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RECEIVED 28 November 2024

ACCEPTED 06 August 2025

PUBLISHED 03 October 2025

CITATION

Esmaili B, Esmaili S, Fahimfar N, Rezaei Tavirani M, Razi F, Nabipour I, Khashayar P and Bandarian F (2025) Remnant cholesterol, not LDL cholesterol, is associated with the risk of hypertension in the middle-aged and elderly population: Bushehr Elderly Health cohort.
Front. Cardiovasc. Med. 12:1483778.
doi: 10.3389/fcvm.2025.1483778

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Remnant cholesterol, not LDL cholesterol, is associated with the risk of hypertension in the middle-aged and elderly population: Bushehr Elderly Health cohort

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Background: Despite available studies, the link between dyslipidemia and hypertension remains unclear, particularly among different ethnicities, age groups, and genders. This study aimed to assess this association in the Iranian elderly population.

Methods: In a cross-sectional study, we used data from phase II of the Bushehr Elderly Health Program (BEHP). Participants were divided into hypertensive and non-hypertensive groups based on their blood pressure. The association between lipid parameters and hypertension (HTN) was evaluated using multiple logistic regression analysis. Additionally, we conducted a subgroup analysis by gender, age, and BMI (Body Mass Index).

Results: In this study, 1,918 people with a mean age of 62.10 ± 8.05 were included. Of them, 1,133 (59.1%) were hypertensive, and 57.2% were females (1,097). Among the lipid profiles, individuals with HTN had higher levels of triglyceride (TG) and remnant cholesterol (RC). There was a negative association between high-density lipoprotein (HDL-c) levels and high blood pressure $0.987(0.978-0.995)$, $p:0.003$, and a positive association between TG and $RC \geq 30$ levels and HTN ($1.003(1.002-1.005)$, $p < 0.001$; $1.36 (1.123-1.648)$, $p:0.002$), respectively). This positive association was observed after full adjustment for age, gender, and BMI. While HDL-C was lower and RC levels were significantly higher only in the hypertensive people aged ≤ 65 ($p < 0.01$), higher RC levels were observed in the hypertensive groups independent of BMI levels ($p = 0.004$). Moreover, the levels of $RC \geq 30$ mg/dl were associated with the risk of HTN only in males.

Conclusion: In the middle-aged and elderly hypertension population, there is a positive and statistically significant association between RC and HTN. This suggests that this indicator is associated with HTN, particularly in those with normal or subnormal levels of traditional risk factors. Moreover, this association may be affected by age and anthropometric parameters as well as life style factors.

KEYWORDS

hypertension, remnant cholesterol, elderly peoples, lipid profile, dyslipidemia

Introduction

High blood pressure (hypertension/HTN) is a major global health challenge with a growing incidence and prevalence, affecting approximately 30% of adults worldwide (1–4). It is a main risk factor for cardiovascular diseases and the third leading cause of disability (3, 5). In Iran, its prevalence among adults aged 25–70 years is approximately 25.6% (6). Therefore, identifying the associated risk factors is important for reducing the burden of this disease.

Several risk factors, such as low physical activity, smoking, and metabolic disorders like dyslipidemia, can increase the risk of HTN (7, 8). Among these factors, both HTN and dyslipidemia share the same pathophysiological mechanisms and have a synergistic effect, increasing the risk of cardiovascular events (9). In this regard, numerous investigations have been conducted on the relationship between HTN and blood lipid profile, as well as its underlying mechanisms (10–14).

While most of the investigations have evaluated the role of traditional lipid parameters (e.g., total cholesterol (Tch), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglyceride (TG)) in HTN, recent studies focused on the effects of non-traditional lipid parameters such as remnant cholesterol (RC) in this context (15, 16). Remnant cholesterol (RC) is the cholesterol content of lipoproteins with a high concentration of triglycerides and is made of very-low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), and chylomicron remnants (17, 18).

Increasing evidence shows the association of RC with cardiovascular risk and HTN development (15, 19). More interestingly, the relationship between RC and HTN is independent of LDL-C levels (20), and its management has been proposed as a new way of controlling or treating hypertensive patients (21). Although the exact mechanisms of this association are not known, evidence shows that RC has more deteriorative effects on vascular damage than traditional lipids (22, 23). In this regard, the established role of RC in inflammation, the endothelial and endocrine system (15, 23–27), has been illustrated by several investigations.

Despite the available studies, the evidence regarding the association of dyslipidemia with HTN is still uncertain, especially across different ethnicities, age groups, and sexes. Therefore, we aimed to assess the relationship between lipid parameters, particularly RC, and HTN in the middle-aged and elderly Iranian population. To the best of our knowledge, no study has

investigated the association of RC with HTN in Iranian middle-aged and elderly populations.

Material methods

In this cross-sectional study, we used data from phase II of the Bushehr Elderly Health Program (BEHP), a community-based prospective cohort study with 3,000 participants. This program aimed to assess the prevalence of non-communicable disease in the middle-aged population. The PoCOSTeo study is an extension to the second stage of BEH, including 2,000 people aged more than 50 years, focusing on musculoskeletal diseases (28). A multistage stratified random sampling method was used to recruit participants. This study was approved by the Research Ethics Committee of the Endocrinology & Metabolism Research Institute (Ethical code: IRTUMS.EMRI.REC.1394.0036). Also, informed consent was obtained from all participants before enrollment.

Information related to the study's design, clinical examination, data collection, biochemical measurements, and methodology can be found elsewhere (28–30). People with systolic blood pressure >140, or diastolic blood pressure >90 (according to the WHO definition) (31), or those taking blood pressure medication were considered hypertensive individuals. We excluded individuals with incomplete data from the study. After measurement of blood lipid and lipoproteins, we used the following formula for the calculation of RC values: total cholesterol minus LDL-cholesterol minus HDL-cholesterol (32, 33).

Data analysis

Demographic characteristics including age, gender, body mass index (BMI), hip circumference (HC), waist circumference (WC), diastolic blood pressure (DBP), and systolic blood pressure (SBP) were collected and reported as mean $\pm$ standard deviation (SD) (for quantitative variables) and frequency with the number and percentage (for categorical variables). The lipid profile, including total cholesterol (TC), high-density lipoprotein (HDL-C), low-density lipoprotein (LDL-C), and remnant cholesterol (RC), as well as other laboratory parameters, including fasting blood sugar (FBS), hemoglobin A1c (HbA1c), was also measured. To reduce RC misestimate, LDL was measured by direct method.

Differences in continuous variables between the two groups were examined by an independent t-test or Mann–Whitney test as appropriate. The chi-square test was used to examine the significant relationship between two qualitative variables. Moreover, we performed a subgroup analysis by age (Age ≤ 65 and Age > 65) and BMI (BMI < 30 and BMI ≥ 30 kg/m²). Then, multivariate logistic regression was used to estimate the relationship between various parameters and HTN and to remove confounders. In the crude model, no variables were adjusted, and in model 1, data was adjusted for age, gender, BMI, smoking and lipid-lowering drug use. For statistical analysis, we used the SPSS software version 23.0 for Windows (IBM, Armonk, New York). A value of $p < 0.05$ was considered statistically significant.

Results

Demographic characteristics of study participants

Generally, 1,918 people with a mean age of 62.10 ± 8.05 years were included in the study, of whom 1,133 (59.1%) were hypertensive, and 57.2% were females (1,097). The baseline characteristics of the participants are presented in Table 1.

Individuals in the HTN group had higher values for age, BMI, FBS, WC, HC, and HbA1c (%), and a lower percentage of current smokers. The non-hypertension group exhibited higher levels of TC, HDL-c, LDL-C, and non-HDL-c ($p < 0.001$), whereas hypertensive individuals showed higher levels of RC and TG ($p < 0.01$). Moreover, the usage of lipid-lowering agents was higher in hypertensive individuals compared to non-hypertensive individuals ($p < 0.001$) (Table 1).

Differences in lipid profiles between hypertensive and non-hypertensive groups based on age and BMI

We performed a subgroup analysis according to age and BMI as shown in Table 2. In both the Age ≤ 65 and Age > 65 groups, we found that TC and LDL-C were higher, and TG levels were lower in the non-hypertensive individuals. Moreover, HDL-c was lower and RC levels were significantly higher only in the hypertensive people aged ≤ 65 ($p < 0.01$). In both the BMI ≤ 30 and BMI > 30 kg/m² groups, TC and LDL-C were higher, and TG levels were lower in non-hypertensive people ($p < 0.01$). Remnant cholesterol was significantly higher in the hypertensive group in individuals with BMI < 30 kg/m² and BMI ≥ 30 kg/m² groups ($p = 0.04$).

TABLE 1 Demographic characteristics and laboratory findings of participants in the hypertensive group compared with the non-hypertensive group.

Characteristics			Total	Hypertension	Non-hypertension	P-value
Number (%)			1,918 (100)	1,133 (59.1)	785 (40.9)	–
Demographic variables	Sex	Men (%)	821 (42.8)	499 (44)	322 (41)	0.18
		Women (%)	1,097 (57.2)	643 (56)	463 (59)	
	Age (years) (mean ± SD)	62.10 ± 8.05	63.89 ± 8.23	59.94 ± 7.28	<0.001*	
Lifestyle factors	Current smoking, <i>n</i> (%)		440 (22.9)	219 (19.4)	221 (28.2)	<0.001*
Medication use	Lipid-lowering agents use, <i>n</i> (%)		552 (28.8)	412 (36.4)	140 (17.8)	<0.001*
Anthropometric	BMI (kg/m ²) (mean ± SD)		28.21 ± 4.92	28.70 ± 4.93	27.51 ± 4.81	<0.001*
	WC (Cm) (mean ± SD)		99.97 ± 11.22	101.68 ± 10.94	97.48 ± 11.15	<0.001*
	HC (Cm) (mean ± SD)		105.71 ± 9.92	106.49 ± 10.02	104.59 ± 9.67	<0.001*
Cardiovascular risk factors	SBP (mmHg) (mean ± SD)		133.10 ± 20.49	142.85 ± 19.34	119.03 ± 12.28	<0.001*
	DBP (mmHg) (mean ± SD)		80.81 ± 10.63	84.23 ± 11.22	75.86 ± 7.30	<0.001*
Laboratory tests	FBS (mg/dl) (mean ± SD)		110.60 ± 42.87	114.10 ± 42.90	105.56 ± 42.35	<0.001*
	HbA1c (%) (mean ± SD)		6.31 ± 1.48	6.46 ± 1.52	6.07 ± 1.39	<0.001*
	TC (mg/dl) (mean ± SD)		187.11 ± 41.64	183.56 ± 42.59	192.23 ± 39.71	<0.001*
	TG (mg/dl) (mean ± SD)		148.81 ± 81.36	156.32 ± 89.51	137.96 ± 66.45	<0.001*
	LDL-C (mg/dl) (mean ± SD)		101.20 ± 3,398	96.90 ± 34.34	107.40 ± 32.50	<0.001*
	HDL-C (mg/dl) (mean ± SD)		49.14 ± 11.39	48.40 ± 11.29	50.20 ± 11.46	<0.001*
	Non_HDL (mg/dl) (mean ± SD)		137.97 ± 40.73	135.15 ± 41.87	142.03 ± 38.68	<0.001
	RC (mg/dl) (mean ± SD)		36.77 ± 28.38	38.25 ± 28.85	34.63 ± 27.58	0.006*

* $p < 0.05$ significant.

FBS, fasting blood sugar; RC, remnant cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; WC, waist circumference; HC, hip circumference; TG, triglyceride; Tch, total cholesterol.

TABLE 2 Subgroup analysis of lipid profile differences between hypertension and non-hypertension according to age and BMI.

Parameter	Non-hypertension N = 607	Hypertension N = 678	p-value	Non-hypertension N = 178	Hypertension N = 455	p-value
	Age ≤ 65 N = 1,285			Age > 65 N = 633		
TC (mg/dl)(mean ± SD)	193.13 ± 40.24	186.57 ± 41.65	0.004*	189.18 ± 37.78	179.06 ± 43.62	0.004*
TG (mg/dl) (mean ± SD)	141.62 ± 68.41	166.12 ± 92.31	<0.001*	125.47 ± 57.75	141.73 ± 83.16	0.005*
LDL (mg/dl) (mean ± SD)	108.24 ± 32.81	98.34 ± 34.39	<0.001*	104.54 ± 31.30	94.62 ± 34.17	<0.001*
HDL (mg/dl) (mean ± SD)	50.07 ± 11.40	47.85 ± 11.34	<0.001*	50.62 ± 11.71	49.22 ± 11.17	0.16
Non-HDL (mg/dl) (mean ± SD)	143.05 ± 39.08	138.72 ± 40.90	0.052	138.56 ± 37.20	129.84 ± 42.77	0.012*
RC (mg/dl) (mean ± SD)	34.81 ± 27.40	40.28 ± 29.82	<0.001*	34.02 ± 28.27	35.22 ± 27.08	0.62
Parameter	Non-hypertension N = 559	Hypertension N = 749	p-value	Non-hypertension N = 226	Hypertension N = 384	p-value
	BMI < 30 N = 1,308			BMI ≥ 30 N = 610		
TC (mg/dl) (mean ± SD)	191.66 ± 40.09	182.48 ± 41.25	<0.001*	193.64 ± 38.80	185.65 ± 45.07	0.021*
TG (mg/dl) (mean ± SD)	134.99 ± 66.15	154.21 ± 93.37	<0.001*	144.29 ± 66.78	160.43 ± 81.43	0.013*
LDL (mg/dl) (mean ± SD)	106.70 ± 31.51	95.89 ± 33.93	<0.001*	109.13 ± 34.84	98.87 ± 35.09	<0.001*
HDL (mg/dl) (mean ± SD)	49.79 ± 11.35	48.16 ± 11.60	0.011*	51.20 ± 11.71	48.88 ± 10.65	0.013*
Non-HDL (mg/dl) (mean ± SD)	141.87 ± 38.85	134.32 ± 40.62	<0.001*	142.43 ± 38.33	136.77 ± 44.23	0.097
RC (mg/dl) (mean ± SD)	35.17 ± 27.81	38.43 ± 29.67	0.044*	33.31 ± 27.02	37.90 ± 27.21	0.044*

*Means significant difference.

Multivariate logistic regression analysis of lipid profile and prevalence of HTN

Based on the crude model in the entire population, an increase in RC ≥ 30 and TG levels was associated with increased risk of HTN [1.390 (1.145–1.686)], *p* = 0.001 and [3.042 (1.865–4.961), *p* < 0.001], respectively. This positive association was observed after adjustment for age, gender, BMI, smoking and lipid-lowering drug use. Both unadjusted and adjusted models showed that an increase in HDL-c exhibited a negative trend with the risk of HTN and reduced the risk of HTN, as shown in Table 3. Relation of other lipid factors including TC, LDL-C and non-HDL-C with HTN are shown in Table 3, also.

In males, before and after adjusting for age, BMI, smoking and lipid-lowering drug use, an increase in RC ≥ 30 increased the risk of HTN [1.430 (1.079–1.898), *p*: 0.013] and [1.572 (1.169–2.113), *p* = 0.003], respectively (Table 4). In females, before and after adjusting for age, BMI, smoking and lipid-lowering drug use there was no significant association between increase in RC ≥ 30 and the risk of HTN (Table 5).

Discussion

In this study, we evaluated the association between lipid parameters, particularly RC, and HTN. We found that in the overall population, hypertensive people were older individuals with higher levels of anthropometric parameters, TGs, and RC. In the subgroup analysis based on the age, only hypertensive people with aged ≤65 had significantly higher levels of RC. Our logistic regression analyses revealed that the risk of HTN increased significantly with an increase in RC ≥ 30 and TG levels.

Even though the available evidence has highlighted the relationship between lipid profile and HTN, the pattern of lipid

TABLE 3 Association between lipid profile and HTN in the whole population.

Lipid parameter	Unadjusted OR (95% CI) P value	Adjusted Model 1 ^a OR (95% CI) P value
HDL-C increase	0.986 (0.975–0.996), <i>p</i> :0.007	0.983 (0.974–0.991), <i>p</i> < 0.001
TC Increase	0.995 (0.993–0.997), <i>p</i> < 0.001	-removed from equation
LDL Increase	0.991 (0.988–0.994), <i>p</i> < 0.001	0.995 (0.992–0.998), <i>p</i> = 0.001
Triglyceride increase	2.907 (1.847–4.576), <i>p</i> < 0.001	3.042 (1.865–4.961), <i>p</i> < 0.001
non-HDL-C increase	0.996 (0.994–0.998), <i>p</i> < 0.001	-removed from equation
RC increase ≥30 mg/dl	1.310 (1.091–1.573), <i>p</i> : 0.004	1.390 (1.145–1.686), <i>p</i> = 0.001

^aAdjusted for age, gender, and BMI, smoking and lipid lowering drug use.

TABLE 4 Association between lipid profile and HTN in males.

Lipid parameter	Unadjusted OR (95% CI) P value	Adjusted Model 1 ^a OR (95% CI) P value
HDL-C increase	0.989 (0.975–1.003), <i>p</i> :0.11	-removed from equation
TC Increase	0.997 (0.993–1.001), <i>p</i> : 0.09	-removed from equation
LDL Increase	0.992 (0.988–0.996), <i>p</i> < 0.001	-removed from equation
Triglyceride increase	2.942 (1.492–5.801), <i>p</i> = 0.002	3.505 (1.654–7.428), <i>p</i> = 0.001
non-HDL-C increase	0.998 (0.994–1.001), <i>p</i> :0.19	-removed from equation
RC increase ≥30 mg/dl	1.430 (1.079–1.898), <i>p</i> : 0.013	1.572 (1.169–2.113), <i>p</i> : 0.003

^aAdjusted for age, BMI, smoking and lipid lowering drug use.

parameters associated with HTN varies considerably among the studies. While Deng et al. showed a positive association between TC, LDL-C, and non-HDL-C levels and HTN, there was no significant association between the levels of TGs and HTN

TABLE 5 Association between lipid profile and HTN in females.

Lipid parameter	Unadjusted OR (95% CI) <i>P</i> value	Adjusted Model 1 ^a OR (95% CI) <i>P</i> value
HDL-C increase	0.982 (0.975–0.996), <i>p</i> = 0.007	0.984 (0.9734–0.9956), <i>p</i> = 0.005
TC increase	0.994 (0.991–0.997), <i>p</i> < 0.001	0.997 (0.994–1.000), <i>p</i> < 0.046
LDL increase	0.990 (0.987–0.994), <i>p</i> < 0.001	0.994 (0.990–0.998), <i>p</i> = 0.002
Triglyceride increase	2.870 (1.559–5.286), <i>p</i> = 0.001	2.441 (1.268–4.698), <i>p</i> = 0.008
non-HDL-C increase	0.995 (0.992–0.998), <i>p</i> < 0.001	-removed from equation
RC increase ≥30 mg/dl	1.23 (0.968–1.569), <i>p</i> = 0.09	-removed from equation

^aAdjusted for age and BMI, smoking and lipid lowering drug use.

among Chinese women (11). Similar results were obtained in a study conducted on Chinese adult males (9). In the Iranian population, a high level of TG in females was associated with HTN (34). In another study, Tohidi et al. showed TG levels were useful indicators of HTN rather than Tch and non-HDL-c levels (35). While the exact reasons for these inconsistent results remain unknown, they may be attributed to age, genetic differences, and lifestyle of the participants (11).

In line with a study conducted on Chinese women (11), the results of this study showed a negative association between HTN and HDL-c levels. HDL-c has anti-inflammatory and vasodilator effects. Its abnormal levels are linked to endothelial dysfunction (36, 37), supporting its association with blood pressure. However, some reports indicated a positive relationship between this indicator and HTN (9, 38). Although most investigations indicated higher levels of Tch and LDL-C in hypertensive people (9, 11), our results showed lower levels of these indicators among hypertensive individuals. These differences may be associated with the age of the participants in this study. Aging has a decreasing effect on LDL-C and TC levels (39). On the other hand, most of the hypertensive participants were lipid-lowering drug users. To verify the findings of this study, another study is required to account for confounding variables, including the impact of treatment on lipid profile levels.

Risk factors such as dyslipidemia and BMI status are the same between HTN and metabolic syndrome, suggesting the pathophysiological mechanisms involved in the development of HTN may be similar to those involved in the metabolic syndrome (9). In both of them, endothelial dysfunction plays an important role (40, 41). Moreover, there is a relationship between BMI and TG levels (42). Even at normal levels of cholesterol, hypertriglyceridemia can increase the risk of cardiovascular diseases (43).

In this study, despite a reduction in Tch and LDL-C levels, the levels of TGs and anthropometric parameters were higher in people with HTN, which shows that in the Iranian elderly, the characteristic indicators of metabolic syndrome may play a more important role in HTN development, which needs further evaluation.

Despite the controversial results related to the relationship of conventional lipid parameters with HTN, most recent studies have shown a positive and significant association between RC and high blood pressure in different populations (15, 20, 24, 27). Recent investigations have suggested that managing RC levels could efficiently reduce persistent residual cardiovascular risk (44, 45). Therefore, numerous studies evaluated and compared the role of this indicator to other conventional lipid parameters in HTN development. The results of these studies revealed that compared with TGs, LDL-C, and Tch levels, the levels of RC had the strongest association with HTN (15, 24). Moreover, this association was stronger in the high RC/low LDL-C group, suggesting the role of RC in HTN incidence beyond traditional cardiovascular risk factors (46).

In our study, the levels of RC were significantly higher in the HTN group. RC serves as a valuable biomarker for assessing hypertension risk in the elderly, which supports longitudinal studies.

Moreover, in the entire population, a positive association was found between RC and HTN, even after adjusting for confounders. In subgroup analysis based on gender, while this association was significant only in males, there was a positive relationship between these parameters after adjusting for age and BMI in females (Tables 4, 5). Consistent with these results, Li et al. showed that the levels of RC were higher in Chinese males with higher BMI. They indicated that among lipid parameters, RC had the highest association with central systolic blood pressure independently of other lipid parameters. This association may be due to the physiological characteristics of this cholesterol (24) and the fact that the cholesterol in residual lipoproteins has an atherogenic and proinflammatory property more than that of cholesterol in LDL-C (19, 47). Kasahara et al. also showed the levels of remnant-like lipoprotein particle cholesterol (RLP-C) were higher in males (48). However, some reports showed females had higher RC levels (20, 27) and this association may be related to the impacts of sex hormones on cholesterol metabolism (49).

Most of the evidence indicated the impact of age, gender, and BMI on the incidence and prevalence of HTN among the participants. Among these factors, aging is a well-documented risk factor (34) due to its role in vascular stiffness (50). However, there are inconsistent results about the impact of gender on the HTN risk (34, 51). While aging increases the incidence rate in both sexes, the prevalence of HTN is higher in males than in females among younger adults (less than 40 years old) (52). In our study, we found that differences in the RC levels were significant only in the hypertensive individuals aged ≤65. In line with these results, Alijanvand et al. demonstrated that the association between RC and HTN increased with obesity in the high-risk group (53). Moreover, Shi et al. showed that the participants in the low LDL-c/high RC group were younger and females with higher BMI and TG levels. They declared that increased levels of RC were linked to HTN independent of LDL levels (20). Wu et al. also demonstrated that RC levels through inflammatory pathways increase the risk of HTN even in normal levels of TC, LDL-C, and HDL-C (27). These results show that

remnant cholesterol has an impressive effect on the development of HTN however this effect may be affected by demographic and anthropometric characteristics of the individuals. Moreover, in the assessment of the HTN risk, we should pay more attention to the levels of RC of the participants, particularly in those with normal or subnormal LDL-C levels.

Limitations

We acknowledge several limitations of the present study. Firstly, we were unable to draw causal conclusions due to the cross-sectional nature of the study. Secondly, we obtained the RC values through indirect measurements with calculation by formula which may introduce bias due to inherent assumptions about the relationship between triglycerides and remnant lipoproteins which can lead to overestimating or underestimating the relationship.

Conclusion

In conclusion, although the levels of traditional lipid parameters were below the normal, the levels of RC and TG were higher in the group with HTN, and an increase in these indicators was associated with the risk of developing HTN. This shows the superior ability of remnant cholesterol in assessing the risk of HTN compared to traditional lipid parameters. Furthermore, this association may be more significant in younger adults with higher anthropometric characteristics.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Ethics Committee of the Endocrinology and Metabolism Research Institute. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

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(9455):217–23. doi: 10.1016/S0140-6736(05)17741-1
2. Fryar CD, Ostchega Y, Hales CM, Zhang G, Kruszon-Moran D. Hypertension prevalence and control among adults: United States, 2015–2016. *NCHS Data Brief*. (2017) (289):1–8.
3. Zhou B, Perel P, Mensah GA, Ezzati M. Global epidemiology, health burden and effective interventions for elevated blood pressure and hypertension. *Nat Rev Cardiol*. (2021) 18(11):785–802. doi: 10.1038/s41569-021-00559-8
4. Peng J, Zhao F, Yang X, Pan X, Xin J, Wu M, et al. Association between dyslipidemia and risk of type 2 diabetes mellitus in middle-aged and older Chinese adults: a secondary analysis of a nationwide cohort. *BMJ Open*. (2021) 11(5):e042821. doi: 10.1136/bmjopen-2020-042821
5. Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S, Murray CJ. Selected major risk factors and global and regional burden of disease. *Lancet*. (2002) 360(9343):1347–60. doi: 10.1016/S0140-6736(02)11403-6
6. Esteghamati A, Etemad K, Koohpayehzadeh J, Abbasi M, Meysamie A, Khajeh E, et al. Awareness, treatment and control of pre-hypertension and hypertension among adults in Iran. *Arch Iran Med*. (2016) 19(7):456–64.

Author contributions

BE: Writing – original draft. SE: Writing – original draft, Supervision, Writing – review & editing. NF: Writing – review & editing, Conceptualization, Formal analysis, Methodology. MR: Writing – review & editing, Data curation. FR: Writing – review & editing, Methodology. IN: Writing – review & editing, Data curation. PK: Writing – review & editing. FB: Conceptualization, Data curation, Methodology, Supervision, Writing – review & editing.

Funding

The author(s) declare that no financial support was received for the research and/or publication of this article.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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7. Sun D, Liu J, Xiao L, Liu Y, Wang Z, Li C, et al. Recent development of risk-prediction models for incident hypertension: an updated systematic review. *PLoS One*. (2017) 12(10):e0187240. doi: 10.1371/journal.pone.0187240
8. Asgari S, Khalili D, Mehrabi Y, Kazempour-Ardebili S, Azizi F, Hadaegh F. Incidence and risk factors of isolated systolic and diastolic hypertension: a 10 year follow-up of the Tehran lipids and glucose study. *Blood Press*. (2016) 25(3):177–83. doi: 10.1093/08037051.2015.1116221
9. Chen S, Cheng W. Relationship between lipid profiles and hypertension: a cross-sectional study of 62,957 Chinese adult males. *Front Public Health*. (2022) 10:895499. doi: 10.3389/fpubh.2022.895499
10. Rafaqat S, Rafaqat S, Klisic A. The role of serum lipid profile in the pathogenesis of arterial hypertension. *Arh Farm*. (2024) 74:76–91. doi: 10.5937/arhfarm74-47908
11. Deng G, Li Y, Cheng W. Association of lipid levels with the prevalence of hypertension in Chinese women: a cross-sectional study based on 32 health check centers. *Front Endocrinol*. (2022) 13:904237. doi: 10.3389/fendo.2022.904237
12. Tan M, Zhang Y, Jin L, Wang Y, Cui W, Nasifu L, et al. Association between atherogenic index of plasma and prehypertension or hypertension among normoglycemia subjects in a Japan population: a cross-sectional study. *Lipids Health Dis*. (2023) 22(1):87. doi: 10.1186/s12944-023-01853-9
13. Ivanovic B, Tadic M. Hypercholesterolemia and hypertension: two sides of the same coin. *Am J Cardiovasc Drugs*. (2015) 15(6):403–14. doi: 10.1007/s40256-015-0128-1
14. Si XB, Liu W. Relationship between blood lipid and arterial stiffness in hypertension. *Clin Invest Med*. (2019) 42(3):E47–e55. doi: 10.25011/cim.v42i3.33092
15. Chen MM, Huang X, Xu C, Song XH, Liu YM, Yao D, et al. High remnant cholesterol level potentiates the development of hypertension. *Front Endocrinol*. (2022) 13:830347. doi: 10.3389/fendo.2022.830347
16. Palmu J, Tikkanen E, Havulinna AS, Vartiainen E, Lundqvist A, Ruuskanen MO, et al. Comprehensive biomarker profiling of hypertension in 36985 Finnish individuals. *J Hypertens*. (2022) 40(3):579–87. doi: 10.1097/HJH.0000000000003051
17. Langsted A, Madsen CM, Nordestgaard BG. Contribution of remnant cholesterol to cardiovascular risk. *J Intern Med*. (2020) 288(1):116–27. doi: 10.1111/joim.13059
18. Zhao L, Zhao X, Tian P, Liang L, Huang B, Huang L, et al. Predictive value of remnant cholesterol level for all-cause mortality in heart failure patients. *Front Cardiovasc Med*. (2023) 10:1063562. doi: 10.3389/fcvm.2023.1063562
19. Varbo A, Nordestgaard BG. Remnant lipoproteins. *Curr Opin Lipidol*. (2017) 28(4):300–7. doi: 10.1097/MOL.0000000000000429
20. Shi L, Zhang D, Ju J, Wang A, Du T, Chen X, et al. Remnant cholesterol associates with hypertension beyond low-density lipoprotein cholesterol among the general US adult population. *Front Endocrinol*. (2023) 14:1260764. doi: 10.3389/fendo.2023.1260764
21. Kunimura A, Miura K. Is remnant cholesterol a new therapeutic target for preventing hypertension? *Hypertens Res*. (2024) 47(5):1227–8. doi: 10.1038/s41440-024-01609-7
22. Bernelot Moens SJ, Verweij SL, Schnitzler JG, Stiekema LCA, Bos M, Langsted A, et al. Remnant cholesterol elicits arterial wall inflammation and a multilevel cellular immune response in humans. *Arterioscler Thromb Vasc Biol*. (2017) 37(5):969–75. doi: 10.1161/ATVBAHA.116.308834
23. Varbo A, Benn M, Tybjaerg-Hansen A, Nordestgaard BG. Elevated remnant cholesterol causes both low-grade inflammation and ischemic heart disease, whereas elevated low-density lipoprotein cholesterol causes ischemic heart disease without inflammation. *Circulation*. (2013) 128(12):1298–309. doi: 10.1161/CIRCULATIONAHA.113.003008
24. Li K, Fan F, Zheng B, Jia J, Liu B, Liu J, et al. Associations between remnant lipoprotein cholesterol and central systolic blood pressure in a Chinese community-based population: a cross-sectional study. *Lipids Health Dis*. (2021) 20(1):60. doi: 10.1186/s12944-021-01490-0
25. Liu J, Fan F, Liu B, Li K, Jiang Y, Jia J, et al. Association between remnant cholesterol and arterial stiffness in a Chinese community-based population: a cross-sectional study. *Front Cardiovasc Med*. (2022) 9:993097. doi: 10.3389/fcvm.2022.993097
26. Varbo A, Benn M, Tybjaerg-Hansen A, Jørgensen AB, Frikke-Schmidt R, Nordestgaard BG. Remnant cholesterol as a causal risk factor for ischemic heart disease. *J Am Coll Cardiol*. (2013) 61(4):427–36. doi: 10.1016/j.jacc.2012.08.1026
27. Wu Y, Wei Q, Li H, Yang H, Wu Y, Yu Y, et al. Association of remnant cholesterol with hypertension, type 2 diabetes, and their coexistence: the mediating role of inflammation-related indicators. *Lipids Health Dis*. (2023) 22(1):158. doi: 10.1186/s12944-023-01915-y
28. Khashayar P, Dimai HP, Moradi N, Fahimfar N, Gharibzadeh S, Ostovar A, et al. Protocol for a multicentre, prospective cohort study of clinical, proteomic and genomic patterns associated with osteoporosis to develop a multidimensional fracture assessment tool: the PoCOsteo study. *BMJ Open*. (2020) 10(9):e035363. doi: 10.1136/bmjopen-2019-035363
29. Ostovar A, Nabipour I, Larijani B, Heshmat R, Darabi H, Vahdat K, et al. Bushehr Elderly Health (BEH) programme, phase I (cardiovascular system). *BMJ Open*. (2015) 5(12):e009597. doi: 10.1136/bmjopen-2015-009597
30. Shafiee G, Ostovar A, Heshmat R, Darabi H, Sharifi F, Raeisi A, et al. Bushehr Elderly Health (BEH) programme: study protocol and design of musculoskeletal system and cognitive function (stage II). *BMJ Open*. (2017) 7(8):e013606. doi: 10.1136/bmjopen-2016-013606
31. World Health Organisation. Hypertension. (n.d.). Available online at: <https://www.who.int/news-room/fact-sheets/detail/hypertension> (Accessed November 10, 2024).
32. Dong W, Yan S, Chen H, Zhao J, Zhang Z, Gu W. Association of remnant cholesterol and newly diagnosed early-onset type 2 diabetes mellitus in Chinese population: a retrospective cross-sectional study. *J Diabetes*. (2024) 16(2):e13498. doi: 10.1111/1753-0407.13498
33. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al. 2019 ESC/EAS guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J*. (2020) 41(1):111–88. doi: 10.1093/eurheartj/ehz455
34. Asgari S, Moazzeni SS, Azizi F, Abdi H, Khalili D, Hakemi MS, et al. Sex-specific incidence rates and risk factors for hypertension during 13 years of follow-up: the Tehran lipid and glucose study. *Glob Heart*. (2020) 15(1):29. doi: 10.5334/gh.780
35. Tohidi M, Hatami M, Hadaegh F, Azizi F. Triglycerides and triglycerides to high-density lipoprotein cholesterol ratio are strong predictors of incident hypertension in middle eastern women. *J Hum Hypertens*. (2012) 26(9):525–32. doi: 10.1038/jhh.2011.70
36. Laaksonen DE, Niskanen L, Nyyssönen K, Lakka TA, Laukkanen JA, Salonen JT. Dyslipidaemia as a predictor of hypertension in middle-aged men. *Eur Heart J*. (2008) 29(20):2561–8. doi: 10.1093/eurheartj/ehn061
37. Yu S, Guo X, Li GX, Yang H, Zheng L, Sun Y. Lower or higher HDL-C levels are associated with cardiovascular events in the general population in rural China. *Lipids Health Dis*. (2020) 19(1):152. doi: 10.1186/s12944-020-01331-6
38. Yang G, Qian T, Sun H, Xu Q, Hou X, Hu W, et al. Adjustment for body mass index changes inverse associations of HDL-cholesterol with blood pressure and hypertension to positive associations. *J Hum Hypertens*. (2022) 36(6):570–9. doi: 10.1038/s41371-021-00548-x
39. Feng L, Nian S, Tong Z, Zhu Y, Li Y, Zhang C, et al. Age-related trends in lipid levels: a large-scale cross-sectional study of the general Chinese population. *BMJ Open*. (2020) 10(3):e034226. doi: 10.1136/bmjopen-2019-034226
40. Kim JA, Montagnani M, Koh KK, Quon MJ. Reciprocal relationships between insulin resistance and endothelial dysfunction: molecular and pathophysiological mechanisms. *Circulation*. (2006) 113(15):1888–904. doi: 10.1161/CIRCULATIONAHA.105.563213
41. Oparil S, Zaman MA, Calhoun DA. Pathogenesis of hypertension. *Ann Intern Med*. (2003) 139(9):761–76. doi: 10.7326/0003-4819-139-9-200311040-00011
42. Shama L, Lurix E, Shen M, Novaro G, Szomstein S, Rosenthal R, et al. Association of body mass index and lipid profiles: evaluation of a broad spectrum of body mass index patients including the morbidly obese. *Obes Surg*. (2011) 21:42–7. doi: 10.1007/s11695-010-0170-7
43. Raposeiras-Roubin S, Rosselló X, Oliva B, Fernández-Friera L, Mendiguren JM, Andrés V, et al. Triglycerides and residual atherosclerotic risk. *J Am Coll Cardiol*. (2021) 77(24):3031–41. doi: 10.1016/j.jacc.2021.04.059
44. Quispe R, Martin SS, Michos ED, Lamba I, Blumenthal RS, Saeed A, et al. Remnant cholesterol predicts cardiovascular disease beyond LDL and ApoB: a primary prevention study. *Eur Heart J*. (2021) 42(42):4324–32. doi: 10.1093/eurheartj/ehab432
45. Wong ND, Zhao Y, Quek RGW, Blumenthal RS, Budoff MJ, Cushman M, et al. Residual atherosclerotic cardiovascular disease risk in statin-treated adults: the multi-ethnic study of atherosclerosis. *J Clin Lipidol*. (2017) 11(5):1223–33. doi: 10.1016/j.jacl.2017.06.015
46. Guo DC, Gao JW, Wang X, Chen ZT, Gao QY, Chen YX, et al. Remnant cholesterol and risk of incident hypertension: a population-based prospective cohort study. *Hypertens Res*. (2024) 47(5):1157–66. doi: 10.1038/s41440-023-01558-7
47. Salinas CAA, Chapman MJ. Remnant lipoproteins: are they equal to or more atherogenic than LDL? *Curr Opin Lipidol*. (2020) 31(3):132–9. doi: 10.1097/MOL.0000000000000682
48. Kasahara A, Adachi H, Hirai Y, Enomoto M, Fukami A, Yoshikawa K, et al. High level of plasma remnant-like particle cholesterol may predispose to development of hypertension in normotensive subjects. *Am J Hypertens*. (2013) 26(6):793–8. doi: 10.1093/ajh/hpt011
49. Ghosh M, Gálman C, Rudling M, Angelin B. Influence of physiological changes in endogenous estrogen on circulating PCSK9 and LDL cholesterol. *J Lipid Res*. (2015) 56(2):463–9. doi: 10.1194/jlr.M055780
50. DuPont JJ, Kenney RM, Patel AR, Jaffe IZ. Sex differences in mechanisms of arterial stiffness. *Br J Pharmacol*. (2019) 176(21):4208–25. doi: 10.1111/bph.14624
51. Katibeh M, Moghaddam A, Yaseri M, Neupane D, Kallestrup P, Ahmadi H. Hypertension and associated factors in the Islamic Republic of Iran: a population-based study. *East Mediterr Health J*. (2020) 26(3):304–14. doi: 10.26719/emhj.19.042
52. Colafella KMM, Denton KM. Sex-specific differences in hypertension and associated cardiovascular disease. *Nat Rev Nephrol*. (2018) 14(3):185–201. doi: 10.1038/nrneph.2017.189
53. Hadi Alijanvand M, Aminorroaya A, Kazemi I, Amini M, Aminorroaya Yamini S, Mansourian M. Prevalence and predictors of prediabetes and its coexistence with high blood pressure in first-degree relatives of patients with type 2 diabetes: a 9-year cohort study. *J Res Med Sci*. (2020) 25:31. doi: 10.4103/jrms.JRMS_472_18