. Norepinephrine and epinephrine release and adrenergic mediation of smoking-associated hemodynamic and metabolic events. *N Engl J Med* 1976; 295:573–577.

48. Minami J, Todoroki M, Yoshii M, Mita S, Nishikimi T, Ishimitsu T, *et al*. Effects of smoking cessation or alcohol restriction on metabolic and fibrinolytic variables in Japanese men. *Clin Sci* 2002; 103:117–122.

49. Bermudez EA, Rifai N, Buring JE, Manson JE, Ridker PM. Relation between markers of systemic vascular inflammation and smoking in women. *Am J Cardiol* 2002; 89:1117–1119.

50. Sesso HD, Buring JE, Rifai N, Blake GJ, Gaziano JM, Ridker PM. C-reactive protein and the risk of developing hypertension. *JAMA* 2003; 290:2945–2951.

51. Noor A, Jatoi PJ-D, Feely J, Mahmud A. Impact of Smoking and Smoking Cessation on Arterial Stiffness and Aortic Wave Reflection in Hypertension. *Hypertension* 2007; 49:981–985.

52. Kim JW, Park CG, Hong SJ, Park SM, Rha SW, Seo HS, *et al*. Acute and chronic effects of cigarette smoking on arterial stiffness. *Blood Press* 2005; 14:80–85.

53. Dochi M, Sakata K, Oishi M, Tanaka K, Kobayashi E, Suwazono Y. Smoking as an independent risk factor for hypertension: a 14-year

54. Halperin RO, Gaziano JM, Sesso HD. Smoking and the risk of incident hypertension in middle-aged and older men. *Am J Hypertens* 2008; 21:148–152.

55. Gee ME, Bienek A, Campbell NR, Bancej CM, Robitaille C, Kaczorowski J, *et al*. Prevalence of, and barriers to, preventive lifestyle behaviors in hypertension (from a national survey of Canadians with hypertension). *Am J Cardiol* 2012; 109:570–575.

56. Mishra V, Arnold F, Semenov G, Hong R, Mukuria A. Epidemiology of obesity and hypertension and related risk factors in Uzbekistan. *Eur J Clin Nutr* 2006; 60:1355–1366.

57. Janghorbani M, Amini M, Gouya MM, Delavari A, Alikhani S, Mahdavi A. Nationwide survey of prevalence and risk factors of prehypertension and hypertension in Iranian adults. *J Hypertens* 2008; 26:419–426.

58. Grotto I, Huerta M, Sharabi Y. Hypertension and socioeconomic status. *Curr Opin Cardiol* 2008; 23:335–339.

59. Esteghamati A, Meysamie A, Khalilzadeh O, Rashidi A, Haghazali M, Asgari F, *et al*. Third national Surveillance of Risk Factors of Non-Communicable Diseases (SuRFNCD-2007) in Iran: methods and results on prevalence of diabetes, hypertension, obesity, central obesity, and dyslipidemia. *BMC Public Health* 2009; 9:167.

60. WHO Global InfoBase team. *The SuRF Report 2. Surveillance of chronic disease risk factors: Country-level data and comparable estimates*. Geneva: World Health Organization; 2005.

61. Mendez-Chacon E, Santamaria-Ulloa C, Rosero-Bixby L. Factors associated with hypertension prevalence, unawareness and treatment among Costa Rican elderly. *BMC Public Health* 2008; 8:275.

62. Mohan V, Deepa M, Farooq S, Datta M, Deepa R. Prevalence, awareness and control of hypertension in Chennai - The Chennai Urban Rural Epidemiology Study (CURES - 52). *J Assoc Physicians India* 2007; 55:326–332.

63. O'Rourke M. Arterial stiffness, systolic blood pressure, and logical treatment of arterial hypertension. *Hypertension* 1990; 15:339–347.

64. Forman DE, Rich MW, Alexander KP, Zieman S, Maurer MS, Najjar SS, *et al*. Cardiac care for older adults. Time for a new paradigm. *J Am Coll Cardiol* 2011; 57:1801–1810.

65. Ko FC. The clinical care of frail, older adults. *Clin Geriatr Med* 2011; 27:89–100.

66. Alavez S, Lithgow GJ. A new look at old compounds. *Aging* 2011; 3:338–339.

67. van Rossum CT, van de Mheen H, Witteman JC, Hofman A, Mackenbach JP, Grobbee DE. Prevalence, treatment, and control of hypertension by sociodemographic factors among the Dutch elderly. *Hypertension* 2000; 35:814–821.

68. Shadpour K. Primary healthcare networks in the Islamic Republic of Iran. *East Mediterr Health J* 2000; 6:822–825.

69. Asadi-Lari M, Sayyari AA, Akbari ME, Gray D. Public health improvement in Iran: lessons from the last 20 years. *Public Health* 2004; 118:395–402.

70. Moghadam MN, Sadeghi V, Parva S. Weaknesses and challenges of primary healthcare system in Iran: a review. *Int J Health Plann Manag* 2012; 27:e121–e131.

71. Wise J. Polypill holds promise for people with chronic disease. *Bull WHO* 2005; 83:885–887.

72. Sepanlou SG, Farzadfar F, Jafari E, Danaei G. Cardiovascular disease prevention using fixed dose pharmacotherapy in iran: updated meta-analyses and mortality estimation. *Arch Iran Med* 2012; 15:531–537.

73. Namazi MH, Mohagheghi A, Ostovaneh MR. Prevention of cardiovascular diseases in developing countries. *Arch Iran Med* 2012; 15:528–530.

Reviewer's Summary Evaluation

Reviewer 1

The strength of the study lies in the large number of study participants, mainly from a rural area as well as a very detailed recording of a great number of associated cardiovascular risk factors and associated parameters. The results are representative of the area studied and to some extent to the Iranian population as well. The study contributes to our knowledge about the global aspect of the prevalence, awareness and treatment of hypertension.

The weakness of the study could be that the prevalence of hypertension might be somewhat overestimated as only one blood pressure measurement was done and often subsequent blood pressure measurement could be somewhat lower. The authors drew attention to this as a limitation of the study.