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ORIGINAL ARTICLE

Pre-hypertension, pre-diabetes or both: which is best at predicting cardiovascular events in the long term?

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The present study aimed to assess the value of pre-diabetes and pre-hypertension in predicting cardiovascular events. A population-based, cross-sectional survey was conducted, representing a large sample of the general Iranian population aged 35 years and older from the Isfahan Province and determined using a random, multistage cluster-sampling 10-year cohort. The five end points considered as study outcome were unstable angina (UA), acute occurrence of myocardial infarction (MI), sudden cardiac death (SCD), brain stroke and cardiovascular disease (CVD). Of the 6323 subjects scheduled for assessment of diabetes state 617 were diabetics and 712 were pre-diabetic. In addition, of these subjects, 1754 had hypertension and 2500 had pre-hypertension. Analysing only pre-hypertension, pre-diabetes and its combination and adjusted for gender and age variables, pre-hypertension and pre-diabetes status together, could only effectively predict occurrence of MI (hazard ratio (HR) = 3.21, 95% confidence interval (CI): 1.06–9.76, $P = 0.04$). In the same COX regression models, pre-hypertension status could predict UA and CVD occurrence (HR = 2.94, 95% CI: 1.68–5.14, $P < 0.001$ and HR = 1.74, 95% CI: 1.23–2.47, $P = 0.002$, respectively). However, pre-diabetes status could not predict any of these events after adjustment for gender and age. Our data provide valuable evidence of the triggering role of pre-hypertension and pre-diabetes together, on appearance and progression of MI even in healthy individuals and the significant predicting value of pre-hypertension on the occurrence of UA and CVD. In this regard, the value of pre-hypertension and pre-diabetes together, and the pre-hypertension state alone, are clearly superior to pre-diabetes state alone in predicting cardiovascular events.

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INTRODUCTION

Cardiovascular diseases (CVDs) are considered one of the main causes of mortality and life-threatening morbidity worldwide.[1] In communities with higher prevalence of CVDs, uncontrolled potential risk factors, such as hypertension and diabetes mellitus, may lead to higher mortality and morbidity.[1] Even a slight change in blood pressure or insulin resistance has been shown to be associated with an increased risk of significant mortality and adverse cardiac events in patients from such communities.[2] In this regard, the two clinical conditions of pre-hypertension or pre-diabetes are not only the precursors to systemic hypertension and diabetes mellitus but can also increase the susceptibility to develop coronary atherosclerosis. In this context, the combination of these two predisposing factors is more likely to lead to severe coronary artery disease (CAD) than expected with either one alone.[3] According to recent reports regarding the high prevalence of these two clinically risky conditions in some countries, their potential role in CVD occurrence should be considered. In two large surveys in the United States and South Korea, the overall prevalence of pre-hypertension was 30% of the general populations.[4,5] The prevalence of pre-diabetes has been estimated in the range of 15.5% in Eastern countries, up to 35% in Western countries and in Iran it is 13%.[6,7] It seems that the prevalence of these conditions may be higher than the reported ranges because of the unawareness of the majority of affected individuals of their risk.[8] The underlying pathophysiological causes related to pre-hypertension and pre-diabetes leading to increased risk of cardiovascular disorders remain unknown. It has been suggested that individuals with these clinical conditions have the same risk factors such as insulin resistance, hypertension, hyperlipidemia, obesity, low physical activity, endothelial dysfunction, abnormal coagulative state and inflammatory conditions, as those linked to increased risk of cardiovascular events.[9] Despite the demonstrated role of pre-hypertension and pre-diabetes in possible progress to hypertension and diabetes mellitus, as well as their status as risk factors for atherosclerotic events, it has remained unclear which of these conditions can predict cardiovascular events more effectively. The present study aimed to assess the impact of pre-diabetes and pre-hypertension, separately and in combination to predict unstable angina (UA), myocardial infarction (MI), brain stroke, sudden cardiac death (SCD) and CVD (consisting either of UA, MI, brain stroke or SCD) in a large longitudinal cohort in Iran.

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MATERIALS AND METHODS

This research was based on a large longitudinal cohort study, begun in 2001. With the use of a random multistage cluster sampling, a large sample was originally selected from urban and rural population of 19 years and older from Isfahan, Najafabad and Arak at the central part of Iran and was followed for 10 years. The detailed methods, sampling and measurements, and population characteristics were previously presented.[8–12] Patients with metabolic and inflammatory disorders and those administered by any agents affecting their carbohydrate and lipid metabolisms were excluded from the study. At the baseline, all the participants were void of CVD or any kidney disease. Before collecting the data, each participant offered his/her written informed consent. The research committee at Isfahan Cardiovascular Research Institute as a collaborating centre of WHO approved the protocol. By the use of a validated questionnaire including demographic features, socioeconomic information, history of medications and risk factors for cardiovascular diseases, the trained medical personnel collected the baseline data. Furthermore, measurements of body weight and height were done on a calibrated beam scale and wall-mounted stadiometer barefoot to the nearest 0.1 kg and 0.1 cm, respectively. Then, body weight (kg) was divided by height (m^2) to obtain body mass index. Also, some questions concerning current smoking and dietary, and lifestyle habits were asked to identify the presence of any cardiovascular risk factors. Those involved in regular smoking of a tobacco product once or more times per day or at any time in the past 30 days were defined as the smokers in this research;[12] hypercholesterolaemia as total cholesterol $\geqslant 5.0$ mmol l^{-1}, high-density lipoprotein-cholesterol $\geqslant 1.0$ mmol l^{-1} in males or $\geqslant 1.1$ mmol l^{-1} in females, and triglycerides $\geqslant 2.0$ mmol l^{-1};[13] positive first-degree family history of CAD in men and women < 55 and 65 years old, respectively;[14] hypertension as being on antihypertensive treatment and/or systolic blood pressure of $\geqslant 140$ mm Hg and/or diastolic blood pressure of $\geqslant 90$ mm Hg;[15] and symptoms of diabetes mellitus associated with at least a plasma glucose concentration of $\geqslant 11.1$ mmol l^{-1}, fasting plasma glucose of $\geqslant 7.0$ mmol/l, or 2 hpp $\geqslant 11.1$ mmol/l.[16] A systolic blood pressure of 120–139 mm Hg and/or a diastolic blood pressure of 80–89 mm Hg was/were determined as a pre-hypertension case.[3]

Fasting blood glucose levels of 100–125 mg dl^{-1} as impaired fasting glucose and/or 2-h postprandial (2 hpp) blood glucose levels of 140–199 mg dl^{-1} after a load of 75 g oral glucose as impaired glucose tolerance were the criteria for pre-diabetes diagnosis according to American Diabetes Association.[17]

Occurrences of brain stroke, UA, MI, SCD and CVD within a follow-up period of 9 years were considered as acute cardiovascular outcomes in this cohort study. Every 2 years, the participants were asked briefly about any CVD occurrences through phone calls. All the measurements were repeated every 5 years. This cohort follow-up procedure is explained in detail elsewhere.[8]

The most recently published studies on the prevalence of pre-hypertension and pre-diabetes in various Middle Eastern countries were reviewed as well. Surveys on normal populations were considered, and specific age groups and communities were excluded from the review.

Chi-square and one-way ANOVA (analysis of variance) tests were employed to compare the percentages between categorical variables and across quantitative variables, respectively. Also, univariate and multiple Cox regression analysis were performed based on statistically significant correlations with cardiovascular events to investigate their independence as the determinants. Moreover, calculations of HR and CIs of 95% were done and *P*-values of 0.05 or less were regarded to be statistically significant. SPSS software, version 15.0 (SPSS Inc., Chicago, IL, USA) was used to conduct all the statistical analyses.

RESULTS

A total of 6323 subjects were studied in 2001, 925 were missing in the follow-ups and the remaining 5398 were followed for 10 years. Subjects at baseline underwent fasting blood sugar and 2 hpp blood sugar assessment, 1754 subjects had hypertension, 2500 subjects were pre-hypertensive, 617 were diabetics, 712 pre-diabetic and 286 had both pre-hypertension and pre-diabetes. Comparisons of baseline characteristics between the groups are presented in Table 1. Both diabetes and pre-diabetes were higher in females than in males. Diabetics and pre-diabetics were older and had higher mean body mass index (BMI), and lower prevalence of current smoking than did non-diabetics. The comparison of baseline data across different groups of blood pressure categories (Table 1) showed higher female gender distribution, higher average age, higher BMI and lower current smoking in those who suffered hypertension than in the pre-hypertensive group, whereas no significant differences were revealed in these parameters between normotensive and pre-hypertensive groups. The participants with pre-hypertension (6.38%) experienced CVDs more than healthy participants (3.11%; Figure 1). Also, both MI and sudden cardiac death were more prevalent in subjects with both pre-hypertension and pre-diabetes (1.07 and 0.72%, respectively). In Table 2, subjects with hypertension or diabetes mellitus were not analysed and after adjustment for gender and age, pre-hypertension status could effectively predict occurrence of CVD and UA (HR = 1.74, 95% CI: 1.23–2.47, $P = 0.002$ and HR = 2.94, 95% CI: 1.68–5.14, $P = < 0.001$, respectively), but did not predict appearance of MI, SCD or brain stroke. In addition, we found that subjects with the combination of pre-hypertension and pre-diabetes status are at risk of MI 3.21-folds more than are other subjects (95% CI: 1.23–2.47, $P = 0.04$). The same Cox regression models used showed that pre-diabetes could not predict any of the CVD events.

A literature review of the most recent studies regarding the prevalence of pre-hypertension and pre-diabetes on normal populations in Middle Eastern countries is provided in

Table 1. Baseline characteristics in subgroups of study population

Characteristics	*Non-diabetic*	*Diabetic*	*Pre-diabetic*	P-*value*
Male gender	2521 (50.5)	264 (42.8)	283 (39.7)	< 0.001
Age, years	49.70 ± 11.33	56.07 ± 11.27	53.51 ± 12.47	< 0.001
Body mass index, kg m^{-2}	26.26 ± 4.37	28.34 ± 4.57	27.79 ± 4.72	< 0.001
Current smoking	820 (16.4)	68 (11.0)	70 (9.8)	< 0.001
Receiving anti-hypertension drugs	466 (77.8)	142 (82.6)	125 (82.2)	0.254
Receiving anti-lipidemic drugs	382 (46.1)	143 (54.8)	72 (45.6)	0.042
Characteristics	*Non-hypertensive*	*Hypertensive*	*Pre-hypertensive*	P-*value*
Male gender	996 (48.1)	757 (43.2)	1315 (52.6)	< 0.001
Age, years	45.92 ± 9.43	57.44 ± 11.68	50.07 ± 11.10	< 0.001
Body mass index, kg m^{-2}	25.62 ± 4.31	27.76 ± 4.55	26.68 ± 4.40	< 0.001
Current smoking	504 (24.4)	290 (16.5)	543 (21.7)	< 0.001
Receiving anti-diabetes drugs	46 (64.8)	158 (72.5)	110 (70.1)	0.465
Receiving anti-lipidemic drugs	110 (39.3)	300 (59.3)	187 (40.6)	< 0.001

Data are shown as number (percentage), or mean ± s.d.

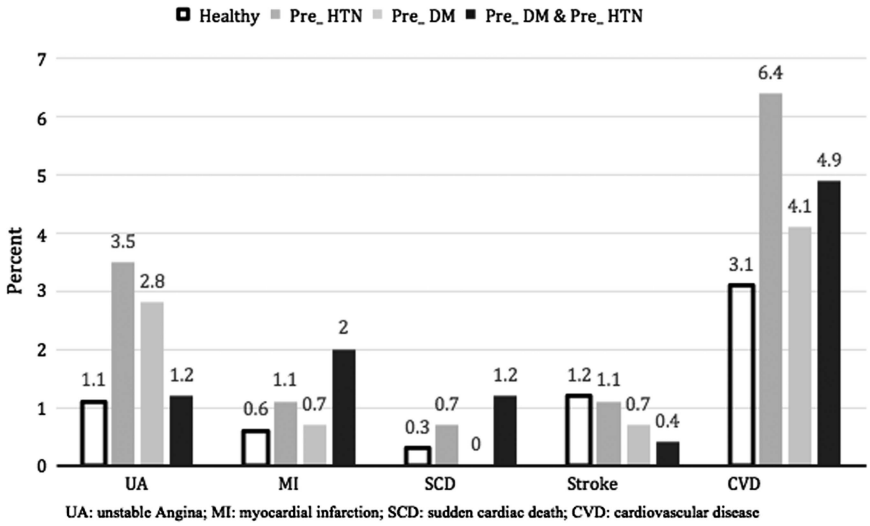

Figure 1. Cardiovascular events in healthy, pre-hypertension, pre-diabetes, and pre-diabetes mellitus and pre-hypertension.

Table 2. Adjusted and non-adjusted HR (95% CI) of developing cardiovascular events according to the presence of pre-hypertension, pre-diabetes or both

Variable	*Healthy,* N = *1542*	*Unadjusted*						*Healthy,* N = *1542*	*Adjusted for sex and age*					
		Pre-HTN, N = *1677*		*Pre-DM,* N = *145*		*Pre-HTN and Pre-DM,* N = *247*			*Pre-HTN,* N = *1677*		*Pre-DM,* N = *145*		*Pre-HTN and Pre-DM,* N = *247*	
		HR (95% CI)	P-*value*	*HR (95% CI)*	P-*value*	*HR (95% CI)*	P-*value*		*HR (95% CI)*	P-*value*	*HR (95% CI)*	P-*value*	*HR (95% CI)*	P-*value*
MI	R	1.79 (0.81, 4.01)	0.15	1.25 (0.16, 9.92)	0.83	3.83 (1.28, 11.46)	0.016	R	1.46 (0.65, 3.28)	0.36	1.28 (0.16, 10.14)	0.81	3.21 (1.06, 9.76)	0.04
Stroke	R	0.96 (0.50, 1.83)	0.90	0.59 (0.08, 4.14)	0.61	0.37 (0.05, 2.75)	0.33	R	0.78 (0.41, 1.51)	0.47	0.55 (0.07, 4.14)	0.56	0.28 (0.04, 2.09)	0.21
SCD	R	2.68 (0.86, 8.32)	0.09	—[a]	—[a]	5.09 (1.14, 22.83)	0.03	R	2.03 (0.65, 6.38)	0.23	—[a]	—[a]	4.01 (0.88, 18.31)	0.07
UA	R	3.25 (1.87, 5.65)	< 0.001	2.69 (0.9, 8.06)	0.08	1.27 (0.37, 4.37)	0.70	R	2.94 (1.68, 5.14)	< 0.001	2.69 (0.90, 8.08)	0.08	1.17 (0.34, 4.02)	0.81
CVD	R	2.05 (1.45, 2.89)	< 0.001	1.39 (0.59, 3.24)	0.45	1.73 (0.92, 3.26)	0.09	R	1.74 (1.23, 2.47)	0.002	1.37 (0.59, 3.21)	0.47	1.47 (0.77, 2.78)	0.24

Abbreviations: CI, confidence interval; CVD, cardiovascular disease; HR, hazards ratio; MI, myocardial infarction; pre-HTN, pre-hypertension; pre-DM, pre-diabetes mellitus; R, reference; SCD, sudden cardiac death; UA, unstable angina. [a]No pre-DM subject had SCD.

Table 3,[18–21] and Table 4,[22–28] respectively. The percentage of individuals with pre-hypertension and pre-diabetes in other countries in the Middle East ranges from 30 to 54.1 and 13.8% to 44.2%, respectively. Our report finds the incidences of pre-hypertension and pre-diabetes are 46.3 and 11.4%, respectively, which is comparable with the findings from other countries in the region.

DISCUSSION

It has been well demonstrated that patients with diabetes or hypertension accelerate coronary artery involvement and thus can aggravate cardiovascular events and related outcomes.[29,30] The present study showed that the combination of pre-hypertension and pre-diabetes can trigger the progression of MI and have been identified as potential risk factors for CVD, though, among pre-hypertension and pre-diabetes conditions, only the former one can effectively predict the occurrence of myocardial infarction, whereas pre-diabetes had no significant value for predicting any of the studied CVD events. In total, both pre-hypertension and pre-diabetes mellitus had high values for predicting CVD events, adjusted for baseline confounders.

Although pre-diabetes has been found to be a potential risk factor for MI (unadjusted for gender and sex), after adjusting these two baseline variables, the predictive role of pre-diabetes for acute CVD events was not indicated. It seems that the value of pre-diabetes for triggering cardiac ischaemic events may be discrepant in men and women as well as in the young and the elderly. This means that partial changes in blood glucose may be successfully tolerable in some gender and age subgroups.

Table 3. Literature review reporting pre-hypertension prevalence in the Middle Eastern countries

Country	*Year*	*Author*	*Total sample*	*Age range mean*	*Study design*	*Diagnostic criteria*	*Finding*	*Conclusion*
Iran (This Study)	2016	Khosravi *et al.*	5398	35 <	Cohort	JNC 7	Pre-HTN = 46.3%, HTN = 32.5%	Pre-HTN and Pre-DM together & Pre-HTN state alone, are superior to Pre-DM in predicting cardiovascular events
Egypt	2012	El-Din *et al.*[18]	5534	20–75	Cross-sectional	JNC 7	Pre-HTN = 49.2%, HTN = 16.8%	Overweight/obesity and diabetes are risk factor for HTN. Public awareness strategies for HTN is needed
Turkey	2010	Gupta *et al.*[19]	10380	20 <	Cross-sectional	JNC 7	Pre-HTN = 36.3%, HTN = 11.8%	Detection of Pre-HTN, during annual health maintenance in disease-free adults, could become an early marker of adverse cardiometabolic risk profile
Lebanon	2015	Matar *et al.*[20]	1685	20 <	Cross-sectional	JNC 7	Pre-HTN = 30%, HTN = 37%	Awareness, treatment, and control rates remain low and should be substantially improved
Oman	2008	Ganguly *et al.*[21]	327	18 <	Cross-sectional	JNC 7	Pre-HTN = 54.1%, HTN = 24.2%	In Pre-DM subjects, male gender, increasing dysglycemia and BMI are the major determinant for Pre-HTN

Abbreviations: BMI, body mass index; JNC 7, Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure; pre-HTN, pre-hypertension. Definition based on JNC 7: systolic blood pressure ranging from 120 to 139 mmHg and/or a diastolic blood pressure ranging from 80 to 89 mmHg

Table 4. Literature review reporting pre-diabetes prevalence in the Middle Eastern countries

Country	*Year*	*Author*	*Total sample*	*Age range mean*	*Study design*	*Diagnostic criteria*	*Finding*	*Conclusion*
Iran (This Study)	2016	Khosravi *et al.*	5398	35 <	Cohort	IFG, IGT	Pre-DM = 11.4%, DM = 13.2%	Pre-HTN and pre-DM together & pre-HTN state alone, are superior to pre-DM in predicting Cardiovascular events
Turkey	2013	Satman *et al.*[22]	26 499	20 <	Cross-sectional	IFG, IGT	Pre-DM = 30.8%, DM = 16.5%	This figure is alarming and underscore the urgent need for national programs to prevent diabetes, to manage the illness and thus prevent complications
Iraq	2015	Al-Azzawi *et al.*[23]	300	30– 75	Cross-sectional	IFG, IGT	Pre-DM = 33.7%	Pre-DM is associated with Metabolic syndrome, increasing the burden on public health care that needs to be addresses globally
Saudi Arabia	2014	Al-Rubeaan *et al.*[24]	53 370	18 <	Cohort	IFG	Pre-DM = 22.6%, DM = 11.9%	Abnormal glucose metabolism has reached an epidemic state. An urgent strategy for launching diabetes primary prevention programs is needed
Lebanon	2014	Ghassibe-Sabbagh *et al.*[25]	998	65	Cross-sectional	HbA1C	Pre-DM = 20.7%, DM = 40.8%	hypertension, hyperlipidemia, and low levels of HDL-C are associated with an increased risk of pre-diabetes and DM. There is an alarming prevalence of pre-diabetes and diabetes
Oman	2011	Al-Shafaee *et al.*[26]	1313	18– 60	Cross-sectional	IFG, IGT	Pre-DM = 44.2%	Customised interventions targeting groups with high risk of pre-diabetes, especially men, the elderly and the obese, are urgently needed
Kuwait	2016	Zhang *et al.*[27]	960	20 <	Cross-sectional	FBG, HbA1C	Pre-DM = 40%, DM = 27%	Improving vitamin D status, even to a small extent, can potentially have a large impact on diabetes prevention in this high-risk population
Qatar	2009	Bener A. *et al.*[28]	1117	20 <	Cross-sectional	IFG, IGT	Pre-DM = 13.8%, DM = 16.7%	Early diagnosis of DM is of major importance to reduce the risk of these diabetes-related conditions

Abbreviations: DM, diabetes mellitus; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; pre-DM, pre-diabetes mellitus; pre-HTN, pre-hypertension. DM: fasting glucose $\geqslant$7.0 mmol l^{-1} or, HbA1C $\geqslant$6.5 % or, plasma glucose concentration $\geqslant$11.1 mmol l^{-1} or, fasting blood glucose $\geqslant$126 mg dl, or use of medications to control diabetes. Definition of Pre-DM used in studies based on: IFG—fasting blood glucose levels from 100 to 125 mg dl^{-1}; IGT—140 to 199 mg dl^{-1} after a 75 g oral glucose load; HbA1C—5.7–6.4%; fasting blood glucose—5.6 to 6.9 mmol l^{-1}.

However, some studies may suggest a continuous relationship between the developing role of pre-diabetes to diabetes, it can be also considered a high-risk factor but with lower triggering value in terms of development of acute ischaemic events.[31,32] It is believed that, like diabetes, pre-diabetes can provoke some molecular processes that impair the structure and functioning of blood vessels, leading to arterial inflammation and vasoconstriction and thus inducing the beginning of atherosclerosis.[33–37] In addition, both pre-diabetes and diabetes status are commonly prevalent in CAD patients (diagnosed in 35% and 31% of patients,

respectively).[38] In addition, >60% of individuals with previously undiagnosed pre-diabetes or diabetes experience myocardial infarction or undergo coronary catheterization and angiography following suspected coronary involvement.[38] Moreover, a strong relationship between pre-diabetes status and two traditional coronary risk factors of obesity and hyperlipidemia has been suggested.[39–41] Individuals with pre-diabetes develop obesity and dyslipidemia, and thus any assessment of a patient with pre-diabetes should consist of the measurement of lipid profile as well as anthropometric parameters, with the aim of CAD risk stratification. However, our results show that pre-diabetes could not effectively predict the occurrence of any cardiovascular events. In our study, the insignificant association between pre-diabetes and increased risk of cardiovascular events may be due to the fact that less than half of our pre-diabetic subjects (45.6%), were under anti-lipidemic drugs and their average BMI (27.79 = overweight), was not classified as obese. In addition, the slight coronary microvascular dysfunction in the patients studied could be the reason why pre-diabetes could not underlie ischaemic events. In sum, pre-diabetes remains a matter of controversy, especially with regard to its management and treatment in healthy individuals.

Some studies may suggest a continuous relationship between systolic blood pressure and the progression rate of coronary atherosclerosis over a broad range of blood pressures extending from 100 mm Hg to the hypertensive range.[42] In this regard, it has been shown that patients who improved from a pre-hypertensive state at baseline to normal blood pressure levels had significantly less progression of an atheroma than did patients who remained pre-hypertensive.[43] It has been revealed that the alteration of coronary flow reserve is significantly impaired in patients with pre-hypertension compared with normotensive subjects; however, in subjects with pre-hypertension, impairment of coronary flow reserve was not as severe as in those with hypertension.[44] In our study, the significant association between pre-hypertension and increased risk of cardiovascular events may be due to great coronary microvascular dysfunction in the patients studied. Therefore, it is reasonable to consider individuals with pre-hypertension to be at high risk for UA and CVD, and thus candidates for coronary diagnostic interventions to reduce the occurrence of acute ischaemic events in pre-hypertensive patients.

To the best of our knowledge, this is the first study in its field among the Middle Eastern countries. Moreover, many Middle Eastern countries lack sufficient data regarding the prevalence of pre-hypertension and pre-diabetes. However, as in Table 3,[18–21] and Table 4,[22–28] the prevalence of pre-hypertension and pre-diabetes of other countries in the region is relatively comparable to that found in Iran, considering the growing rate of this incidence in these regions.

Despite the diversity and inequalities found in Middle Eastern countries, they still have several health issues in common. This is possibly related to their relatively similar cultural backgrounds, socioeconomic circumstances and religion, which result in similar lifestyles with specific and preventable known risk factors. The Middle East is predicted to be among the regions that will experience a tripling of Coronary heart disease and stroke mortality over the next two decades.[45] Therefore, based on this study, Middle Eastern countries should consider pre-hypertension in particular as a strong risk factor for cardiovascular events.

LIMITATION

The fact that our sample was Iranians limits the generalisability of our findings beyond the Middle East region. Also, no similar study could be found in the Middle East, so we were unable to compare our results with other Middle Eastern countries. In the literature review on the prevalence of pre-hypertension and pre-diabetes, only a certain number of countries studied the incidence of these two factors in their nations, resulting in a limited number of possible comparisons. In addition, some of the factors such as subfractions of cholesterol, smoking status, anti-hypertension drugs, anti-diabetes drugs and anti-lipidemic drugs were not adjusted in the model in this study.

In conclusion, our data provide valuable evidence of the triggering role for the combination of pre-hypertension and pre-diabetes in predicting myocardial infarction, and pre-hypertension in the occurrence of unstable angina and cardiovascular diseases even in apparently healthy individuals. In this regard, the value of pre-hypertension for predicting cardiovascular events is clearly superior to pre-diabetes state and thus the presence of mildly elevated blood pressure should be considered seriously by clinicians or health professionals while planning for preventive or screening programs.

What is known about topic?

- Cardiovascular diseases (CVDs) are considered one of the main causes of mortality and life-threatening morbidity worldwide
- Despite the demonstrated role of pre-hypertension and pre-diabetes in possible progress to hypertension and diabetes mellitus, as well as their status as risk factors for CVDs, it has remained unclear, which of these conditions can predict cardiovascular events more effectively.

What this study adds?

- There is a valuable evidence of the triggering role for the combination of pre-hypertension and pre-diabetes in predicting myocardial infarction which is 3.21-folds more than other subjects, and pre-hypertension in the occurrence of unstable angina and cardiovascular diseases even in apparently healthy individuals.
- The value of pre-hypertension for predicting cardiovascular events is clearly superior to pre-diabetes state and thus the presence of mildly elevated blood pressure should be considered seriously by clinicians or health professionals while planning for preventive or screening programs.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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