Identifying Factors Associated With Hypertension Using Structural Equation Modeling: Evidence from a Large Kurdish Cohort Study in Iran

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Abstract

Background

Identifying the risk factors leading to hypertension can help explain why some populations are at a greater risk for developing hypertension than others. The present study seeks to identify the causal paths among the risk factors of hypertension in 35- to 65-year-old participants in western Iran.

Methods

The secondary analysis was conducted using the data obtained in the recruitment stage of Ravansar Non-Communicable Disease (RaNCD) cohort. Each of the latent variables were confirmed by confirmatory factor analysis. Using Structural Equation Modeling (SEM), we assessed the direct and indirect effects of the risk factors associated with hypertension.

Results

Socioeconomic status (SES), physical activity, lipid profile, obesity, Diabetes and family history of hypertension had a diverse impact on the blood pressure, directly and (or) indirectly. When investigating the latent and observers risk factors and the interrelations between different risk factors, The standardized total effect (the sum of direct and indirect effects, β_t) of SES, physical activity, lipid profile, obesity, on the blood pressure was(-0.09 vs -0.14), (-0.04 vs -0.04), (0.13 vs 0.13), (0.24 vs 0.15) in men and women respectively. Diabetes had a direct relationship with the blood pressure in women (0.03).

Conclusion

With regard to control of high blood pressure, public health interventions must target obesity,SES, lifestyle and nutritional factors such as hyperlipidemia and hyperglycemia in Iranian population

Introduction

Hypertension is one of the most important risk factors for chronic heart diseases(1, 2). The incidence of hypertension has increased over the last few decades; the number of adults with hypertension has increased from 595 million in 1975 to 1.13 billion in 2015 (1). the prevalence of hypertension is predicted to increase 29.2% by 2025 and This increase has largely occurred in low-to middle-income countries(3, 4). The relationship between high blood pressure and cardiovascular disease and its mortality has been addressed in a number of observational studies(5). Hypertension shows an independent relationship with the incidence of several cardiovascular events such as stroke, myocardial infarction, heart failure and peripheral arterial disease as well as kidney disease. This relationship is shown for all ages and in all ethnic groups(6, 7).

Hypertension have a wide range of risk factors including, genetic, behavioral, environmental origin or other medical conditions(8, 9). Identifying the risk factors associated with hypertension can help explain why some populations are at a greater risk for developing hypertension than others. Studies have shown that, after adjustments for age and gender in different populations, hypertension are associated with body mass index (BMI), the level of physical activity and genetic factors, overweight/obesity, smoking, high cholesterol, diabetes mellitus, and other lifestyle factors (10–12). Nonetheless, these risk factors have not yet been simultaneously examined in a series that assesses the causal relationships leading to the outcome. By assessing the effect of the latent variables, Structural Equation Modeling (SEM) is the most useful method for the concurrent testing of complex relationships between variables(13). SEM is a powerful multivariate analysis method of multivariate regression that allows for the simultaneous verification of a series of regression equations(14) and a concurrent assessment of the relationships between different variables(15) .

SEM reduces measurement errors by involving several overt variables for each latent variable. Unlike traditional regression models that treat each covariate in the model as an independent direct effect, SEM allows to test the model with several dependent variables and assess the concurrent direct and indirect effects of several independent variables on the dependent variable. Available research allows us to hypothesize a causal model that depicts the relationships between factors related to the development of hypertension in terms of direct and indirect (i.e, mediator) effects. The present research was conducted to use SEM to identify the (direct and indirect) causal paths between the risk factors associated with hypertension in in the Ravansar Non-Communicable Disease (RaNCD) cohort.

Materials And Methods

Study design and participants

We used data from (RaNCD) cohort study. Ravansar is a city in Kermanshah Province which is located in western Iran close to the border with Iraq, with a population mainly comprised of Kurdish ethnicity. The RaNCD cohort is part of the large PERSIAN (Prospective Epidemiological ReSearch in IrAN) study. The study began in November 2014 and continues to date. Data from the recruitment phase of the study has been collected and includes general data, a nutrition questionnaire, and biological samples. More information is available in the cohort protocol and preliminary results (16, 17) .

Inclusion and exclusion criteria

The data used in this study pertained to more than 10000 participants aged 35 to 65 who had voluntarily entered the study. For the purpose of this study we excluded those with a clinical history of stroke (50 subjects), myocardial infarction (65 subjects), renal failure (53 subjects).

Definitions and measurements

Anthropometric indices including body weight, height, waist to hip ratio and body mass index, waist circumference were measured according to standard methods. Body weight was measured using Bio-Impedance Analyzer BIA (Inbody770, Inbody Co, Seoul, Korea) with a precision of 0.5 kg. Height was measured by BSM370 (Biospace Co, Seoul, Korea) with the precision of 0.1cm. Body mass index (BMI was measured by dividing weight (kg) by the square of height (m). The Waist to Hip Ratio (WHR) was calculated by dividing the waist circumference by the hip circumference. WC was measured with a flexible measuring tape at a level midway between the lower rib margin and the iliac crest to the nearest 0.5 cm (18).

The standard physical activity questionnaire of PERSIAN cohort was implemented to assess participants' physical activity. The questionnaire consisted of 22 questions regarding the amount of an individual's daily activity. Finally, metabolic equivalent of task (MET), as an indicator for level and measure of physical activity, was extracted and entered into the model. MET is the amount of oxygen consumed at rest (about 3.5 ml 02/kg/min) and is equal to resting metabolic rate. MET for each activity was extracted using a compendium of physical activities(19). Diabetes was defined as having an FBG 126 mg/dl and/or being on diabetes medication and/or if the diabetes was confirmed by a health practitioner (20).self-report family history of hypertension including living and deceased were any biological blood relatives, ever told by a health professional that they have hypertension.

The outcome variable in this study Blood pressure were classified as latent variable with tow markers including SBP and DBP used quantitatively. Blood pressure was measured after 15 minutes of rest in sitting position. Both arms were measured twice with the cuff size adjusted to the arm circumference. Four BP measurements were taken to mean systolic and diastolic pressure (SBP and DBP) (21).

Statistical Methods

First, we conducted an exploratory factor analysis (EFA) to identify the latent variables underlying the observation variables. The principal component analysis (PCA) and varimax rotation was conducted to estimate the latent variables. The number of the extracted factors was chosen based on the factor eigenvalue (1). The economic welfare (wealth) variable was measured using 12 questions regarding housing, car, home appliances and other amenities by PCA method. Second, In order to create constructs (or factors), we applied confirmatory factor analysis (CFA) and we constructed an initial SEM. The objective of confirmatory factor analysis is to test whether the data fit a hypothesized measurement model. In the next step, SEM with maximum likelihood estimation (MLE) was applied to assess the conceptual model (Figure1). The SEM was used to study the direct and indirect relationships between a set of variables associated with hypertension. In the conceptual model, there are four latent variables including the main dependent variable, which is blood pressure, with the indicator of systolic and diastolic blood pressure (SBP, DBP). Considering that BMI, WHR and WC represent obesity indicators, a latent variable named 'obesity ' was constructed. The other latent variable that play the role of independent variable in the model include SES with three indicators: economic prosperity (Wealth); education level; and place of residence (place). The four latent variable named 'lipid profile' was constructed to reflect TC/HDL and LDL/HDL. Path standardized coefficients (β) as the effect sizes of this model were calculated. CMIN/DF , CFI , GFI , RMSEA , NFI and AGFI were applied to assess fitness of the model. Also, data were described using the appropriate method (mean ± standard deviation for quantitative variables and number and percentage (%) for qualitative variable). All of the statistical analysis was performed using AMOS-SPSS 22 and STATA 14.0 (STATA Corp, College Station, TX). P-value less than 0.05 was considered as statistically significant.

Results

Characteristics of study participants

From among 10065 participants, 9705 subjects enrolled in this study. The mean age ± SD of the participants was 47.53 ± 8.47years. About 52% of the participants were female and 47% were male. The mean systolic blood pressure was 107.52±15.45 and the mean diastolic blood pressure was 69.65±9.35. The BMI of >= 30 was 35% in women and 16% in men. The waist-to-hip ratio (WHR) >= 90 was 3257 (53%) in women and 2908 (47%) in men. The general characteristics of the study participants are shown in Table 1.

Table1: Demographic features in 35-65-year-old by sex at RaNCD chort study

The values outside the parentheses are the number of people and the values inside the parentheses are the percentages. Data are expressed as mean SD. P values were estimated using analysis variance or test.

Results of latent analysis variables

Exploratory factor analysis was conducted and the Kaiser-Meyer-Olk statistic was determined to be 0.697, which indicated that the data were suitable for factor analysis. The four latent factors included SES, blood pressure, obesity, lipid profile were extracted with eigenvalue greater than 1. The extraction results of the latent variables are shown in Table2. In the CFA between the latent variable in the model, correlation and fitting indexes were acceptable : chi-square value ( ) =624.897, the ratio of   to the degrees of freedom = 25, root mean square error of approximation (RMSEA) = 0.05 , comparative fit index (CFI) = 0.98 , goodness of fit index (GFI) = 0.987 ,tuker- lewis index(TLI) = 0.981. (Table3)

Table 2: Extraction results of latent analysis variables (Varimax rotation)

The result of exploratory factor analysis: Kaiser-meyer-olk in measure Of sampling adequacy (kmo) = 0.697, Bartlett test of sphericity approx: Chi-square = 56799.689 , p SES socioeconomic status, SBP systolic blood pressure, DBP diastolic Blood pressure, WC waist circumference, BMI   body mass index, WHR waist to hip ratio, LDL low-density lipoproteins, TC total cholesterol, HDL High-density lipoprotein.

Table 3 : standardized factor loading of the confirmatory factor analysis

SES socioeconomic status, SBP systolic blood pressure, DBP diastolic blood pressure, WC waist circumference, BMI body mass index, WHR waist to hip ratio, LDL low-density lipoproteins, TC total cholesterol, HDL High-density lipoprotein

Results of the model structure

The conceptual model of the study included the variables extracted from the results of previous studies and a review of literature plus consultation with experts. The final model was constructed of the different models (Figure1) and was determined to be the most suitable and identified as the final model. In figure 2 and 3, variables of obesity, Diabetes, lipid profile and METs play a mediation effect which then lead to blood pressure. Table 4 shows the direct and indirect effects of risk factors associated with blood pressure for two groups. Obesity in women were associated with blood pressure directly (ß= 0.15) and corresponding values in men were (ß= 0.24). In men and women, the direct effect of SES on the blood pressure came out negative (ß = -0.13 vs ß = -0.17), but it was positive indirect effect (ß = 0.04 vs ß = 0.03). The mediators for the indirect effect of SES on blood pressure were obesity, Diabetes and Mets (Figure 2, 3). Diabetes was directly associated with blood pressure in women (ß = 0.03) but the association was not statistically significant in men. Mets were inversely indirect associated with blood pressure (ß = -0.04 vs ß = -0.04), in men and women. The mediators for the indirect effect of Mets on blood pressure were obesity, Diabetes and lipid profile. Having positive family history of hypertension especially in the first-degree relatives were associated with a higher risk of hypertension in men and women. lipid profile were direct effect(ß = 0.05 vs ß = 0.09) and indirect effect(ß = 0.08 vs ß = 0.04) in men and women. The mediators for the indirect effect of lipid profile on blood pressure were obesity, Diabetes. Taking antihypertensive drugs were inversely directly associated with blood pressure (ß = -0.29 vs ß = -0.33) in men and women. Table (4) shows the association between the variable.

Figure 2 and 3: shows structural equation models for assessing direct and indirect effects on blood pressure for both males and females by standardized path coefficient and goodness of fit indices. "e" represent the errors. **Note**. SBP systolic blood pressure; DBP diastolic blood pressure; WHR waist to hip ratio ; BMI body mass index; SES socioeconomic status, WC waist circumference, LDL low-density lipoproteins, TC total cholesterol, HDL High-density lipoprotein, HTNfamily Family history ohypertension, HTNdrug antihypertensive drugs,

Table 4. Direct and indirect effects derived from a SEM in people 35-65 from the RaNCD cohort study. **Note**. SBP systolic blood pressure; DBP diastolic blood pressure; WHR waist to hip ratio ; BMI body mass index; SES socioeconomic status, WC waist circumference, LDL low-density lipoproteins, TC total cholesterol, HDL High-density lipoprotein, HTNfamily Family history of hypertension, HTNdrug antihypertensive drug,

Discussion

hypertension is a major public health problem globally(22). Although many studies have examined the effect of risk factors for hypertension separately, only a few limited studies have evaluated the direct and indirect effects of risk and protective factors of hypertension by considering the role of the mediator variables. The present study was conducted to determine the direct and indirect effects of modifiable and non-modifiable risk factors of hypertension using SEM. Therefore, we constructed the latent variable path graph and the SEM model based on past theories. For a proper model fit, modifications had to be implemented on the conceptual model over the course of the statistical analysis based on adjustable indices suggested by the software. In our study, due to the high sample size Chi-square tests are not suitable for model fitting (23). although other fitting indices unrestricted by the sample size are good. Comparative fit index (FCI), incremental fit index (IFI), and normed fit index (NFI) equal to or greater than 0.90 and Root Mean Square Error of Approximation (RMSEA) equal to less than 0.08 were applied to confirm the fit of the model.

With development of the medical research field, it has become important to study and analyze the relationship between social and behavioral factor that affect people's health. This study has demonstrated that individual with a higher level of SES had a direct negative and indirect positive effect through (obesity, MET, Diabetes) on hypertension and at increased risk for lipid profile and obesity in both sexes. Increased awareness, accessibility of medical treatment and opportunities to prevent, diagnosis of hypertension have been indicated a protective effect of higher SES on raised blood pressure. However, unfavorable living habits, unhealthy diet including the consumption of high-calorie foods (the average energy consumed by our whole population was 3865.56kcal/d, which was higher than the recommended levels) ,obesity and physical inactivity have been indicated an indirect positive effect of higher SES on raised blood pressure. This finding is consistent whit previous research that found that individual with a higher level of SES had a direct and indirect effect on hypertension with structural equation model(24, 25). Individuals with high level of SES should pay more attention to prevent the hypertension, since SES as a distal risk factor, indirectly influenced obesity, MET, Diabetes, Lipid profile through this pathway.

Obesity was the most important risk factor that directly affected the development of hypertension in our study in both sexes. Consistent with the results of SEM previous studies(24, 26).Overall, individuals who participated in the RaNCD 27.6% of all participants had a normal BMI, while the majority were overweight or obese, especially among women. For waist-to-hip ratio, there was a big difference between men and women. From a total of 9705 people (82.4%) with an abnormal value, 60.4% and 39.6% Were women and men, respectively(17). Hypertension and obesity were associated with biological, behavioral, social and environmental risk factors(27). Obesity is a major risk factor for hypertension, and the association between hypertension and obesity has been confirmed in the past two decades. The combination of obesity and hypertension leads to an increased risk of developing cardiovascular complications(28).

In the present study, the lipid profile was directly associated with hypertension in both sexes, and was associated with obesity directly in Men and women. Many clinical studies have shown that the lipid profile is a strong marker for predicting the risk of atherosclerosis and heart diseases(29, 30). In most studies, old age, hypertension and obesity were significantly associated with an increased lipid profile and consequent dyslipidemia(31). The presence of hyperlipidemia is known to be a prognostic risk factor in patients with hypertension (32, 33).

The association between diabetes mellitus and serum lipids has been much debated over the past decades (34, 35). Type 2 diabetes mellitus (T2DM) is usually associated with abnormal levels of serum lipids. The interaction between impaired lipid metabolism and blood sugar plays an important role in the onset and progression of diabetes and related chronic complications(36, 37). In the present study, the lipid profile was directly associated with Diabetes in women. Higher level of Physical activity are associated with a decreased risk of CVD(38). We found that higher levels of physical activity were negative indirectly effect through decrease of mediator variables (obesity, lipid profile, Diabetes) on blood hypertension. in other words, physical activity was associated with a lower proportion of obesity, lipid profile, Diabetes consistent with previous SEM studies(25, 26).

Strengths And Weaknesses

This study has strengths and weaknesses. The most important strength of the present study was the sample size which was large enough to investigate the association between all the above mentioned variables with hypertension. Our study reveals advantages of SEM application for hypertension compared with the traditional analysis methods. In fact, SEM includes causal modeling, analysis of covariance structures, latent variable and robust model. SEM reduces measurement errors by involvement of several overt variables for each latent variable instead of single-measurement particularly with variables that are measured by multiple indicators, e.g.(SES, obesity, lipid profile) (39). However, our study is cross-sectional, which challenges the causal relationship between the variables. As well as the nature of hypertension which more than 90% of its causes are unknown, it was impossible to draw a model with a large number of variables due to the limitations of working with the software. Our study showed that although there are other factors associated with increased hypertension, among the modifiable risk factors obesity and antihypertensive drugs had the strongest direct effect on the outcome studied in this model. For future works we suggest conducting next studies on other incidence cases that may affect the development of hypertension, such as the role of various diseases, dietary patterns, drug use, the role of psychological and behavioral factors, and so on.

Conclusion

the present study demonstrated that high blood pressure was related to SES, physical activity, lipid profile, obesity and Diabetes directly and (or) in directly. Future interventions to prevent and control hypertension among Ravansar province should focus on SES, obesity, increasing physical activity and improving the life style.

Declarations

Ethics approval and consent to participate: the present study was conducted according to the Helsinki Declaration. The study was approved by the ethics committee of the vice chancellery of research and technology, Kermanshah University of Medical Sciences(IR.KUMS.REC.1394.315) and the written informed consent was obtained from each participant after explaining the purpose of research.

Consent for publication: Not applicable

Availability of data and materials: The RaNCD cohort is not an open-access database. However, we would encourage external investigators to consider applying to use the data for secondary analyses, to maximize the scientific output from the data. All the information on how to access the RaNCD public data archive, with a list of current proposals and papers under preparation, can be found on our website: www.persiancohort.com

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: Farid Najafi interpretation of data and analysis and revised**..Mehdi Moradinazar** design of work **, *Shahab Rezayan*** contributions to the conception and revised **, *Reza Azarpazhooh*** contributions to the conception and revised. **Parastoo jamshidi** interpretation of data and writing and analysis.

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Tables

Table 1 is available in the Supplemental Files section.

Table 2: Extraction results of latent analysis variables (Varimax rotation)

Latent variable	Indicator variable	Loading coefficient	Cronbach's coefficient
Blood pressure	SBP	0.953	0.863
	DBP	0.958	
			0.589
	Education	0.832	
SES	Wealth	0.802	
	Place	0.585	0.962
Lipid profile	LDL: HDL	0.973	0.549
	TC: HDL	0.972	
	BMI		
Obesity	WC	0.916	
	WHR	0.905	
		0.836	

The result of exploratory factor analysis: Kaiser-meyer-olk in measure Of sampling adequacy (kmo) = 0.697, Bartlett test of sphericity approx: Chi-square = 56799.689 , $p < 0.001$

SES socioeconomic status, SBP systolic blood pressure, DBP diastolic Blood pressure, WC waist circumference, BMI body mass index, WHR waist to hip ratio, LDL low-density lipoproteins, TC total cholesterol, HDL High-density lipoprotein

Table 3 : standardized factor loading of the confirmatory factor analysis

Latent variables	Indicator variables	Loading cofficint
Blood pressure	SBP	0.958
	DBP	0.950
SES	Education	0.644
	Wealth	0.801
	Place	0.335
Lipid profile	LDL: HDL	0.959
	TC: HDL	0.980
	BMI	0.741
Obesity	WC	0.696
	WHR	0.925

SES socioeconomic status, SBP systolic blood pressure, DBP diastolic blood pressure, WC waist circumference, BMI body mass index, WHR waist to hip ratio, LDL low-density lipoproteins, TC total cholesterol,HDL High-density lipoprotein

Table 4: Direct and indirect effects derived from a SEM in people 35-65 from the RaNCD cohort study.

Variables	Male			Female		
	Total effect **(95%CI)**	Direct effect **(95%CI)**	Indirect effect **(95%CI)**	Total effect **(95%CI)**	Direct effect **(95%CI)**	Indirect effect **(95%CI)**
Obesity —> BP	0.24(0.21 - 0.27)	0.24(0.21 - 0.27)	—	0.15(0.12 - 0.18)	0.15(0.12 - 0.18)	—
Lipid profile–-> BP	0.13(0.10 - 0.16)	0.05(0.02 - 0.08)	0.08(0.06 - 0.09)	0.13(0.10 , 0.15)	0.09(0.07 , 0.12)	0.04(0.02 , 0.05)
SES —> BP	-0.09(-0.13, -0.06)	-0.13(-0.17, - 0.09)	0.04(0. 02 , 0.05)	-0.14(-0.18, -0.06)	-0.17(-0.20, -0.13)	0.03(0.02 , 0.04)
Diabetes—> BP	—	—	—	0.03(0.02 , 0.05)	0.03(0.02 , 0.05)	—
MET —> BP	-0.04(-0.07, -0.01)	—	-0.04(-0.07, -0.01)	-0.04(-0.07, -0.02)	—	-0.04(-0.07, -0.02)
HTNDRUG —> BP	-0.29 (-0.32, -0.25)	-0.29 (-0.32, -0.25)	—	-0.33 (-0.36, -0.30)	-0.33 (-0.36, -0.30)	—
HTN family—> BP	0.02(0.02 , 0.05)	0.02(0.02 , 0.05)	—	0.03(0.01 , 0.06)	0.03(0.01 , 0.06)	—
MET —> obesity	-0.11 (-0.15, -0.08)	-0.08 (-0.11, -0.05)	-0.03 (-0.04, -0.02)	-0.08 (-0.11, -0.05)	-0.07 (-0.10, -0.04)	-0.01 (-0.01, -0.03)
MET—> lipid profile	-0.11 (-0.13, -0.07)	-0.11 (-0.13, -0.07)	—	-0.07 (-0.09 , -0.04)	-0.07 (-0.09 , -0.04)	—
MET—> Diabetes	-0.06 (-0.09, -0.03)	-0.06 (-0.09 -0.03)	—	-0.03(-0.09, -0.03)	-0.02 (-0.05, -0.03)	-0.01 (-0.01, -0.03)
Lipidprofile—>obesity	0.32(0.30 , 0.35)	0.32(0.30 , 0.35)	—	0.21(0.18 , 0.24)	0.21(0.18 , 0.24)	—
SES—> METs	-0.39 (-0.41, -0.36)	-0.39 (-0.41, -0.36)	—	-0.23 (-0.26, -0.19)	-0.23 (-0.26, -0.19)	—
SES—> Obesity	0.13 (0.09 , 0.16)	0.08 (0.04 , 0.12)	0.05 (0.03 , 0.06)	0.10 (0.06 , 0.13)	0.08 (0.04 , 0.12)	0.02 (0.01 , 0.02)
SES—> Lipid profile	0.04 (0.03 , 0.05)	—	0.04 (0.03 , 0.05)	0.01 (0.01, 0.02)	—	0.01 (0.01, 0.02)
Lipid profile -–>Diabetes	—	—	—	0.04 (0.01,0.07)	0.04 (0.01,0.07)	—

SBP systolic blood pressure, DBP diastolic blood pressure, SES socioeconomic status, HTN family:Family history of hypertension, HTNdrug antihypertensive drugs

Figures

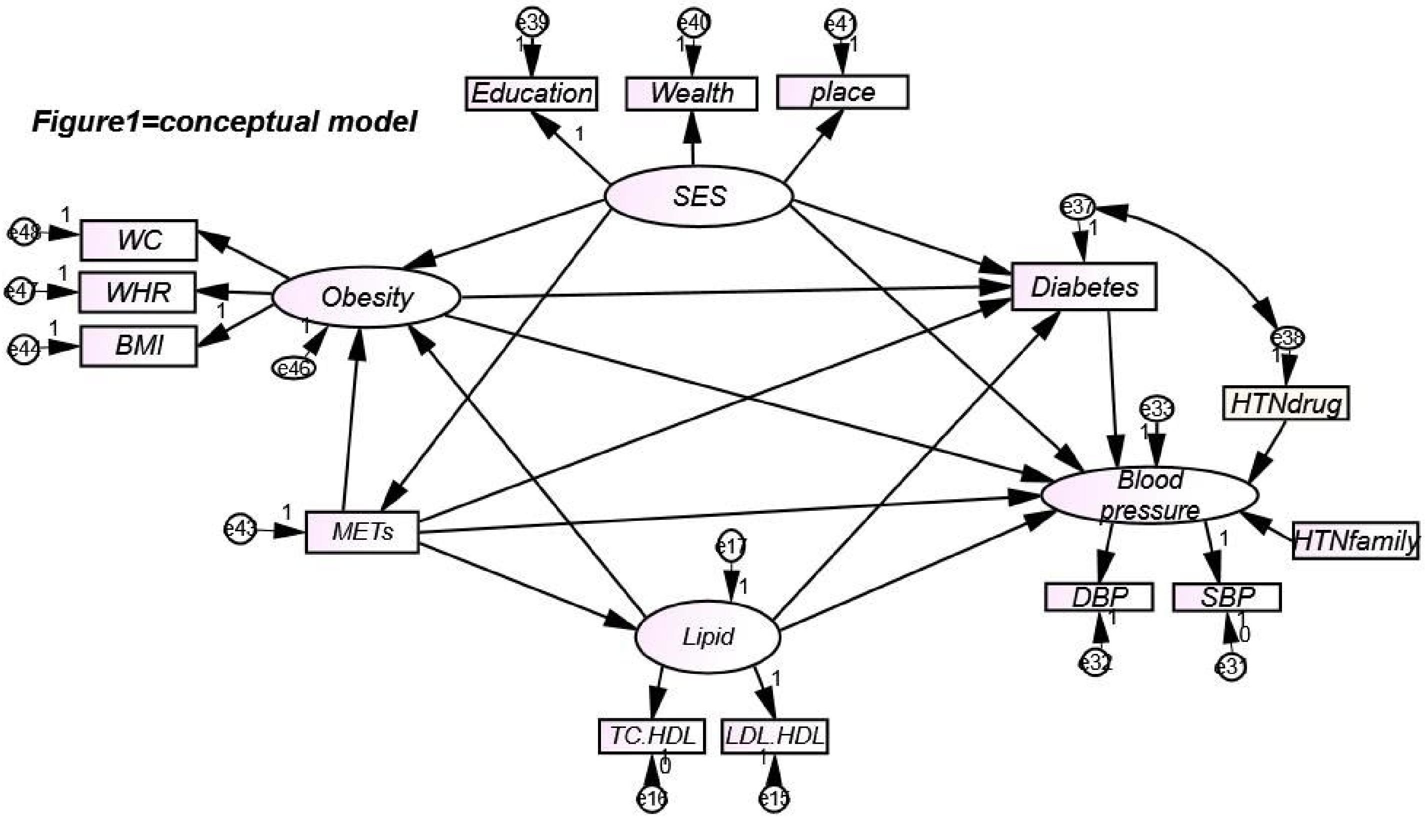

Figure 1

The conceptual model diagram for risk factors relationship with blood pressure.

SES socioeconomic status, SBP systolic blood pressure, DBP diastolic Blood pressure, WC waist circumference, BMI body mass index, WHR waist to hip ratio, LDL low-density lipoproteins, TC total cholesterol, HDL High-density lipoprotein, HTNfamily Family history of hypertension, HTNdrug antihypertensive drugs

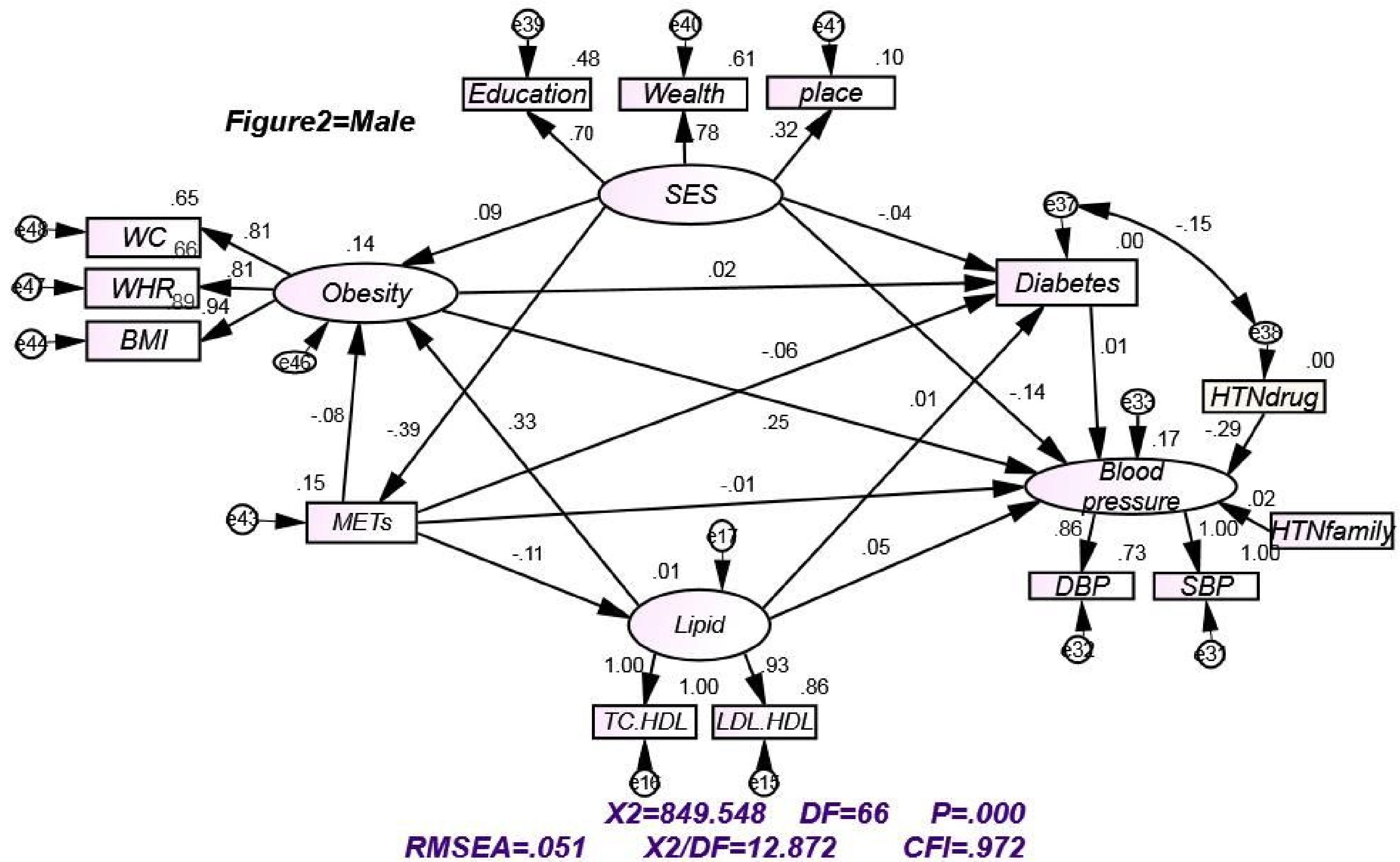

Figure 2

Figure 2: shows structural equation models for assessing direct and indirect effects on blood pressure for both males and females by standardized path coefficient and goodness of fit indices. "e" represent the errors. **Note**. SBP systolic blood pressure; DBP diastolic blood pressure; WHR waist to hip ratio ; BMI body mass index; SES socioeconomic status, WC waist circumference, LDL low-density lipoproteins, TC total cholesterol, HDL High-density lipoprotein, HTNfamily Family history ohypertension, HTNdrug antihypertensive drugs,

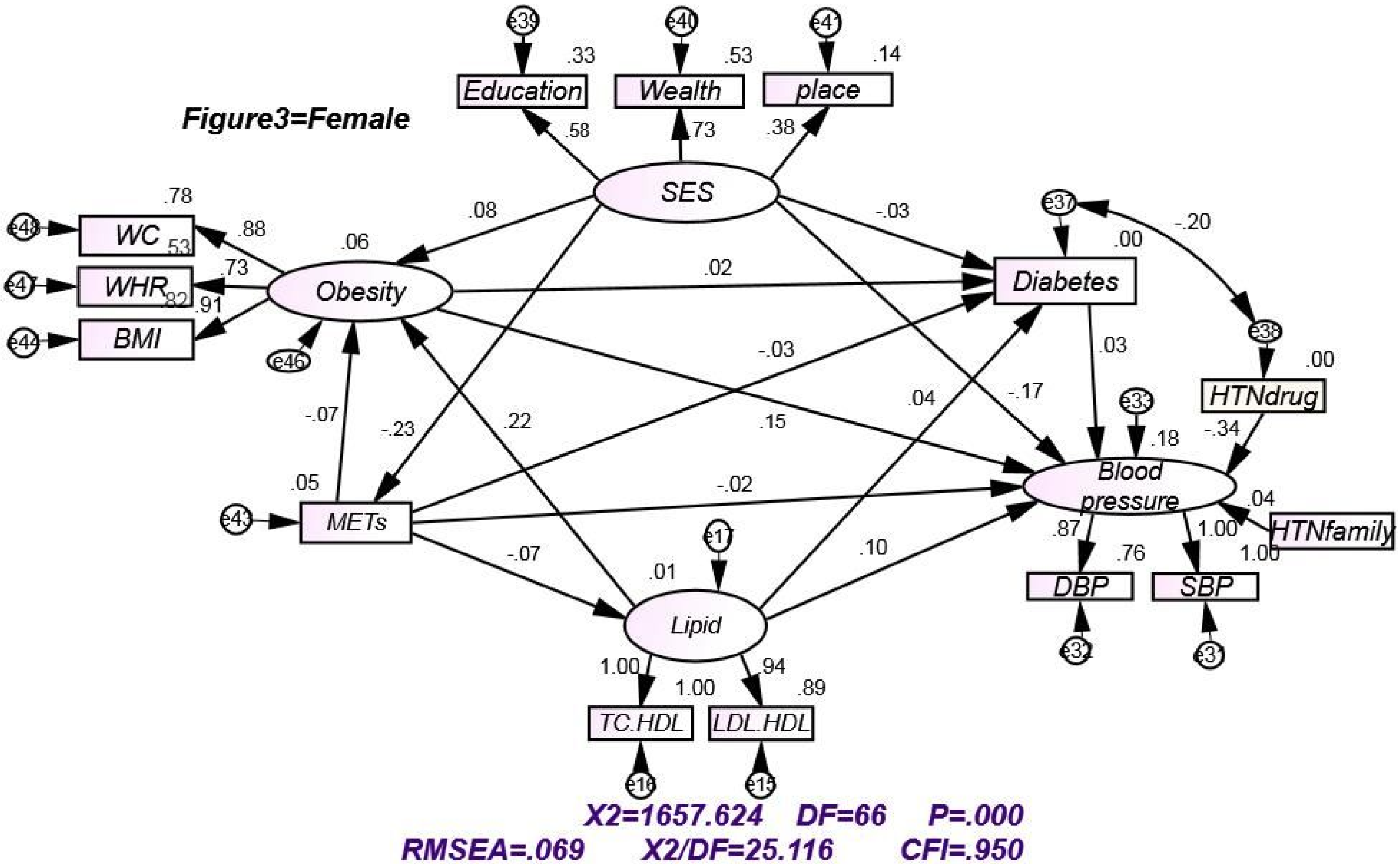

Figure 3

Figure 3: shows structural equation models for assessing direct and indirect effects on blood pressure for both males and females by standardized path coefficient and goodness of fit indices. "e" represent the errors. **Note**. SBP systolic blood pressure; DBP diastolic blood pressure; WHR waist to hip ratio ; BMI body mass index; SES socioeconomic status, WC waist circumference, LDL low-density lipoproteins, TC total cholesterol, HDL High-density lipoprotein, HTNfamily Family history ohypertension, HTNdrug antihypertensive drugs,

Supplementary Files

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- Table1.jpg