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ORIGINAL ARTICLE

Triglycerides and triglycerides to high-density lipoprotein cholesterol ratio are strong predictors of incident hypertension in Middle Eastern women

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Dyslipidemia has been reported as a risk factor for incident hypertension in a few prospective studies, however, no study has specifically assessed different lipid measures including the lipid ratios, that is, total cholesterol (TC)/high-density lipoprotein cholesterol (HDL-C) and triglycerides (TGs)/HDL-C as predictors of hypertension among Middle Eastern women with high prevalences of dyslipidemia and hypertension. The study population consisted of 2831 non-hypertensive women, aged ⩾20 years. We measured lipoproteins, and calculated non-HDL-C and the lipid ratios. The risk-factor-adjusted odds ratios for incident hypertension were calculated for every 1 standard deviation (s.d.) change in TC, log-transformed TG, HDL-C, non-HDL-C, TC/HDL-C and log-transformed TG/HDL-C using multivariate logistic regression analysis. Over a mean follow-up of 6.4 years, 397 women developed hypertension. An increase of 1 s.d. in TG, TC/HDL-C and TG/HDL-C increased the risk of incident hypertension by 16, 19 and 18%, respectively, and 1 s.d. increase in HDL-C decreased the risk of hypertension by 14% in the multivariable model (all $P \leqslant 0.05$). In models excluding women with diabetes and central or general obesity, TG, TG/HDL-C and TC/HDL-C remained as independent predictors of incident hypertension. In conclusion, dyslipidemia, using serum TG and TG/HDL-C, in particular, may be useful in identification of women at risk of hypertension, even in those without diabetes and central or general obesity.
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Introduction

The rapid change of life styles including high-calorie diets and acquiring of sedentary life styles might explain the higher prevalence of hypertension and dyslipidemia among residents of the Middle Eastern region, especially in women.[1,2] The prevalence of hypertension among Iranian women increased from 24.8% in 2005 to 28.6% in 2007, whereas during the same period the prevalence of hypertension among Iranian men did not change, remaining around 25%;[3] findings were supported by a systematic review of cardiovascular disease (CVD) risk factors in the Middle East, highlighting the higher prevalence of hypertension in women, compared with men (23 versus 20.1%).[2]

It is of importance that only 45 and 53% of Tehranian women had desirable levels of total cholesterol (TC) and triglycerides (TGs), respectively.[4] The Iranian dietary pattern, *per se*, was significantly associated with dyslipidemia among women and changing to western dietary patterns, accentuated this issue.[5] Recently we showed that dyslipidemia is commonly associated with diabetes and CVD events among Iranian populations.[6,7]

Dyslipidemia could lead to hypertension by mechanisms such as endothelial dysfunction resulting in impaired nitric oxide production, release and activity, and structural changes in large arteries following atherosclerosis.[8,9] Additionally, hypertension and dyslipidemia, as the components of metabolic syndrome may have universal mechanistic pathways.[10–12]

Few prospective studies among North America and European population highlighted the role of dyslipidemia as a predictor of incident

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hypertension.[13–15] In the current study, using data from a large-population-based cohort in the Middle East, we examined the association between different lipid measures and indices including TC, TG, high-density lipoprotein cholesterol (HDL-C), non-HDL-C, TC/HDL-C and TG/HDL-C with incident hypertension, during a 6.4 year follow-up in Iranian adult women, free of hypertension at baseline.

Subjects and methods

Study population

Subjects in this study were selected from among participants of the Tehran Lipid and Glucose Study (TLGS), a prospective study conducted to determine the risk factors and outcomes for non-communicable diseases.[16,17] To summarize, 15 005 people aged 3 years and over, residents of district-13 of Tehran, underwent a baseline examination between February 1999 and August 2001. After this cross-sectional (phase 1), subjects were categorized into the cohort and intervention groups, the latter to be educated for implementation of life-style modifications. For the current study, 5971 women, aged $\geqslant 20$ years were selected to be included; after exclusion of women with prevalent hypertension at baseline ($n=1387$) and those with missing data regarding baseline hypertension and other covariates ($n=323$), there were 4261 non-hypertensive women who were reassessed in the two consecutive phases at approximately 3-year intervals; the second phase examinations were carried out between 2001 and 2005, and the third phase between 2005 and 2008 (Figure 1). Finally, 2831 women who either developed hypertension (in phases 2 or 3; $n=397$) or completed the phase 3 examinations ($n=2434$) were included in this study. The ethical committee of the Research Institute for Endocrine Sciences approved this study, and informed written consent was obtained from all subjects.

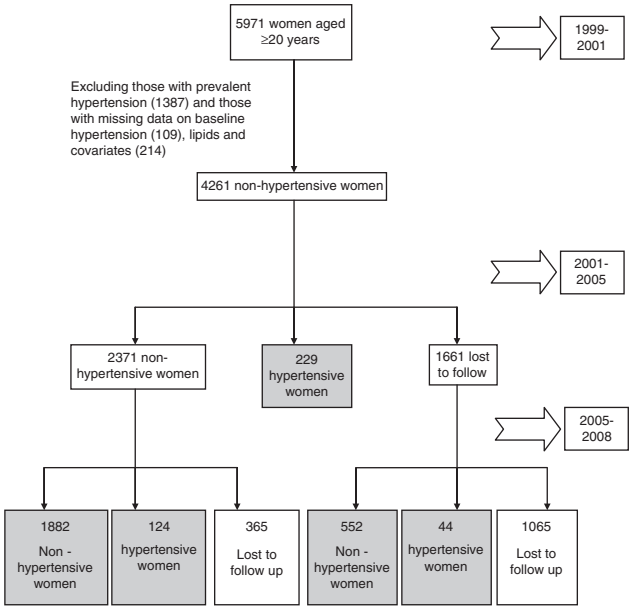

Figure 1 Follow-up status of the Tehran Lipid and Glucose Study participants.

Clinical and laboratory measurements

All information including demographic data, past medical history of CVD, medication use and smoking behaviour were collected by a trained interviewer, using a pretested questionnaire. Weight was measured, while subjects were minimally clothed without shoes, using digital scales (Seca 707, Seca Corp., Hanover, MD, USA; range 0.1–150 kg) and recorded to the nearest 100 g. Height was measured in a standing position without shoes, using stadiometer with shoulders in normal alignment. Body mass index was calculated as weight (kg) divided by square of height (m^2). Waist circumference (WC) was measured at umbilical level, using an unstretched tape metre, without any pressure to body surface over light clothing and hip circumference at the maximal level over light clothing. Waist to hip ratio (WHR) was calculated as WC (cm) divided by hip circumference (cm). Two systolic blood pressure (SBP) and diastolic blood pressure (DBP) measurements were taken using a standardized mercury sphygmomanometer (calibrated by the Iranian Institute of Standards and Industrial Researches) on the right arm, after a 15 min rest in a sitting position; mean of the two measurements was considered as subject's blood pressure. A blood sample was drawn between 0700 and 0900 hours from all study participants, after 12–14 h overnight fasting. All the blood analyses were done at the TLGS research laboratory on the day of blood collection. Plasma glucose was measured using an enzymatic colorimetric method with glucose oxidase. TC was assayed using enzymatic colorimetric method with cholesterol esterase and cholesterol oxidase. HDL-C was measured after precipitation of the apolipoprotein-B-containing lipoproteins with phosphotungstic acid. TG was assayed using an enzymatic colorimetric method with glycerol phosphate oxidase. These analyses were performed using commercial kits (Pars Azmoon Inc., Tehran, Iran) and a Selectra 2 auto analyzer (Vital Scientific, Spankeren, The Netherlands). Non-HDL-C was calculated by subtracting HDL-C from TC; TC/HDL-C and TG/HDL-C were calculated by dividing TC and TG to HDL-C, respectively. The intra- and inter-assay coefficients of variation (CV) for both were 2.2% for glucose. For both total and HDL-Cholesterol, intra- and inter-assay CVs were 0.5 and 2%, respectively. Intra- and inter-assay CVs were 0.6 and 1.6% for TG, respectively.

Definition of terms

Hypertension status included a record of using antihypertensive drugs and/or SBP $\geqslant 140$ mm Hg or

DBP $\geqslant$ 90 mm Hg.[18] General obesity was defined as body mass index $\geqslant 30\,kg\,m^{-2}$ and central obesity as WC $\geqslant$ 90 cm[19] or WHR > 0.90. Metabolic syndrome was defined according to the 2009 scientific consensus[20] using WC cutoff points for Iranian men and women to predict cardiovascular risk factors (WC $\geqslant$ 90 cm in both genders).[19] Diabetes was defined as using antidiabetic drugs or having fasting plasma glucose $\geqslant 7\,mmol\,l^{-1}$.[21] History of CVD reflected any history of ischaemic heart disease and/or cerebrovascular accidents. Smoking status categorized as 'current' smokers included a record of current regular or occasional smoking; 'past' smokers were those who used to smoke in the past, while those who had never smoked were called 'never' smokers. Menopause status was defined as an absence of spontaneous menstrual bleeding for over 12 months.

Statistics

Mean (standard deviation: s.d.) values for continuous and frequencies (%) for categorical variables of the baseline characteristics including lipid measures are given for women with and without incident hypertension. As TG and TG/HDL-C had skewed distribution, they are shown as median (interquartile range). Comparison of baseline characteristics between participants with and without hypertension was done by Student's *t*-test for continuous variables, χ^2-test for categorical variables and Mann-Whitney test for skewed variables. Logistic regression analysis was used to study the associations of lipid measures with incident hypertension.

To select covariates to be included in the multivariate logistic regression models, univariate analysis was used for each candidate covariate (age, history of CVD, intervention group, diabetes, baseline SBP, WC, smoking behaviour, menopause status and lipid lowering drugs use); following this, each covariate that had a *P*-value <0.2 in the univariate analysis, was selected to be included in a stepwise backward (*P* remove: 0.1) multivariate logistic regression analysis. Final covariates were age, WC, diabetes and baseline SBP. Each final model included these covariates plus one of the lipid measures (TG and TG/HDL-C were added as log-transformed value) or lipid categories. Age and multivariate odds ratios (ORs), with 95% confidence intervals (CI), were calculated for every 1 s.d. increase in the value of each lipid parameters. Model fitness was assessed using Hosmer-Lemeshow test; statistically significant χ^2 statistics from this test indicate poor model fitness. The predictive ability of each model was examined with area under the receiver operating characteristic (aROC) curves.

In another analysis, ORs and 95% CI of incident hypertension for each lipid measure (TC, HDL-C, TG, non-HDL-C, TC/HDL-C, TG/HDL-C) were determined by the quartiles, using the first quartile as the reference group, in age- and multivariable-adjusted models. We also evaluated National Cholesterol Education Project (NCEP) cut points for incident hypertension in multivariable-adjusted models.

SPSS program (SPSS Inc., Chicago, IL, USA; Version 15) was used for data analysis and two tailed *P*-values $\leqslant 0.05$ were considered statistically significant.

Results

The study population consisted of 2831 women with a mean age of 38 ($\pm$12) years. After a median follow-up of 6.4 years, 397 (14% of the population) women developed hypertension (incidence rate 2.2% per year). Table 1 shows the baseline characteristics of women according to incident hypertension. Compared with women, who did not have hypertension during follow-up, those who did were older and had higher prevalence of cardiovascular disorders, smoking behaviour, menopause status, diabetes, lipid lowering drugs use, WC and metabolic syndrome, at baseline. Levels of all lipid parameters were higher in women who developed hypertension than those without the condition, except HDL-C, which was higher in women without incident hypertension. Baseline SBP and DBP were higher in women who developed hypertension than those who remained normotensive.

The ORs of a 1 s.d. change in each lipid marker or index are presented in Table 2. In the age-adjusted model, there were significant associations between all lipid measures with incident hypertension; however, after further adjustment with baseline WC, SBP, diabetes and age—TC and non-HDL-C were no longer associated with hypertension. An increase of 1 s.d. in TG, TC/HDL-C and TG/HDL-C increased the risk of incident hypertension by 16, 19 and 18%, respectively, in the multivariable model. Also, a $0.29\,mmol\,l^{-1}$ increase in HDL-C decreased the risk of hypertension by 14% along with other risk factors. The Hosmer-Lemeshow test did not reject the goodness of fit for the models (all $P>0.1$). Predictive ability of these models was statistically equal (all aROC $\approx$ 0. 84).

In categorical analysis, we evaluated the risk of hypertension for quartiles of lipid indexes in the age- and multivariable-adjusted models (Table 3). Compared with women in the lowest TC quartile, there was no significant increase in risk of hypertension in higher quartiles of TC, in both the age and multivariable-adjusted models. HDL-C and TG/HDL-C had significant associations with development of hypertension in the both models, so that in the multivariable model, the women in the second and third quartiles of HDL-C level had a 39 and 33% decreased risk of hypertension, respectively, compared with the lowest quartile of HDL-C, whereas the highest quartile of TG/HDL-C was associated

Table 1 Baseline characteristics of women with and without incident hypertension

	Incident hypertension (397)	*No hypertension (2434)*	P-*value*
Age (year)	48 ± 12	37 ± 11	<0.001
Intervention group (%)	37.0	39.1	0.4
History of cardiovascular disease (%)	3.2	1.1	0.001
Smoking (%)			<0.001
Never	96.4	94.6	
Past	0.8	3.7	
Current	2.8	1.7	
Menopause status	37.4	15.3	<0.001
Lipid lowering drug use (%)	7.4	1.8	<0.001
Diabetes (%)	16.9	3.0	<0.001
Metabolic syndrome	61.5	23.8	<0.001
Body mass index (kg m^{-2})	29.0 ± 4.5	26.6 ± 4.7	<0.001
Waist circumference (cm)	92 ± 11	84 ± 12	<0.001
Waist to hip ratio	0.87	0.81	<0.001
Systolic blood pressure (mm Hg)	122 ± 10	110 ± 10	<0.001
Diastolic blood pressure (mm Hg)	80 ± 7	73 ± 7	<0.001
TC (mmol l^{-1})	5.88 ± 1.22	5.24 ± 1.13	0.01
HDL-C (mmol l^{-1})	1.13 ± 0.28	1.17 ± 0.29	<0.001
Non-HDL-C (mmol l^{-1})	4.75 ± 1.20	4.07 ± 1.15	<0.001
TG (mmol l^{-1})	1.95(1.30–2.80)	1.31(0.91–1.94)	<0.001
TC/HDL-C	5.47 ± 1.67	4.74 ± 1.60	<0.001
TG/HDL-C	1.87(1.11–2.69)	1.14(0.74–1.88)	<0.001

Abbreviations: HDL-C, high-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.
Mean ± s.d. are shown for continuous variables and *P*-value is calculated with *t*-test; % is shown for categorical variables with *P*-value according to χ^2; TG and TG/HDL are shown as median (interquartile range) and *P*-value according to Mann-Whitney test.

Table 2 Odds ratio of lipid measures for incident hypertension in women

	s.d. (mmol l^{-1})	Age adjusted model		*Multivariable adjusted model*			
		Odds ratio (95%CI)	P-*value*	*Odds ratio (95%CI)*	P-*value*	P-*value H–L χ^2-test*	*aROC (95%CI)*
TC	1.7	1.13(1.00–1.28)	0.04	1.02(0.89–1.16)	0.8	0.3	0.84(0.82–0.86)
HDL-C	0.29	0.81(0.72–0.91)	0.001	0.86(0.75–0.98)	0.02	0.4	0.84(0.82–0.86)
Non-HDL-C	1.18	1.19(1.06–1.34)	0.004	1.06(0.93–1.20)	0.4	0.5	0.84(0.82–0.86)
TG	0.55	1.44(1.28–1.63)	<0.001	1.16(1.01–1.33)	0.03	0.2	0.84(0.82–0.86)
TC/HDL-C	1.63	1.21(1.09–1.34)	<0.001	1.19(1.00–1.27)	0.05	0.2	0.84(0.82–0.86)
TG/HDL-C	0.69	1.42(1.26–1.59)	<0.001	1.18(1.04–1.35)	0.01	0.2	0.84(0.82–0.86)

Abbreviations: aROC, area under the receiver operating characteristic curve of each model; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; H–L χ^2, Hosmer and Lemeshow goodness of fit test; TC, total cholesterol; TG, triglyceride.
Odd ratios indicate the increase risk for a 1 s.d. increase of each lipid measure. Multivariable models were adjusted for age, waist circumference, diabetes and baseline systolic blood pressure.

with a 71% increased risk of hypertension, compared with the lowest quartile. As for non-HDL-C and TC/HDL-C, the second, third and fourth quartiles had increased risk of hypertension compared with those in lowest quartiles in age-adjusted model (*P* for trend: 0.005 for non-DHL-C and <0.001 for TC/HDL-C); in the multivariable model, although the highest quartile of TC/HDL-C significantly increased the risk of hypertension by 55%, compared with the lowest level, but the overall pattern of increased risk among TC-HDL-C categories were nonsignificant (*P* for trend = 0.1) and for non-HDL-C, after adjustment with other risk factors, the ORs attenuated and were not longer significant. The higher levels of TG were associated with higher risk of hypertension in the age-adjusted model; in full-adjusted model, the highest level of TG increased the risk of hypertension by 43%, which was marginally significant.

In another analysis, we divided the lipid measures by the NCEP clinical cut points (Table 4). The overall pattern of associations between these lipid cut points and incident hypertension were parallel with the quartiles analyses. Higher levels of TC and non-HDL-C were not associated with incident hypertension in the multivariable model. Compared with TC/HDL-C ratios <4, those over 6 were associated with a 37% increased risk of hypertension,

Table 3 Odds ratios and 95% CI of incident hypertension by quartiles of lipid measures in women

Lipid measures	*Quartiles of each lipid*				P-*value*
	First	*Second*	*Third*	*Fourth*	
TC	⩽4.48	4.49–5.20	5.21–6.03	>6.3	
No. of women	710	724	693	704	
No. of hypertension cases	49	77	106	165	
Age-adjusted OR (95% CI)	1	1.06(0.72–1.57)	1.19(0.81–1.74)	1.31(0.89–1.93)	0.4
Multivariable adjusted OR (95% CI)	1	0.91(0.60–1.38)	0.96(0.64–1.45)	0.95(0.62–1.44)	0.9
HDL-C	⩽1.1	1.01–1.09	1.10–1.37	>1.37	
No. of women	1049	390	885	507	
No. of hypertension cases	171	52	108	66	
Age-adjusted OR (95% CI)	1	0.69(0.48–0.99)	0.63(0.47–0.83)	0.66(0.47–0.91)	0.004
Multivariable adjusted OR (95% CI)	1	0.61(0.41–0.90)	0.67(0.49–0.90)	0.76(0.53–1.09)	0.02
Non-HDL	⩽3.31	3.32–4.07	4.08–4.87	>4.87	
No. of women	715	717	707	698	
No. of hypertension cases	37	90	104	166	
Age-adjusted OR (95% CI)	1	1.80(1.19–2.72)	1.64(1.09–2.48)	1.96(1.30–2.96)	0.005
Multivariable adjusted OR (95% CI)	1	1.41(0.91–2.18)	1.22(0.79–1.90)	1.31(0.85–2.04)	0.5
Triglycerides	⩽0.95	0.96–1.38	1.39–2.07	>2.07	
No. of women	716	702	707	706	
No. of hypertension cases	41	69	108	179	
Age-adjusted OR (95% CI)	1	1.34(0.88–2.03)	1.69(1.13–2.50)	2.75(1.88–4.01)	<0.001
Multivariable adjusted OR (95% CI)	1	0.96(0.62–1.50)	1.04(0.68–1.60)	1.43(0.94–2.17)	0.06
TC/HDL-C	⩽3.69	3.70–4.61	4.62–5.68	>5.68	
No. of women	708	711	703	709	
No. of hypertension cases	49	79	106	163	
Age-adjusted OR (95% CI)	1	1.38(0.93–2.03)	1.63(1.12–2.37)	2.17(1.51–3.11)	<0.001
Multivariable adjusted OR (95% CI)	1	1.14(0.75–1.73)	1.25(0.84–1.87)	1.55(1.05–2.29)	0.1
TG/HDL-C	⩽0.77	0.78–1.20	1.21–2.01	>2.01	
No. of women	707	709	707	708	
No. of hypertension cases	44	76	104	173	
Age-adjusted OR (95% CI)	1	1.39(0.93–2.09)	1.64(1.11–2.42)	2.79(1.93–4.03)	<0.001
Multivariable adjusted OR (95% CI)	1	1.16(0.75–1.78)	1.12(0.74–1.71)	1.71(1.14–2.57)	0.01

Abbreviations: CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; OR, odds ratio; TC, total cholesterol; TG, triglyceride.
Multivariable models were adjusted for age, waist circumference, diabetes and baseline systolic blood pressure. Lipids are shown as SI units.

Table 4 Multivariable adjusted odds ratio and 95% CI for NCEP clinical cut points of each lipid measure

Lipid measures	*First*	*Second*	*Third*	P-*value*
TC	<5.18	5.180–6.213	⩾6.213	
Multivariable OR (95% CI)	1	1.04(0.76–1.41)	1.07(0.77–1.48)	0.9
HDL-C	<1.036	1.036–1.551	⩾1.551	
Multivariable OR (95% CI)	1	0.67(0.52–0.87)	0.69(0.45–1.05)	0.01
Non-HDL-C	<4.144	4.144–4.918	⩾4.918	
Multivariable OR (95% CI)	1	1.05(0.76–1.44)	1.06(0.77–1.44)	0.9
Triglycerides	<1.695	1.695–2.259	⩾2.259	
Multivariable OR (95% CI)	1	1.34(0.97–1.96)	1.52(1.14–2.04)	0.01
TC/HDL-C	<4	4–6	⩾6	
Multivariable OR (95% CI)	1	1.01(0.73–1.39)	1.37(0.96–1.95)	0.08
TG/HDL-C	<1.09	1.09–2.18	⩾2.18	
Multivariable OR (95% CI)	1	1.26(0.93–1.71)	1.67(1.21–2.31)	0.007

Abbreviations: CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; NCEP, National Cholesterol Education Project; OR, odds ratio; TC, total cholesterol; TG; triglyceride.
Multivariable models were adjusted for age, waist circumference, diabetes and baseline systolic blood pressure. Lipids are shown as SI units.

which was nearly significant (1.37 (0.96–1.95)) along with other risk factors. In the multivariable model, women with HDL-C level between 1.0 and 1.5 mmol l^{-1} had 33% lower risk of hypertension compared with those having HDL-C levels <1.0 mmol l^{-1}. Women with high-TG levels, based

on NCEP cut points (TG level $>2.3\,mmol\,l^{-1}$) had a 52% increased risk of hypertension, compared with those with normal TG levels ($<1.7\,mmol\,l^{-1}$) independent of other risk factors. The OR of TG/HDL-C >2.18 was 1.67, compared with reference level of $<1.09\,mmol\,l^{-1}$.

In another multivariate analysis, we adjusted body mass index as a covariate instead of WC; the ORs of lipid parameters for incident hypertension did not change with controlling for general obesity instead of central obesity (data not shown).

We then excluded the women with general obesity and diabetes. The multivariate ORs(95%CI) of a 1 s.d. change in lipid parameters for incident hypertension were as follows: for TC, 1.05(0.89–1.25; $P=0.8$); for HDL-C, 0.90(0.76–1.07; $P=0.2$); for TG, 1.25(1.04–1.48; $P=0.01$); for non-HDL-C, 1.08(0.91–1.28; $P=0.3$); for TC/HDL-C, 1.15(0.98–1.34; $P=0.08$) and for TG/HDL-C, 1.24(1.04–1.46; $P=0.01$).

We also limited analysis to those without central obesity (WC <90 cm or WHR <0.9) and diabetes. The multivariate ORs of lipid measures for incident hypertension in this analysis were as follows: for TC, 1.06(0.85–1.33; $P=0.6$); for HDL-C, 0.88(0.72–1.09; $P=0.3$); for TG, 1.28(1.02–1.60; $P=0.03$); for non-HDL-C, 1.11(0.88–1.38; $P=0.3$); for TC/HDL-C, 1.20(0.99–1.46; $P=0.05$) and for TG/HDL-C, 2.28(1.03–1.59; $P=0.03$).

Discussion

To the best of our knowledge, this study is the second population-based prospective study to compare head-to-head different lipid parameters for the prediction of incident hypertension among a female population who were initially normotensive. Results highlighted that higher levels of TGs, TC/HDL-C and TG/HDL-C and lower levels of HDL-C were independently associated with risk of incident hypertension over a 6.4 year follow-up. Applying the NCEP[22] cut points demonstrated the same association between baseline lipids and incident hypertension among Iranian women, although, the trend was nonsignificant for TC/HDL-C in multivariate analysis. The relationship between TG, TG/HDL-C and TC/HDL-C (nearly significant) and incident hypertension, persisted even after the exclusion of women with central or general obesity and diabetes, however, in these groups, HDL-C did not remain as a predictor.

Limited data from prospective studies is available examining different lipid measures for prediction of incident hypertension. A 14.1 year follow-up of 3110 initially non-hypertensive men in the Physician' Health Study demonstrated that in multivariate analyses, men in the highest quintile of TC, non-HDL-C, and TC/HDL-C had increased risks of 23, 39, and 54% of developing hypertension, respectively, compared with participants in the lowest quintile; also men in the highest quintile of HDL-C had a 32% decreased risk of developing hypertension compared with those in the lowest quintile. Halperin *et al.*[13] also showed that models using NCEP cut points highlighted the same association between baseline lipids and incident hypertension.

In the Sesso *et al.*[15] study, of 16 130 adult women followed up for 10.8 years, 4593 developed hypertension. In multivariate analyses, the relative risks of incident hypertension from the lowest (referent) to the highest quintile of baseline TC were 1.00, 0.96, 1.02, 1.09 and 1.12 ($P=0.002$ for trend); for HDL-C, 1.00, 0.93, 0.87, 0.87 and 0.81 ($P<0.001$ for trend); for non-HDL-C, 1.00, 1.06, 1.11, 1.12 and 1.25 ($P<0.001$ for trend); and for the TC/HDL-C, 1.00, 1.10, 1.14, 1.20 and 1.34 ($P<0.001$ for trend). In Iranian women, the comparable multivariate OR of incident hypertension from the lowest (referent) to the highest quartile of baseline TG were 1.00, 0.96, 1.04 and 1.43 ($P=0.06$ for trend); for HDL-C, 1.00, 0.61, 0.67 and 0.76 ($P=0.02$ for trend); and for the TG/HDL-C, 1.00, 1.16, 1.12 and 1.71 ($P=0.01$ for trend). Furthermore, in our findings, contrary to the Women's Health Study, only the fourth quartile of TC/HDL-C (that is, TC/HDL-C >5.68) showed a 55% independent risk for incident hypertension in comparison to the reference group. Additionally, using clinical guideline cut points of lipid measures for prediction of hypertension, both the Women's Health Study and the TLGS highlighted the same association between baseline lipids and incident hypertension. However, in the Sesso *et al.*[15,22] study, levels of HDL-C, non-HDL-C and TC/HDL-C and in the TLGS, levels of HDL-C, TGs and TG/HDL-C were the strongest independent predictors of hypertension, based on popular clinical guidelines.

Recently Laaksonen *et al.*[14], in a 7-year follow-up of 311 Finnish men, without hypertension at baseline highlighted the importance of the dyslipidemia characteristics of metabolic syndrome in development of hypertension, independent of features related to insulin resistance. Using factor analysis, they found that the 'TG factor' seemed to mainly explain incident hypertension, whereas the 'low-density lipoprotein factor' only was likely to be associated with new onset hypertension. In line with the Laaksonen *et al.* study, we found that among Iranian women even without general or central obesity and diabetes at baseline, in multivariate analyses TG and TG/HDL-C remained as independent predictors of new onset hypertension.

In the current study, we do not deal with the mechanisms by which the lipid parameters might increase the risk of hypertension; although the issue has been addressed in many studies. Dyslipidemia leads to impairment in endothelial function and resulting in defective vasoregulation,[8] increasing arterial stiffness, decreasing arterial compliance[9] and renal microvascular disease.[23] It has been shown that high levels of cholesterol and low levels

of HDL-C are toxic for endothelial cells and impair the nitric oxide production, release and later activity,[8,24] furthermore high levels of HDL-C stimulates nitric oxide production and has antithrombotic and antioxidant activity.[24–26]

Additionally, some studies suggest that insulin resistance, which includes dyslipidemia, might be an underlying factor of hypertension due to the sympathetic overactivity.[27] Lipid abnormality and hypertension are the components of metabolic syndrome, which are highly prevalent among Iranian women[28] and insulin resistance induces the occurrence of these components of the syndrome simultaneously.[10,11] It remains unclear, however, why hypertension develops in patients with metabolic syndrome as an early- or late-stage manifestation.[10,11,13] The high prevalences of metabolic syndrome, high TG, low HDL-C and hypertension were reported in Tehranian women.[28] Importantly, the incidence of metabolic syndrome was 23.1% in Iranian women during 3 years of follow-up,[29] and the incidence rate of diabetes was about 1%.[30] In the current study, however, TG and TG/HDL-C and TC/HDL-C remained predictive of incident hypertension, even after limiting the study population to those without general or central adiposity and diabetes, suggesting that central obesity and the underlying insulin resistance and metabolic syndrome might not explain the association of dyslipidemia and incident hypertension, a finding that was also reported by Sesso *et al.*[15] in women without general obesity and diabetes.

Finally, if lipid measures predict incident hypertension, is it possible to conclude that lowering lipid values translate to lowering blood pressures? Esmaillzadeh *et al.*[5] showed that subjects in the top quintile of the healthy dietary pattern were less likely to have dyslipidemia (OR = 0.36, 95%CI: 0.19–0.53) and hypertension (OR = 0.33, 95%CI: 0.17–0.60) compared with the lowest quintile. The Iranian dietary pattern, however, was significantly associated with dyslipidemia (OR = 1.73, 95%CI: 1.02–2.99).[5] Furthermore, Strazzullo *et al.*[31] in a meta-analysis of randomized, controlled trials highlighted that statin therapy has a relatively small but clinically meaningful effect on blood pressure.

There are potential limitations regarding the interpretation of our results. First, we measured TC, HDL-C and TG only once at baseline per subject; thus, the potential bias resulting from regression dilution of TG and HDL-C could not be ignored.[32] Second, we did not have data regarding dietary pattern of the study population; hence, we did not consider this parameter in our analysis. Third, we did not evaluate low-density lipoprotein cholesterol because it was calculated, rather than measured in TLGS (that is, requiring exclusion of participants with TG $\geqslant$ 4.52 mmol l^{-1}). Additionally, we used WC and WHR criteria for diagnosis of central obesity instead of direct measurement of visceral adiposity, criteria that are more feasible in population-based studies. Finally, extrapolation of our findings to other ethnic groups and men might not be possible.

Finally, our findings suggested that dyslipidemia, especially high TG and high TG/HDL-C, independently predict incident hypertension. Hence, identifying dyslipidemia, implementing drastic changes in dietary patterns and increasing physical activity among Iranian women would reduce the burden of CVD.

What is known about this topic

- Few prospective studies in north America and Europe have shown that dyslipidemia might be a risk factor for incident hypertension.

What this study adds

- High triglycerides and triglycerides /high-density lipoprotein cholesterol, independently predict incident hypertension in Middle Eastern women, even in those without diabetes and central or general obesity.

Conflict of interest

The authors declare no conflict of interest.

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