



Differences in Lipid Profiles and Atherogenic Indices Between Hypertensive and Normotensive Populations: A Cross-Sectional Study of 11 Chinese Cities

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Background: Several previous studies have reported that dyslipidemia is associated with the risk of hypertension, but these studies are mainly conducted in European and US populations, with a very few studies in the Asian population. Moreover, the effects of atherosclerotic indices, including atherogenic coefficient (AC) and atherogenic risk of plasma (AIP), on hypertension in Asians have not been well described so far.

Methods: From 2010 to 2016, altogether 211,833 Chinese adults were ultimately recruited at the health centers in 11 Chinese cities (including Shanghai, Beijing, Nanjing, Suzhou, Shenzhen, Changzhou, Chengdu, Guangzhou, Hefei, Wuhan, and Nantong). Differences in continuous variables between the two groups were analyzed by the Mann–Whitney test, while those in categorical variables were examined by the Chi-squared test. Logistic regression was applied to evaluate the association between lipid profiles and the risk of hypertension. The predictive values of AC and AIP for the incidence of hypertension were analyzed using the area under the receiver operating characteristic (ROC) curve. Meanwhile, Bayesian network (BN) models were performed to further analyze the associations between the different covariates and the incidence of hypertension.

Results: A total of 117,056 participants were included in the final analysis. There were significant differences in baseline characteristics between normotension and hypertension groups ($p < 0.001$). In multivariate logistic regression, the risk of hypertension increased by 0.2% (1.002 [1.001–1.003]), 0.2% (1.002 [1.001–1.003]), and 0.2% (1.002 [1.001–1.003]) per 1 mg/dl increase in total cholesterol (TC), low-density lipoprotein (LDL), and non-high-density lipoprotein cholesterol (non-HDL-c), respectively. However, after adjusting for body mass index (BMI), an increase in HDL level was associated with a higher risk of hypertension (p for a trend < 0.001), and the risk of hypertension increased by 0.6% per 1 mg/dl increase in HDL-c (1.006 [1.003–1.008]). In women, AC had the highest predictive value for the incidence of hypertension with an area under the curve (AUC) of 0.667 [95% confidence interval (CI): 0.659–0.674].

BN models suggested that TC and LDL were more closely related to the incidence of hypertension.

Conclusions: Overall, lipid profiles were significantly abnormal in the hypertensive population than in the normotensive population. TC and LDL were strongly associated with the incidence of hypertension. TC, LDL, and non-HDL-c levels show a positive association, HDL-c shows a negative association, while TG is not significantly associated with the risk of hypertension. After adjusting for BMI, HDL-c turns out to be positively associated with the risk of hypertension. In addition, AC has a good predictive value for the incidence of hypertension in women.

Keywords: lipid, triglycerides, high-density lipoprotein cholesterol, low density lipoprotein, total cholesterol, hypertension, Bayesian network model

INTRODUCTION

Hypertension is not only one of the most prevalent public health problems in the world, but also a major contributor to the global burden of disease and death (1). It is clinically characterized by prolonged, sustained elevation of blood pressure (2). The overall prevalence of hypertension is estimated to be 29.2% by 2025 (3), in other words, there will be 1.56 billion people with hypertension, having one-third of the hypertension population in China (4, 5).

Generally, dyslipidemia consists of the elevated total cholesterol (TC) or low-density lipoprotein cholesterol (LDL-c), or elevated triglycerides (TG), or decreased high-density lipoprotein cholesterol (HDL-c).

Dyslipidemia and hypertension are two different diseases, but both of them may induce the risk of cardiovascular diseases (CVDs) and commonly occur synergistically in the affected individuals (6). Studies have suggested that patients with dyslipidemia and hypertension are associated with a significantly higher risk of cardiovascular mortality than the pooled risk caused by dyslipidemia and hypertension separately (7, 8). In this regard, such a synergistic effect is crucial to elucidate the relationship between dyslipidemia and hypertension. As reported in several previous studies, dyslipidemia is associated with the risk of hypertension, but these studies are conducted mainly in European and US populations (9–11), while a few of them focus on the Asian population. Moreover, the effects of atherosclerotic indices, including atherogenic coefficient (AC) and atherogenic risk of plasma (AIP), on hypertension in Asians have not been well described so far. Therefore, the present cross-sectional study based on over 100,000 Chinese was conducted to compare the lipid differences and atherosclerotic indices between hypertensive and normotensive populations and to further determine the relationship between lipid levels and atherosclerotic indices and the incidence of hypertension.

METHODS

Study Design and Data Extraction

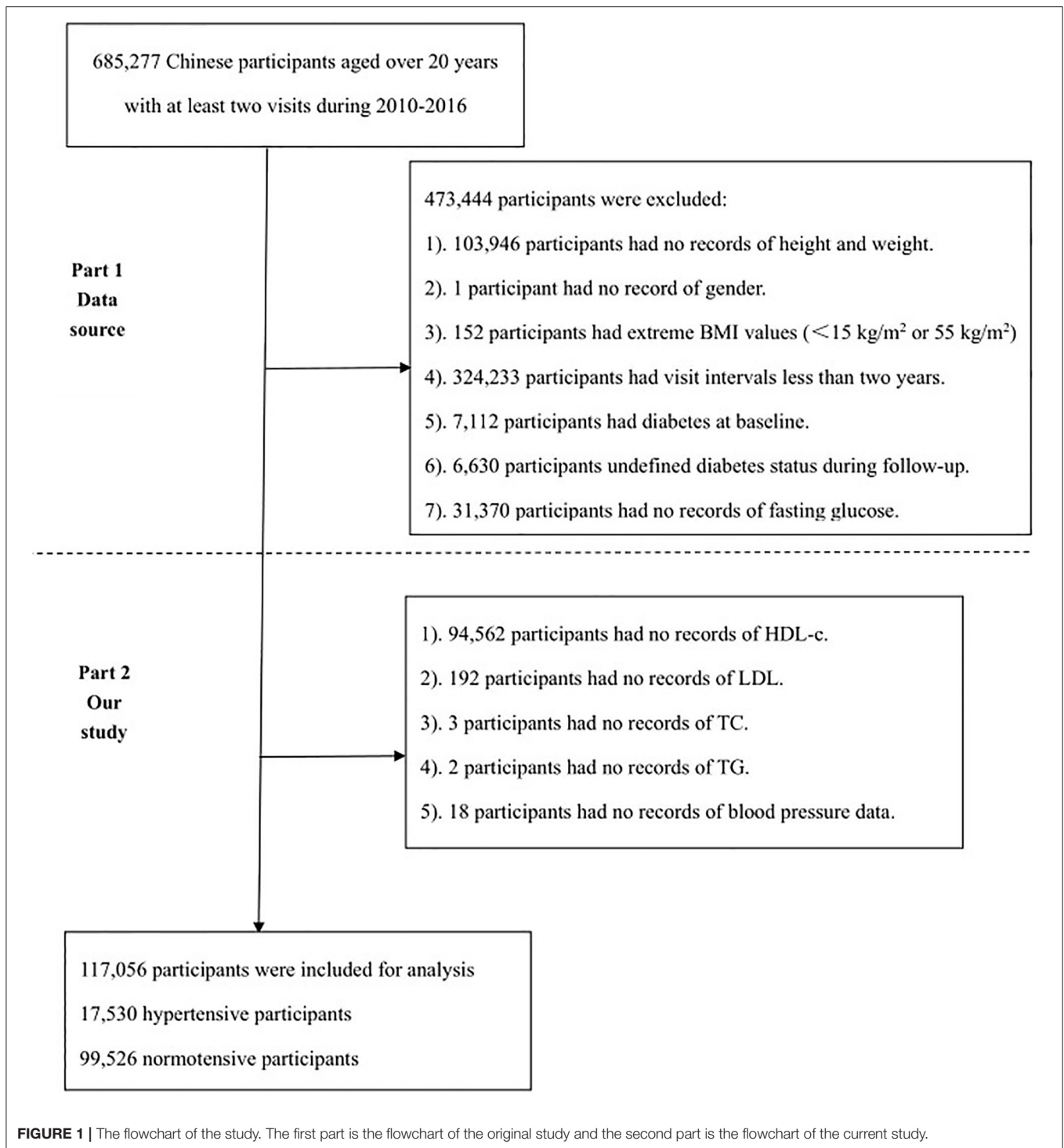
This was a cross-sectional study performed based on the DATADRYAD database (www.Datadryad.org), a computerized

database established by the Rich Healthcare Group of China. The original data were provided by Chen et al. (12). The raw data were downloaded from this site free of charge. Specifically, the original study aimed to assess the associations of body mass index (BMI) and age with the incidence of diabetes in Chinese adults. From 2010 to 2016, altogether 211,833 Chinese adults were ultimately recruited from the healthcare centers in 11 Chinese cities (namely, Shanghai, Beijing, Nanjing, Suzhou, Shenzhen, Changzhou, Chengdu, Guangzhou, Hefei, Wuhan, and Nantong). All participants completed a detailed questionnaire assessing demographics, lifestyle, and family history of chronic disease during their initial visit to a healthcare center. Baseline information, including clinical and biochemical measurements, was recorded. Clinical measurements, including weight, height, and blood pressure, were taken by the trained staff. The following biochemical parameters were measured, including TC, HDL-c, LDL-c, serum creatinine (Scr), blood urea nitrogen (BUN), alanine aminotransferase (ALT), and aspartate aminotransferase (AST). BMI was equal to the weight divided by height squared. All data were collected under standardized conditions and performed following the uniform procedures.

As Chen et al. waived all copyrights and related ownership of raw data, these data could be used for secondary analyses without infringing on authors' rights. In addition, the original study was approved and informed consent was waived by the Rich Healthcare Group Review Board, and baseline information was retrieved retrospectively (13). This study was in compliance with the Declaration of Helsinki.

Study Population

Initially, 685,277 Chinese adults who were aged over 20 years were recruited from 32 health screening centers in 11 cities in China from 2010 to 2016. As shown in **Figure 1**, the participant selection process consisted of two parts. The first part was the flowchart of the original study, which included 211,833 participants, where the reasons for their exclusion were as follows: (1) participants with no records of height or weight ($n = 103,946$); (2) participants with no records of gender ($n = 1$); (3) participants with extreme BMI values ($<15 \text{ kg/m}^2$ or 55 kg/m^2) ($n = 152$); (4) participants whose visit intervals were less than 2 years ($n = 334,233$); (5) participants with diabetes at baseline (n



= 7,112); (6) participants with undefined diabetes status during a follow-up ($n = 6,630$); and (7) participants with no records of fasting glucose ($n = 31,370$). The second part is the flow chart of the current study, with the following reasons for their exclusion: (1) participants with no records of HDL-c ($n = 94,562$); (2) participants with no records of low-density lipoprotein (LDL)

($n = 192$); (3) participants with no records of TC ($n = 3$); (4) participants with no records of TG ($n = 2$); and (5) participants with no records of blood pressure data ($n = 18$). Ultimately, a total of 117,056 participants, including 17,530 hypertensive and 99,526 normotensive participants, were participated in this study for further analysis.

Exposures of Interest and Outcome Measures

The exposures of interest were plasma lipid profiles, including TC, TG, LDL, HDL-c, and non-HDL-c, and atherosclerotic indices, including AC and AIP. AC, AIP, and non-HDL-c were calculated using the following formulas (14): $AC = (TC - HDL-c) / HDL-c$; $AIP = \text{Log}(TG / HDL-c)$; and $\text{non-HDL} = TC - HDL-c$. With reference to the Chinese guidelines for the prevention and treatment of hypertension (2018 version) (15), participants were divided into hypertensive and normotensive groups according to their baseline blood pressure levels. Hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg. Moreover, hypertension was further subdivided into mild hypertension (Grade I; SBP 140–159 mmHg or DBP 90–99 mmHg), moderate hypertension (Grade II; SBP 160–179 mmHg or DPB 100–109 mmHg); and severe hypertension (Grade III; SBP ≥ 180 mmHg or DBP ≥ 110 mmHg). Normotension was defined as SBP < 140 mmHg and DBP < 90 mmHg.

The primary outcome of this paper was to assess the differences in lipid profiles, AC, and AIP between hypertensive and normotensive groups, and the association of different lipid levels and combinations with the incidence of hypertension. The secondary outcome was to construct a Bayesian model to assess the potential relationships between baseline characteristics and the incidence of hypertension. Moreover, the importance of lipid levels, AC, and AIP for the incidence of hypertension was assessed.

Statistical Analyses

All continuous variables with a skewed distribution were expressed as median and interquartile range (IQR), whereas categorical variables were expressed as percentages. For continuous variables, differences between the two groups were analyzed using the Mann–Whitney test, while differences in categorical variables were examined using the Chi-squared test. According to blood pressure levels, the total population was divided into four groups, including Normal, Grade I, Grade II, and Grade III. Then, multiple comparisons of lipid levels, AC, and AIP were performed by Kruskal–Wallis one-way analysis of variance (ANOVA) with Dunn's test. Subgroup analyses stratified by age (< 60 years, ≥ 60 years), gender (male, female), BMI (< 23 kg/m², ≥ 23 kg/m²), ALT (< 40 U/L, ≥ 40 U/L), and AST (< 40 U/L, ≥ 40 U/L) were performed. In addition, TC, TG, LDL, HDL-c, non-HDL-c, AC, and AIP were categorized into quartiles. A *p* for trend was employed to assess the trend of associations between lipid profiles, AC, and AIP and the incidence of hypertension. The predictive values of AC and AIP for the incidence of hypertension were analyzed using the area under the receiver operating characteristic (ROC) curve. Moreover, age, gender, BMI, fasting plasma glucose (FPG), ALT, AST, BUN, Scr, smoking status, drinking status, and family history of diabetes were adjusted for regression analyses. Statistical analyses were conducted by SPSS 26.0 and GraphPad 9.0.

Bayesian Network

The Bayesian network (BN) model is one of the probabilistic graphical models, which combines probability theory and graph theory to reveal the probabilistic dependencies between variables (nodes). In short, it is about inferring the probability of occurrence of an outcome in the presence of multiple conditional variables. Firstly, in the SPSS Modeler (version 18.0) model section, the BN model is constructed based on the tree augmented naive (TAN) algorithm, and the parameter learning method is selected as a Bayesian adjustment for small cell counts (16). The arrow connecting two nodes indicates that the two random variables are causally or unconditionally independent; if there is no arrow connecting two nodes, it indicates that the random variables are conditionally independent (17). Meanwhile, the importance of the variables is obtained.

RESULTS

Demographic data and baseline characteristics of eligible participants are displayed in **Table 1**. In total, 117,056 participants, including 54,099 (46.2%) women, were recruited, with the age ranging from 34 to 53 (median, 41) years. According to baseline blood pressure levels, participants were generally divided into normotensive and hypertensive groups. Compared with the normotensive group, the hypertensive group had older age, higher percentages of current smokers and drinkers, and higher levels of BMI, FPG, ALT, AST, BUN, and Scr, whereas percentages of women and family history of diabetes were lower. As for lipid profiles and atherogenic indices, the hypertensive group had higher levels of TC, LDL, non-HDL-c, AC, and AIP, and lower levels of HDL-c, while TG was not significantly different between the two groups.

Subgroup Analyses of Differences in Lipid Profiles and Atherosclerotic Indices Between Normotensive and Hypertensive Groups

As displayed in **Table 2**, subgroup analyses stratified by gender, age, BMI, AST, and ALT were conducted. The results of lipid profiles indicated that TC, LDL, and non-HDL-c levels increased significantly in the hypertensive population, regardless of gender, BMI, AST, and ALT levels. Meanwhile, HDL levels decreased significantly in the hypertensive population in some specific subgroups (like women, or BMI < 23 kg/m², or AST and ALT < 40 U/L). However, in the hypertensive population with BMI ≥ 23 kg/m², their HDL-c levels were mildly higher than those of non-hypertensive people. In all subgroups, there were no significant differences in TC level between the two groups.

Comparisons of the atherosclerotic indices in the normotensive and hypertensive groups indicated that AC was significantly increased in the hypertensive population, regardless of gender and gender, age, BMI, AST, and ALT levels. Similarly, AIP was higher in the hypertensive population regardless of age and BMI yet this association was not observed in men and in those with elevated AST and ALT.

TABLE 1 | Baseline information of the overall population*.

	Total (n = 117,056)	Normotension (n = 99,526)	Hypertension (n = 17,530)	p value
Age (years)	41 (34–53)	39 (33–50)	53 (41–63)	< 0.001
Female (%)	54,099 (46.2)	48,304 (48.5)	5,795 (33.1)	< 0.001
Current smoker (%)	6,674 (5.7)	5,520 (5.5)	1,154 (6.6)	< 0.001
Current drinker (%)	872 (0.7)	651 (0.6)	221 (1.3)	< 0.001
Family history of diabetes (%)	2,651 (2.3)	2,367 (2.4)	284 (1.6)	< 0.001
BMI (kg/m ²)	23.2 (21–25.5)	22.9 (20.8–25.1)	25.1 (23–27.3)	< 0.001
FPG (mmol/L)	5.0 (4.61–5.35)	4.95 (4.6–5.3)	5.19 (4.8–5.62)	< 0.001
ALT (U/L)	18.2 (13–27.8)	18 (12.9–26.8)	22 (15.7–33)	< 0.001
AST (U/L)	22.0 (18.7–26.9)	21.8 (18.2–26)	24.2 (20.7–29.7)	< 0.001
BUN (mmol/L)	4.57 (3.85–5.4)	4.53 (3.81–5.35)	4.78 (4.06–5.63)	< 0.001
Scr (μmol/L)	71.3 (59.3–83.0)	70.5 (58.8–82.4)	75.8 (64.23–86.0)	< 0.001
Lipid profiles and atherosclerotic indices				
TC (mg/dl)	181.70 (159.67–204.90)	179.77 (158.51–202.97)	191.75 (168.56–216.50)	< 0.001
TG (mg/dl)	97.46 (67.34–146.19)	97.46 (67.34–146.19)	97.46 (67.34–147.08)	0.772
LDL (mg/dl)	104.38 (88.53–121.78)	103.22 (87.76–120.62)	110.95 (93.94–128.74)	< 0.001
HDL-c (mg/dl)	51.80 (45.23–59.92)	52.19 (45.23–59.92)	51.42 (44.46–59.15)	< 0.001
Non-HDL-c (mg/dl)	127.96 (108.25–151.16)	126.03 (106.70–148.84)	138.40 (117.53–162.37)	< 0.001
AC	2.43 (1.95–3.1)	2.38 (1.91–3.04)	2.72 (2.21–3.46)	< 0.001
AIP	0.28 (0.1–0.47)	0.28 (0.10–0.46)	0.29 (0.11–0.48)	< 0.001

*Continuous data are expressed as median (interquartile range) due to the skewed distribution. The p-value is a comparison between the normotension and hypertension groups. FPG, fasting plasma glucose; TG, triglycerides; TC, total cholesterol; HDL-c, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; AC, atherogenic coefficient; AIP, atherogenic risk of plasma; Scr, serum creatinine; BUN, blood urea nitrogen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index.

Multivariate Logistic Analyses of Lipid Profiles, and Atherosclerotic Indices and the Incidence of Hypertension

As shown in **Table 3**, TC, TG, LDL, HDL-c, non-HDL-c, AC, and AIP were treated as the continuous variables and divided into quartiles, with the first quartile as a reference group. In the crude model, no covariables were adjusted; in model 1, age and gender were adjusted; in model 2, all the covariables, including BMI, FPG, ALT, AST, BUN, Scr, smoking status, drinking status, and family history of diabetes, were fully adjusted. In the crude model, there was no significant increase in the risk of hypertension with increasing TG level (p for trend = 0.767), and the results were maintained after adjusting for full covariables (p for trend = 0.844). However, in the crude model, the risk of hypertension increased significantly as the levels of TC, LDL, HDL-c, non-HDL-c, AC, and AIP increased (p for trend < 0.001), and this association persisted after adjusting for gender and age, except for AIP.

In model 2, after fully adjusting for all the covariates, the incidence of hypertension increased by 0.2% (1.002[1.001–1.003]), 0.2% (1.002[1.001–1.003]), and 0.2% (1.002[1.001–1.003]), respectively, per 1 mg/dl increase in TC, LDL, and non-HDL. Surprisingly, after fully adjusting for covariates, an increase in HDL was associated with a higher risk of hypertension (p for trend < 0.001), to be specific, the risk of hypertension increased by 0.6% (1.006[1.003–1.008]) with a 1 mg/dl increase in HDL-c. In addition, after fully adjustment for all variables, AIP was not

significantly associated with the incidence of hypertension. AC was positively associated with the incidence of hypertension only at less than 3.1, and the trend p for AC and risk of hypertension was 0.459.

Predictive Value of AC and AIP for the Incidence of Hypertension

As shown in **Table 4**, AC had a predictive value for the incidence of hypertension, regardless of age, sex, BMI, AST, and ALT. In women, AC had the highest predictive value for the incidence of hypertension with an area under the curve (AUC) of 0.667 [95% confidence interval (CI): 0.659–0.674]. However, the predictive value of AIP for the incidence of hypertension was low.

Differences in Lipid Profiles, and Atherosclerotic Indices Between Normotensive and Hypertensive Groups

Based on the baseline blood pressure levels, hypertension was further classified into Grades I–III. As shown in **Figure 2**, TG, TC, and non-HDL-c levels were significantly increased in Grades I–III groups compared with the normotensive group (p < 0.05), whereas TG, TC, and non-HDL-c levels significantly increased in Grades II and III groups relative to the Grade I group (p < 0.05). Similarly, HDL-c and LDL levels were significantly higher in Grades I–III groups than in the normotensive group (p <

TABLE 2 | Subgroup analysis of differences in lipid profiles and atherosclerotic indices between normotension and hypertension according to gender, age, BMI, AST, and ALT*.

	Normotension	Hypertension	p-value	Normotension	Hypertension	p-value
Gender	Male			Female		
TC (mg/dl)	181.70 (160.05–204.90)	189.43 (167.40–212.63)	< 0.001	177.84 (158.12–201.80)	199.87 (175.90–225.77)	< 0.001
TG (mg/dl)	97.46 (67.34–147.96)	97.46 (66.45–147.08)	0.274	97.46 (68.22–146.19)	99.23 (67.34–147.08)	0.319
LDL (mg/dl)	104.77 (88.92–122.17)	109.02 (92.78–126.80)	< 0.001	101.29 (86.21–119.07)	115.59 (98.58–134.54)	< 0.001
HDL-c (mg/dl)	49.1 (42.14–56.44)	49.1 (42.14–56.83)	0.073	56.06 (48.71–64.18)	54.51 (47.17–62.63)	< 0.001
Non-HDL-c (mg/dl)	131.06 (110.95–154.64)	139.18 (118.30–162.37)	< 0.001	120.62 (102.06–143.43)	143.82 (121.59–169.33)	< 0.001
AC	2.64 (2.12–3.38)	2.77 (2.25–3.56)	< 0.001	2.15 (1.74–2.68)	2.62 (2.14–3.25)	< 0.001
AIP	0.31 (0.13–0.49)	0.30 (0.13–0.49)	0.148	0.25 (0.07–0.43)	0.26 (0.09–0.45)	< 0.001
Age	< 60 years			≥ 60 years		
TC (mg/dl)	177.84 (158.12–201.03)	189.43 (167.01–212.63)	< 0.001	197.16 (173.97–222.68)	199.49 (175.90–224.61)	< 0.001
TG (mg/dl)	97.46 (67.34–147.08)	97.46 (67.34–145.30)	0.267	97.46 (67.34–147.08)	98.35 (67.34–148.85)	0.349
LDL (mg/dl)	101.68 (86.60–119.07)	109.02 (92.40–126.80)	< 0.001	114.82 (97.42–134.15)	115.59 (98.58–134.54)	0.074
HDL-c (mg/dl)	52.19 (45.23–60.70)	50.64 (43.30–58.38)	< 0.001	52.58 (44.85–61.08)	51.80 (44.07–60.50)	0.002
Non-HDL-c (mg/dl)	124.10 (105.15–146.91)	137.63 (116.37–160.83)	< 0.001	143.82 (121.39–167.40)	146.33 (124.48–170.49)	< 0.001
AC	2.34 (1.88–2.99)	2.67 (2.18–3.43)	< 0.001	2.72 (2.18–3.42)	2.81 (2.26–3.5)	< 0.001
AIP	0.28 (0.1–0.46)	0.29 (0.12–0.48)	< 0.001	0.27 (0.1–0.46)	0.28 (0.11–0.47)	0.04
BMI	< 23 kg/m²			≥ 23 kg/m²		
TC (mg/dl)	174.36 (154.64–197.17)	189.43 (166.24–214.95)	< 0.001	185.57 (164.31–209.54)	193.69 (171.26–218.04)	< 0.001
TG (mg/dl)	97.46 (67.34–147.08)	97.46 (66.45–147.96)	0.820	97.46 (67.34–147.08)	97.46 (67.34–146.19)	0.799
LDL (mg/dl)	99.36 (84.67–115.98)	109.02 (92.01–127.19)	< 0.001	107.47 (91.62–125.65)	112.11 (95.49–130.28)	< 0.001
HDL-c (mg/dl)	55.28 (47.94–63.40)	54.90 (47.17–62.63)	0.007	49.48 (42.53–56.83)	49.87 (42.53–57.60)	< 0.001
Non-HDL-c (mg/dl)	117.91 (100.13–139.56)	133.38 (112.11–156.57)	< 0.001	135.31 (114.82–158.51)	143.04 (121.78–166.62)	< 0.001
AC	2.34 (1.88–2.99)	2.67 (2.18–3.44)	< 0.001	2.72 (2.18–3.42)	2.81 (2.27–3.5)	< 0.001
AIP	0.28 (0.1–0.46)	0.29 (0.12–0.48)	< 0.001	0.27 (0.1–0.46)	0.28 (0.11–0.47)	0.04
AST	< 40 U/L			≥ 40 U/L		
TC (mg/dl)	179.0 (158.51–202.19)	190.98 (167.34–216.50)	< 0.001	189.43 (166.24–215.72)	197.36 (173.97–227.13)	< 0.001
TG (mg/dl)	97.46 (67.34–146.19)	97.46 (67.34–147.08)	0.583	97.46 (67.34–143.98)	98.35 (69.11–150.62)	0.201
LDL (mg/dl)	102.84 (87.76–120.23)	110.57 (93.94–128.35)	< 0.001	107.86 (91.24–127.96)	114.63 (95.49–135.31)	< 0.001
HDL-c (mg/dl)	52.19 (45.61–60.31)	51.80 (44.85–59.15)	< 0.001	50.26 (42.91–57.99)	51.03 (43.30–57.99)	0.510
Non-HDL-c (mg/dl)	125.26 (106.32–148.45)	138.02 (116.75–161.60)	< 0.001	138.01 (114.43–162.76)	146.33 (126.03–173.0)	< 0.001
AC	2.37 (1.94–2.95)	2.62 (2.19–3.25)	< 0.001	2.68 (2.16–3.48)	2.84 (2.39–3.61)	< 0.001
AIP	0.27 (0.1–0.46)	0.28 (0.11–0.47)	0.004	0.29 (0.12–0.48)	0.31 (0.13–0.50)	0.263
ALT	< 40 U/L			≥ 40 U/L		
TC (mg/dl)	178.22 (158.51–201.42)	192.14 (169.33–216.50)	< 0.001	192.14 (169.72–216.50)	197.55 (175.90–222.68)	< 0.001
TG (mg/dl)	178.22 (158.51–201.12)	192.14 (169.33–216.50)	0.547	97.46 (67.34–145.30)	97.46 (69.11–143.53)	0.540
LDL (mg/dl)	102.06 (86.99–119.46)	110.57 (94.33–128.74)	< 0.001	110.58 (93.94–129.51)	114.43 (96.65–132.99)	< 0.001
HDL-c (mg/dl)	52.58 (45.62–61.08)	51.42 (44.07–59.54)	< 0.001	47.94 (40.98–55.67)	48.32 (40.98–56.06)	0.411
Non-HDL-c (mg/dl)	124.49 (105.16–147.29)	139.18 (117.91–162.76)	< 0.001	142.66 (120.62–167.40)	148.45 (127.0–172.42)	< 0.001
AC	2.33 (1.87–2.95)	2.67 (2.17–3.37)	< 0.001	2.92 (2.32–3.80)	3.0 (2.43–3.93)	< 0.001
AIP	0.27 (0.1–0.46)	0.28 (0.11–0.47)	< 0.001	0.31 (0.14–0.50)	0.31 (0.14–0.5)	0.764

*Continuous data are expressed as median (interquartile range) due to the skewed distribution. TG, triglycerides; TC, total cholesterol; HDL-c, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; AC, atherogenic coefficient; AIP, atherogenic risk of plasma; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index.

0.05), while LDL levels were higher in the Grade II group than in the Grade I group ($p < 0.05$).

Similarly, as shown in **Figure 3**, AC and AIP were significantly higher in Grades I–III groups compared with the normotensive group ($p < 0.05$), while AC and AIP were higher in the Grade II group compared with the Grade I group ($p < 0.05$). However, only a higher AIP was observed in the Grade III group than in the Grade I group ($p < 0.05$).

BN Analysis of the Relationship Between Baseline Characteristics, Lipid Profiles, and Atherosclerotic Indices and the Incidence of Hypertension

In the BN model, each circle represents a predictor, and the depth of its color indicates the importance for the occurrence of hypertension, with a darker color indicating higher importance.

TABLE 3 | Multivariable logistic regression model evaluating the association between serum lipid levels and hypertension.

	Crude model		Model 1		Model 2	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
TG						
Q 1 (≤ 67.3 mg/dl)	Ref					
Q 2 (67.3–97.5 mg/dl)	0.967 (0.923–1.012)	0.149	0.979 (0.932–1.028)	0.394	0.960 (0.889–1.037)	0.296
Q 3 (97.5–147.1 mg/dl)	0.995 (0.951–1.040)	0.822	0.993 (0.947–1.042)	0.781	1.007 (0.934–1.085)	0.862
Q 4 (≥ 147.1 mg/dl)	0.984 (0.940–1.029)	0.478	0.979 (0.933–1.027)	0.378	0.993 (0.920–1.071)	0.849
Per 1 mg/dl increase	1.000 (1.000–1.000)	0.624	1.000 (1.000–1.000)	0.938	1.000 (1.000–1.000)	0.160
ρ for trend	0.767		0.512		0.844	
TC						
Q 1 (≤ 160.4 mg/dl)	Ref					
Q 2 (160.4–181.7 mg/dl)	1.355 (1.286–1.428)	< 0.001	1.178 (1.115–1.245)	< 0.001	0.979 (0.901–1.065)	0.31
Q 3 (181.7–205.7 mg/dl)	1.821 (1.733–1.913)	< 0.001	1.382 (1.312–1.457)	< 0.001	1.093 (1.008–1.184)	0.013
Q 4 (≥ 205.7 mg/dl)	2.529 (2.411–2.653)	< 0.001	1.561 (1.483–1.643)	< 0.001	1.105 (1.021–1.196)	< 0.001
Per 1 mg/dl increase	1.010 (1.009–1.010)	< 0.001	1.005 (1.004–1.006)	< 0.001	1.002 (1.001–1.003)	< 0.001
ρ for trend	< 0.001		< 0.001		< 0.001	
LDL						
Q 1 (≤ 88.5 mg/dl)	Ref					
Q 2 (67.3–104.4 mg/dl)	1.322 (1.257–1.391)	< 0.001	1.143 (1.083–1.206)	< 0.001	0.979 (0.901–1.065)	0.625
Q 3 (104.4–122.2 mg/dl)	1.671 (1.592–1.755)	< 0.001	1.283 (1.218–1.351)	< 0.001	1.093 (1.008–1.184)	0.031
Q 4 (≥ 122.2 mg/dl)	2.208 (2.107–2.314)	< 0.001	1.402 (1.334–1.475)	< 0.001	1.105 (1.021–1.196)	0.013
Per 1 mg/dl increase	1.010 (1.009–1.011)	< 0.001	1.005 (1.004–1.006)	< 0.001	1.002 (1.001–1.003)	< 0.001
ρ for trend	< 0.001		< 0.001		0.001	
HDL-c						
Q 1 (≤ 44.8 mg/dl)	Ref					
Q 2 (44.8–52.2 mg/dl)	0.838 (0.801–0.875)	< 0.001	0.948 (0.904–0.994)	0.026	1.091 (1.012–1.176)	0.023
Q 3 (52.2–60.3 mg/dl)	0.801 (0.7666–0.837)	< 0.001	0.947 (0.903–0.994)	0.026	1.194 (1.107–1.288)	< 0.001
Q 4 (≥ 60.3 mg/dl)	0.719 (0.687–0.752)	< 0.001	0.877 (0.835–0.922)	< 0.001	1.192 (1.100–1.292)	< 0.001
Per 1 mg/dl increase	0.989 (0.988–0.990)	< 0.001	0.995 (0.994–0.997)	< 0.001	1.006 (1.003–1.008)	< 0.001
ρ for trend	< 0.001		< 0.001		< 0.001	
Non-HDL-c						
Q 1 (≤ 107.9 mg/dl)	Ref					
Q 2 (107.9–128 mg/dl)	1.558 (1.476–1.664)	< 0.001	1.267 (1.197–1.341)	< 0.001	1.042 (0.955–1.137)	0.354
Q 3 (128–152.3 mg/dl)	2.186 (2.077–2.301)	< 0.001	1.485 (1.407–1.568)	< 0.001	1.144 (1.052–1.244)	0.002
Q 4 (≥ 152.3 mg/dl)	3.059 (2.911–3.214)	< 0.001	1.708 (1.620–1.8)	< 0.001	1.148 (1.056–1.248)	0.001
Per 1 mg/dl increase	1.011 (1.010–1.012)	< 0.001	1.006 (1.005–1.007)	< 0.001	1.002 (1.001–1.003)	< 0.001
ρ for trend	< 0.001		< 0.001		< 0.001	
AC						
Q 1 (≤ 1.95)	Ref		Ref		Ref	
Q 2 (1.95–2.43)	1.756 (1.664–1.853)	< 0.001	1.428 (1.350–1.511)	< 0.001	1.193 (1.091–1.305)	< 0.001
Q 3 (2.43–3.10)	2.373 (2.253–2.498)	< 0.001	1.595 (1.510–1.685)	< 0.001	1.205 (1.104–1.315)	< 0.001
Q 4 (≥ 3.10)	2.962 (2.816–3.115)	< 0.001	1.712 (1.621–1.807)	< 0.001	1.084 (0.99–1.187)	0.083
Per 1-unit increase	1.350 (1.331–1.370)	< 0.001	1.148 (1.130–1.167)	< 0.001	0.981 (0.954–1.009)	0.178
ρ for trend	< 0.001		< 0.001		0.459	
AIP						
Q 1 (≤ 0.104)	Ref		Ref		Ref	
Q 2 (0.104–0.279)	1.073 (1.025–1.124)	0.003	1.038 (0.989–1.091)	0.131	1.012 (0.937–1.093)	0.757
Q 3 (0.279–0.466)	1.099 (1.050–1.151)	< 0.001	1.037 (0.988–1.090)	0.141	0.990 (0.917–1.069)	0.805
Q 4 (≥ 0.466)	1.128 (1.077–1.180)	< 0.001	1.042 (0.992–1.094)	0.10	0.971 (0.899–1.049)	0.453
Per 0.1-unit increase	1.179 (1.111–1.251)	< 0.001	1.044 (0.980–1.113)	0.184	0.960 (0.868–1.063)	0.437
ρ for trend	< 0.001		0.127		0.367	

OR, odds ratio; CI, confidence interval; Q, quartile. Model 1 adjust age and gender. Model 2 adjust Model 1+ BMI (kg/m²), FPG (mmol/L), ALT (U/L), AST (U/L), BUN, Scr, smoking status (current smoker or not), drinking status (current drinker or not), family history of diabetes (Yes or No).

TABLE 4 | Predictive value of AC and AIP for the incidence of hypertension according to BMI, age, gender, AST and ALT.

		AUC	95%CI	p-value
BMI < 23 kg/m ²	AC	0.607	0.598–0.616	< 0.001
	AIP	0.503	0.494–0.512	0.550
BMI ≥ 23 kg/m ²	AC	0.541	0.536–0.547	< 0.001
	AIP	0.496	0.491–0.502	0.181
Age < 60 years	AC	0.612	0.607–0.618	< 0.001
	AIP	0.515	0.510–0.521	< 0.001
Age ≥ 60 years	AC	0.527	0.518–0.536	< 0.001
	AIP	0.509	0.500–0.518	0.04
Male	AC	0.545	0.540–0.551	< 0.001
	AIP	0.496	0.490–0.502	0.148
Female	AC	0.667	0.659–0.674	< 0.001
	AIP	0.517	0.509–0.525	< 0.001
AST < 40U/L	AC	0.596	0.589–0.603	< 0.001
	AIP	0.511	0.504–0.518	0.004
AST ≥ 40U/L	AC	0.558	0.531–0.584	< 0.001
	AIP	0.516	0.488–0.544	0.263
ALT < 40U/L	AC	0.613	0.608–0.618	< 0.001
	AIP	0.511	0.506–0.516	< 0.001
ALT ≥ 40U/L	AC	0.530	0.519–0.542	< 0.001
	AIP	0.502	0.490–0.514	0.763

AUC, area under curve; CI, confidence interval; AC, atherogenic coefficient; AIP, atherogenic risk of plasma; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index.

When two predictors are connected along the arrows, it indicates the existence of a direct relationship; otherwise, it indicates an indirect relationship.

As shown in **Figures 4A,B**, the results of the BN model showed that, among the baseline characteristics of the participants, age, BMI, and FPG indirectly affected the incidence of hypertension, whereas age directly affected BMI and FPG. Age, BMI, and FPG had a greater effect on the incidence of hypertension. In addition, as shown in **Figures 5A,B**, in terms of lipids and atherosclerotic indices, TC and LDL levels were indirectly related to the incidence of hypertension, while TC directly influenced LDL levels. TC and LDL were more closely related to the incidence of hypertension.

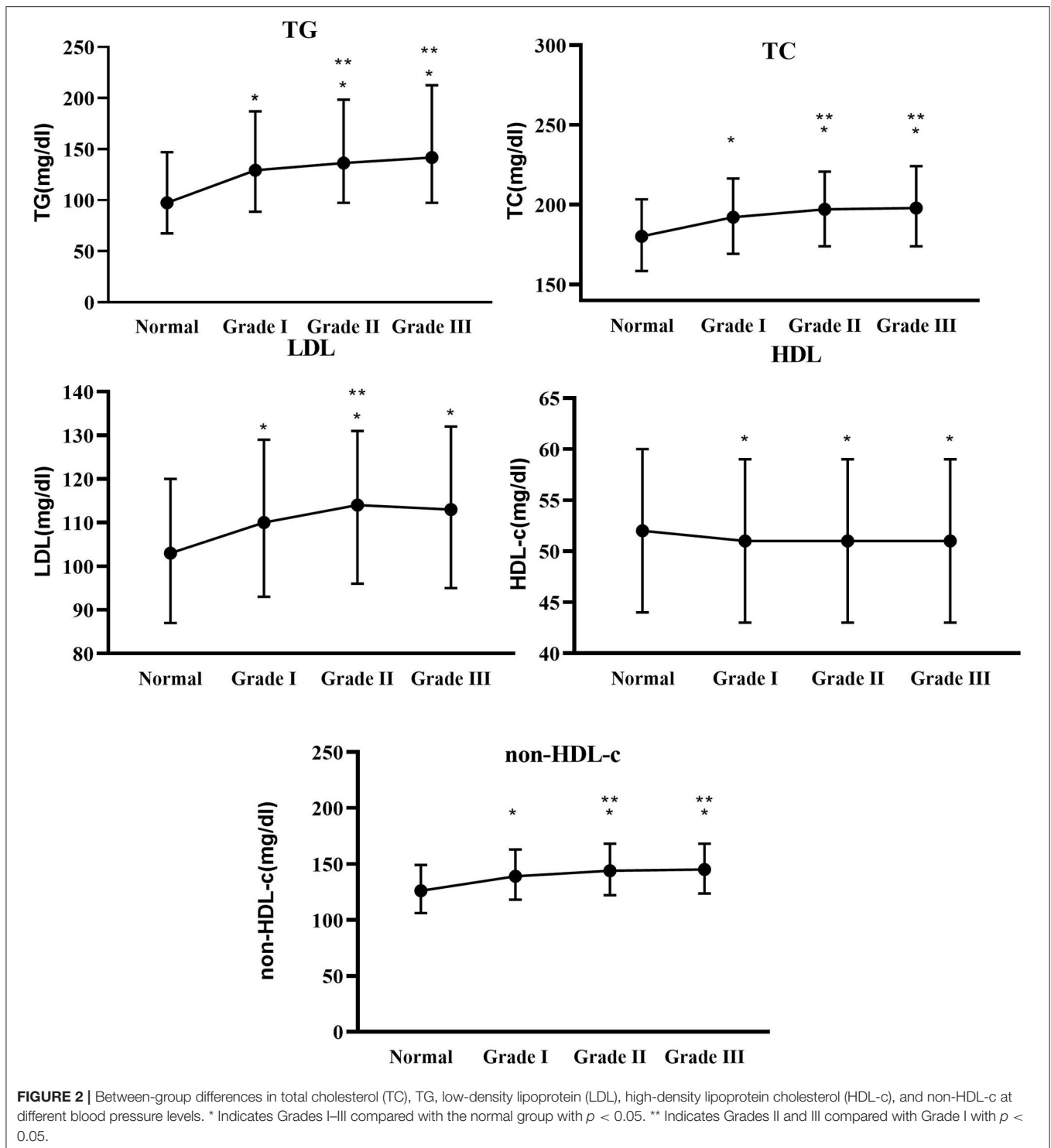
DISCUSSION

This cross-sectional study was conducted based on data collected from 32 healthcare centers in 11 Chinese cities and included a total of 117,056 participants. The following results were obtained in this study. (1) There were significant differences in baseline information and lipid profiles between normotensive and hypertensive groups. (2) Lipid profiles were higher in the hypertensive population, with higher serum levels of TC, LDL, non-HDL-c, and lower HDL-c levels. AC and AIP were higher in the hypertensive population. (3) Subgroup analyses also reached similar results, but HDL-c levels were increased in the hypertensive population with BMI ≥ 23 kg/m². (4) In addition, in the hypertensive population, AIP was not

significantly increased in men and in those with elevated AST and ALT.

In multivariable logistic regression, HDL-c levels were positively associated with the risk of hypertension after adjusting for BMI; AIP was not associated with the incidence of hypertension; AC was positively associated with the incidence of hypertension only at less than 3.1. (5) TG, TC, LDL, non-HDL-c, AC, and AIP were higher in the hypertensive population (regardless of the grade) than in the normotensive group, while HDL-c levels were lower than in the normotensive group. (6) The results of the BN model showed that age, BMI, and FPG were strongly associated with the incidence of hypertension among baseline characteristics. The BN model of lipid profile and atherosclerotic indices showed that TC and LDL were closely associated with the risk of hypertension. (7) AP has a good predictive value for the incidence of hypertension, with the highest predictive value in women.

Dyslipidemia is strongly associated with the development of hypertension. Previous cross-sectional studies have supported the hypothesis of a biological interrelationship between blood pressure and lipids (18, 19), while the relationship between lipid profiles and the risk of new-onset hypertension is further confirmed in cohort studies (20, 21). Nevertheless, different patterns of dyslipidemia have exhibited inconsistent results across diverse ethnic groups. As reported in an East Asian cohort study, HDL-c exerts a protective effect on the risk of hypertension in women, whereas TC and TG were not significantly associated with the risk of hypertension (22). Additionally, a cohort study based on 16,130 US women shows a protective effect of HDL-c



on the risk of hypertension, a positive association of non-HDL-c with the risk of hypertension, and no significant association between LDL and the risk of hypertension (9). Also, a study based on 14,215 Japanese men suggests that elevated serum TC, LDL, and non-HDL-c levels are associated with an increased risk of hypertension, whereas there is no significant evidence

to support the relation between elevated TG levels and the risk of hypertension. Meanwhile, Otsuka et al. suggested that HDL-c levels were not linearly related to the risk of hypertension, but rather in a U-shaped curve (11). To some extent, the above findings are similar to the results of our study (11). Recently, a study from China shows that HDL-c is negatively

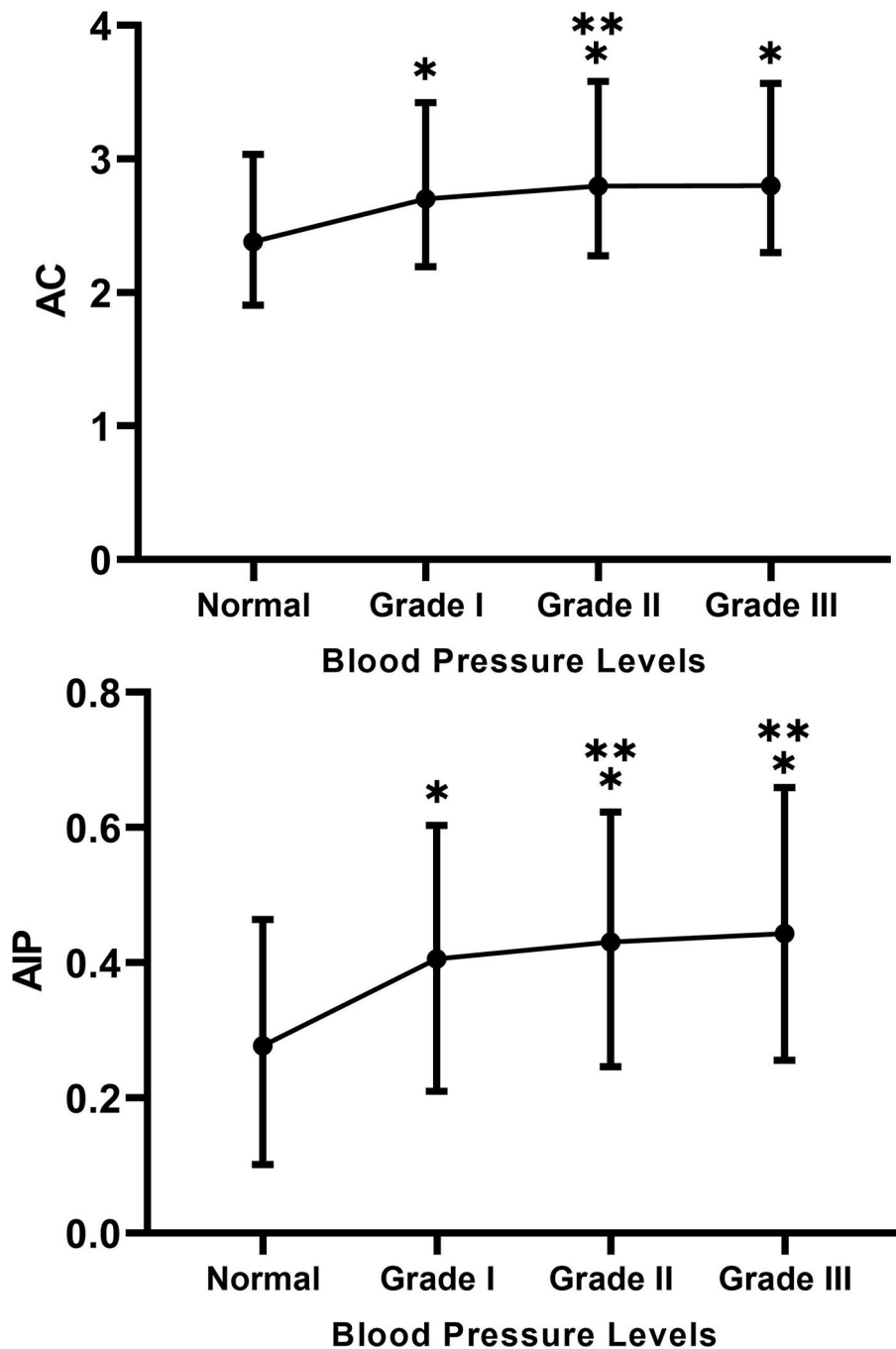
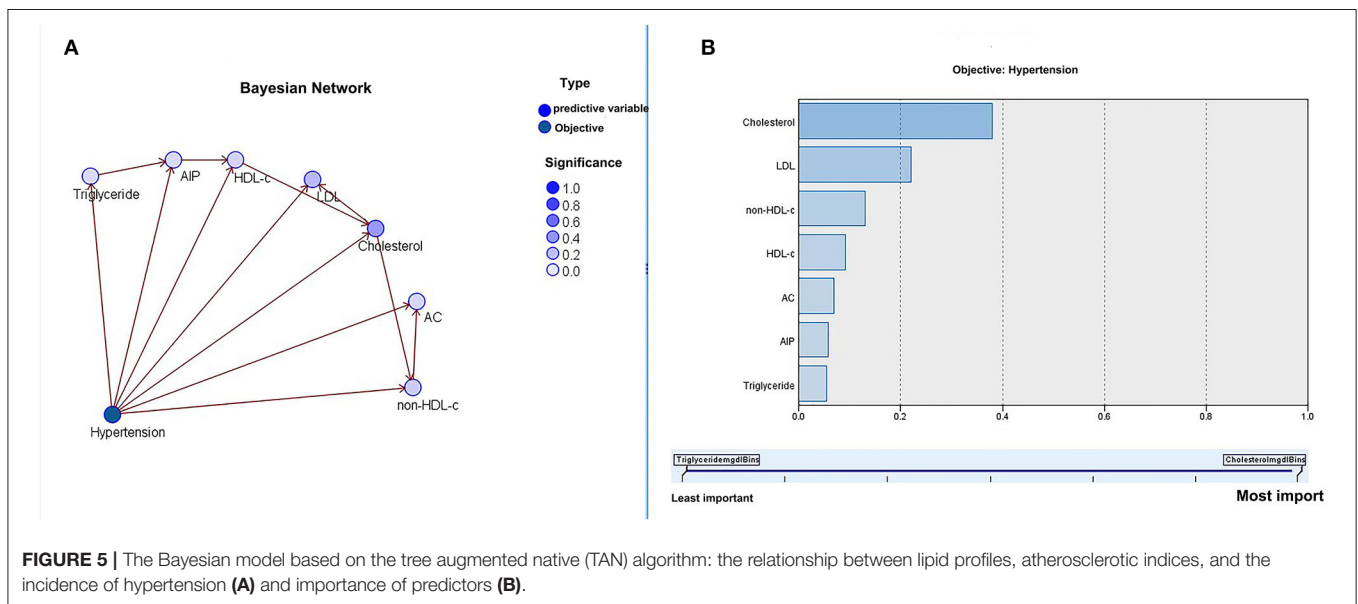
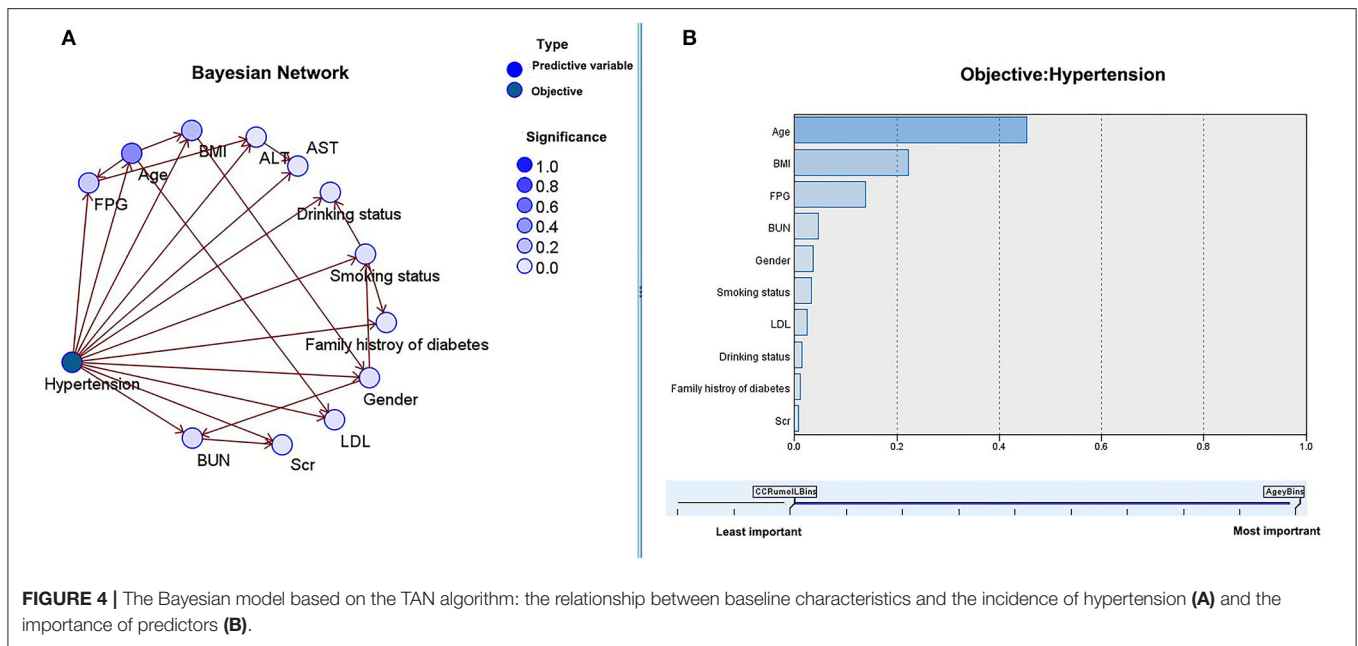


FIGURE 3 | Between-group differences in atherogenic coefficient (AC) and atherogenic risk of plasma (AIP) at different blood pressure levels. * Indicates Grades I–III compared with the normal group with $p < 0.05$. ** Indicates Grades II and III compared with Grade I with $p < 0.05$.

associated with the risk of hypertension in women, but not in men. Meanwhile, the protective effect of HDL-c on the risk of hypertension is only found in people less than 60 years, and HDL-c shows a positive association with the risk of hypertension after adjusting for BMI, consistent with our findings (23). At the same time, another study from China discovers that low or high HDL-c levels are associated with a high risk of cardiovascular

events (24). In China, compared with normotensive individuals, patients with hypertension over 60 years may have other CVDs, and those with a BMI $> 23 \text{ kg/m}^2$ tend to suffer from some metabolic diseases. These individuals may have undergone early lifestyle and pharmacological interventions, such as low-salt and low-fat diet, antihypertensive therapy, lipid-lowering therapy, and improvement of endothelial function, which may



passively increase HDL-c levels. Indeed, the anti-atherosclerotic function of HDL-c is achieved by means of reverse cholesterol transport, maintenance of endothelial cell homeostasis, and its potent antioxidant properties (25, 26). Moreover, randomized clinical trials (RCTs) have confirmed that there is no additional benefit from the pharmacological increase of HDL-c (27). This may partly explain the elevated HDL-c levels in the specific hypertensive population.

Atherogenic coefficient and AIP, as predictors of arteriosclerosis, have been widely used in CVD screening and risk stratification (14, 28–30), while relevant studies in the hypertensive population are still limited (31, 32). In this study, we observed that AC and AIP were higher in the hypertensive

population than in the normotensive population, which was associated with an increased proportion of dyslipidemia in the hypertensive population. However, in multivariate logistic regression, AIP was not significantly associated with the incidence of hypertension, which is consistent with the findings of Choudhary et al. (33). In addition, in the analysis of AC and AIP to predict the incidence of hypertension, we found a good predictive value of AC, especially in women. In **Table 2**, we can find that TC was significantly higher in women than in the other groups, which may partly explain the better prediction of the incidence of hypertension by AC in women. The mechanism behind this remains unclear, and we speculate that a significant increase in TC may be related to female hormone levels.

In addition, from the results of this study, we found no obvious evidence to support the association of TG with an increased risk of hypertension, which was inconsistent with previous studies (34, 35). It is well known that TG reflects the degree of visceral fat accumulation (36). However, visceral adipose tissues should differ between countries due to differences in race, diet, and lifestyle (1). Nazare et al. reported that the visceral adipose tissues of the Chinese differed significantly from those of European and US populations, so there might be differences in the effect of TG on the risk of hypertension (37). In the BN model analysis, TC had the highest importance value on the effect of hypertension, and TC directly affected LDL; as a result, TC might play a “pivotal” role in the development of lipids and hypertension. Indeed, in the Framingham Study, Castelli et al. and Anderson et al. found a strong correlation between blood pressure and serum cholesterol in patients with hypertension. They also suggested the need for early treatment of hypercholesterolemia in these patients with hypertension (38, 39). As well, Gaziano et al. pointed out a potential interaction, rather than independence, between TC and hypertension in the development of myocardial infarction (MI) (40).

Lipids may be involved in the following biological mechanisms in the pathogenesis of hypertension. (1) Lipid abnormalities may act on vascular endothelial cells and affect the production, release, and function of nitric oxide (NO), which may lead to atherosclerosis (41). (2) Dyslipidemia can lead to smooth muscle cell hypertrophy and collagen deposition, which further aggravates arterial wall atherosclerosis. Concurrently, dyslipidemia can induce renal capillary damage, resulting in the development of secondary hypertension (42). (3) There are some genes that identically interact between hyperlipidemia and hypertension, such as apolipoprotein (apo) A-I, apo E, microsomal TG transporter protein, and lipoprotein lipase genes (43). (4) Lipid abnormalities and insulin resistance are associated with sympathetic hyperfunction, and the latter may be related to the development of hypertension (44).

The following limitations should be noted in this work. (1) First, this is a cross-sectional study and our results do not support a causal relationship. (2) Second, the population studied was mainly from eastern China, and the results in this paper were only partially representative of this region. (3) This study did not collect details on medication use or other chronic disease conditions that might partially affect the results of lipids and the risk of hypertension, this deficiency should be improved in the design of future studies.

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CONCLUSIONS

Overall, compared with the normotensive group, TC, TG, LDL-c, and non-HDL-c levels are significantly higher, while HDL-c levels are significantly lower in the hypertensive group. TC and LDL were strongly associated with the incidence of hypertension. TC, LDL, and non-HDL-c levels show a positive association, HDL-c shows a negative association, while TG is not significantly associated with the risk of hypertension. After adjusting for BMI, HDL-c turns out to be positively associated with the risk of hypertension. In addition, AC has a good predictive value for the incidence of hypertension in women.

DATA AVAILABILITY STATEMENT

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found below: <https://datadryad.org/stash/dataset/doi:10.5061/dryad.ft8750v>.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Rich Healthcare Group Review Board. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

WKC and SWC designed. WKC drafted, analyzed, and interpreted this study. WKC, LLW, and SWC critically reviewed the study. All authors finally agreed and read and approved the submitted manuscript.

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