



Insulin Resistance, Serum Calcium and Hypertension: A Cross-Sectional Study of a Multiracial Population, and a Similarity Assessment of Results from a Single-Race Population's Study

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Background: Recent research suggests the need to assess more ethnic disparities in hypertension (HTN). On the other hand, studies reveal impressive mortality rates due to cardiovascular diseases for some race and ethnic groups compared to others.

Methods: We referred to a recent study on serum calcium (SC) and insulin resistance associated with HTN incidence to compare different race groups in the latter found relationship. We compare the current study outcomes with those from the Wu et al study.

Results: From 425 participants of the National Health and Nutrition Examination Survey (NHANES) data, we found a significant association between race and hypertension; Cramer's V (0.006) = 0.21 when adjusted with non-hypertensives and hypertensives. Mc Auley index (McA) was negatively related to hypertension, $r(355) = -0.24, p < 0.0001$. SC associated with HTN in all race groups significance persisted only in non-Hispanic Whites after multivariate adjustments R^2 of 74.1 ($p = 0.03$). McA was a mediator on SC-HTN in non-Hispanic Whites (NHW) (Coef_{IE} = 13.25, [CI] = 1.42–32.13), and a moderator in other Hispanics interaction (0.04) = 0.27 and NHW interaction (0.001) = 0.028.

Conclusion: SC was associated with hypertension, similarly to the baseline study. SC and HTN association persisted in NHW compared to other race groups. Homeostasis model assessment (HOMA-IR) was not a mediator on SC-HTN, but with McA, this in NHW only. McA played a moderator role in OH and NHW. We suggest that race is a factor implicated in our findings, which may be investigated further in future research.

Keywords: Mc Auley index, HOMA-IR, serum calcium, hypertension incidence, ethnicity

Introduction

The link between ethnicity and race disparities with hypertension (HTN) is still lacking. Fewer studies performed comparisons between pure races in native homeland population and health status.¹ On the other hand, studies reveal impressive mortality rates according to the Race group membership; Blacks are more likely to die of heart disease (three times more) than Whites, with a lower rate of control and effective treatment of hypertension in this case.^{2–4} Thus, it is of great interest to focus on any potential risk factor for better awareness of the disease for its prevention.

An association between serum calcium (SC), insulin resistance (IR) and hypertension risk (HR) was recently found on an Asian race population,⁵ yet the SC

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effect on hypertension is yet a controversial issue. Indeed, some studies show that SC would be inversely proportional to the onset of hypertension,⁶ while others suggest that a high level of SC would contribute to the high blood pressure.^{7–9}

Like inheritance passed down from generation to generation, many studies have shown the impact of ethnicity or race on the occurrence of HTN; the racial/ethnic factor is an indicator or inducer which may even be a predictor of cardiovascular disease and high blood pressure.^{2,10–14} Hence, racial demarcations of hypertension incidence have been observed in a population with the same level of knowledge and management of the hypertensive disease.^{15,16} Similarly, in Brazil Browns, Black, Yellow, Brazilian mixed-race, and the more influential group of the region had a lower prevalence of hypertension when compared with Whites.¹⁷

Although previous studies present the HTN prevalence among race and ethnic group population, there are least, if any, which make the comparison, focused on nutritional component risk factors. Therefore, our study aimed to evaluate the SC and the IR thru HOMA-IR and Mc Auley (McA) in an association with the Hypertension risk in a multiracial population background, compared to a single racial population background.

A causal relationship between serum calcium and the hypertension risk has recently been found in a typically Chinese population; our study aims to evaluate this risk factor for hypertension in a multiracial population (namely, Mexican Americans, other Hispanics, non-Hispanic Whites, and non-Hispanic Blacks) in comparison with a single racial population.

Materials and Methods

Study Population

Our data were taken from the NHANES. The NHANES collects data from the US civilian population using a complex four-stage sampling design. With the weights assigned to the samples, each cycle of data produced is intended to be comparable to data collected from the entire US population.¹⁸ The present study is a cross-sectional and prospective study. We collected the data variable, according to the outcomes from the study of Wu et al,⁵ which is our reference Study. From this study, which population consisted entirely of Adult Chinese, we conformably retained the main study variables for analysis assessing SC, IR as a risk factor for Hypertension. We

collected five two-year cycles (from 2007 to 2016). After excluding: patients who had taken calcium supplement 30 days before the day of data sampling, patients with diabetes and cancer comorbidity to avoid overestimation of their SC and IR levels, we collected data on 425 self-reported diagnosed hypertensive patients, from the NHANES database.

Outcome Variables

Hypertension Occurrence

We considered all sequences of participants with available data on blood pressure. From all participants self-reported hypertensives and taking antihypertensive drugs, we selected those with at least stage I hypertension according to the 2018 ACC-AHA Hypertension guidelines for hypertension,¹⁹ which defines 130/90mmHg as high blood pressure. Arithmetical mean of 3 times measurement of the diastolic and systolic blood pressure was used. We first analyzed data considering only stage II hypertension (140/90mmHg) patients, and secondly, we included stage I hypertensives and found no significant difference in the results.

Insulin Resistance

IR was assessed by two indexes, the HOMA-IR and the Mc Auley. HOMA-IR was calculated as per Eq1i.²⁰ We calculated the Mc Auley index by using the formula of Eq2ii.²¹ For both computations, we needed fasting insulin (uU/mL), fasting glucose (mmol/l), and 2h-glucose (mmol/l) and fasting triglycerides (mmol/l) from participants' records.

Serum Calcium

Serum calcium in mmol/L data was available from the Laboratory Dataset.

Covariates

For comparison, we collected from the NHANES all related available data according to the reference study variables. Patients' age in year, gender (male and female), and race (Mexican-Americans, other Hispanics, non-Hispanic Whites and non-Hispanic Blacks) were collected from the Demographic Dataset. Drinking status (frequency of drinking any type of alcoholic beverage in the past 12 months), smoking status, physical activity (How much time usually spend sitting on a typical day, excluding sleeping time), was collected from the Questionnaire Dataset. Caloric intake (in Kcal) was fetched from the

Dietary Dataset. BMI values were taken from the Examination Dataset. Glycohemoglobin records were fetched from the Laboratory data.

Data Analysis

The baseline study was a study on the Harbin Cohort Study on Diet, Nutrition and Chronic Non-Communicable Disease (HDNNCDS) population, in which details are available online. The baseline study aimed to analyze SC related to hypertension risk thru IR (HOMA-IR and Gutt Index), using logistic regressions, cross-lagged path analysis, and mediation for statistical analysis. We used Stata 15.0 for Windows, JMP Pro 13.0.0 and Excel 2007 for data importation, and IBM SPSS statistics 24 for data analysis. A sample weight corresponding to a ten-year cycle was applied before analysis. The first step analysis was to state the relationship between race and hypertension incidence; for this purpose, Chi-square and Cramer's V tests were performed. We used Pearson product-moment correlation to examine the relationship between SC levels, HOMA-IR, Mc Auley index, and hypertension occurrence, in the whole present study

population. OR was assessed to evaluate the hypertension risk related to the SC, HOMA-IR, and McA levels in each race group of the present study. We used logistic regressions to build mediation model 4 and moderation model 1 analysis adjusted one by one with race and gender, and further race with confounders. We cross-checked the moderation and mediation models confidence intervals (CI) in MACRO PROCESS[®] for SPSS. The moderation model was built to perceive a partial temporal relation between SC and HTN. We performed logistic regressions to assess the HTN incidence and its various associated risks in each race group of the present study. We finally compared our results to those of the baseline study standing as our baseline.

Results

Population Characteristics

Table 1 shows population characteristics among each studied racial group. MA had the highest mean age (58 years old). Meanwhile, the highest frequencies were found in NHW (179). MA tends to have the highest mean BMI and HOMA-IR (32.14 and 4.51). As for the highest mean McA

Table 1 Variables Distribution per Race Group

	Mexican-Americans	Other Hispanics	Non-Hispanic Whites	Non-Hispanic-Blacks
	Mean (P-value)			
	N=58	N=55	N=179	N=133
Age	58 (0.146)	47.09 (0.8)	47.60 (0.004)	46.97(0.007)
BMI (Kg/m ²)	32.14 (0.25)	28.17 (0.51)	28.66 (0.000*)	29.57 (*)
Systolic (mmHg)	134.02 (0.02)	127.47 (*)	128.20 (*)	136.19(*)
Diastolic (mmHg)	78.59 (0.003)	72.39 (0.1)	73.79 (0.005)	77.05 (*)
Caloric intake (Kcal)	1770.22 (0.37)	1772.34 (0.001)	1959.9 (*)	1798.9 (0.001)
Serum calcium (mmol.l ⁻¹)	2.31 (0.2)	2.36 (0.002)	2.33 (*)	2.35 (0.06)
HbA1c (%)	5.59 (0.63)	5.75 (*)	5.53 (*)	5.74 (*)
HOMA-IR	4.51 (*)	3.37 (*)	2.83 (*)	3.32 (*)
Mc Auley Index	1.84 (0.017)	1.93 (0.005)	1.97 (0.224)	2.02 (0.61)
Percentages (%)				
HTN cases	29.8	37	43.1	48.9
Physical activity	57.9	50	70.9	64.9
Alcohol consumers	89	80	0.6	1.59
Smoking status	39.7	50.9	69	63

Note: (*) P-value less than 0.001.

Table 2 Reference and Present Study Variables Overview

	Present Study N= 425	Reference Study N= 8653
Age	49.89	47.89
BMI (Kg/m ²)	29.63	24.46
Systolic (mmHg)	131.47	134.91
Diastolic (mmHg)	75.45	81.95
Caloric intake (Kcal)	1825.34	2443.45
Serum calcium (mmol.l ⁻¹)	2.34	2.26 ^μ
HbA1c (%)	5.65	5.12 ^μ
HOMA-IR	3.5	1.96 ^μ

Notes: ^μGiven values for baseline and follow-up. Data from Wu et al.⁵

and Hypertension cases, they were found in non-Hispanic Blacks. Other Hispanics had the highest mean level in Serum calcium.

An Overview of Both Baseline and Current Study Variables

Table 2 globally provides for both RS and current study variables, averaging the studied variables values. A notable

difference was observed in energy intake means, which was more significant in the baseline study, and in the HOMA IR index, which increased almost half in the baseline study.

Hypertension Occurrence and Race

To test whether there was a difference between race group and hypertension occurrence, we used a χ^2 of independence. For this analysis, we first crossed the categorical race variable and the HTN occurrence variable, and secondly, we crossed the same variable by the hypertension occurrence. Table 3 presents Hypertension occurrence in all Race groups and normotensives and hypertensives. There was a significant Pearson Chi-square among all races ($p = 0.005$). There was also a meaningful significance of the Cramer’s V for all race groups 0.17 (0.005). Pearson’s Chi-squares was consistently significant when analyzing per hypertension occurrence, $p = 0.03$ and $p = 0.05$, respectively, in normotensives and hypertensives. Cramer’s V’s slightly increased, 0.19 (0.03) in non-hypertensives and 0.21 (0.05) in hypertensives. These analyses stipulate a dependence between hypertension and race, which is more likely to increase depending on different factors.

Hypertension Correlation with Serum Calcium Level, HOMA-IR, and Mc Auley in All Races Groups

A Pearson product-moment correlation was conducted to examine the relationship between SC levels, HOMA-IR,

Table 3 Correlation Between Hypertension Incidence and Race

All Races N= 412		
Pearson’s χ^2	12.9 (0.005)	
Cramer’s V	0.17 (0.005)	
Nonhypertensive and Hypertensives		
	Normotensives N = 238	Hypertensives N = 174
Pearson’s χ^2	8.45 (0.03)	7.8 (0.05)
Cramer’s V	0.19 (0.03)	0.21 (0.05)

Table 4 HTN, Serum Calcium, Mc Auley, and HOMA-IR in the Study Population

	Serum Calcium N= 373	HOMA-IR N= 355	Mc Auley N= 355
Pearson correlation	0.15	0.18	-0.24
Standard Deviation	0.086	3.41	0.33
N	368	350	350
P-value	0.003	0.001	<0.00001

Mc Auley index, and systolic blood pressure, in the con-founded four race group population. McA was negatively correlated with systolic blood pressure, $r(355) = -0.24$, $p < 0.0001$. On the other hand, the HOMA-IR index was more significantly positively related to systolic blood pressure, $r(355) = 0.18$, $p = 0.001$ than the SC. Table 4 presents the correlations, and Figure 1 presents the scatter-plot of SC and HTN. These findings indicated that Mc Auley explains much more of the variability in systolic HTN than does both SC and HOMA-IR.

Hypertension Occurrence Likelihood in Races

We analysed the occurrence of hypertension in each race group by performing a logistic regression between races and Hypertension occurrence. We used MA as a reference group for this analysis. Table 5 shows the results of our analysis. We found in our population a significant OR = 2.68, 95% CI = [0.45–1.02] in NHB. These results infer that NHB, compared to MA, OH, and NHW, was more

likely to have hypertension. The least risk was found in NHW, OR = 0.9, 95% CI = [0.43–1.02].

Hypertension Occurrence, Serum Calcium, and Insulin Resistance Within Race Groups

A standard multiple regression was conducted on split race groups in the baseline study population, to assess the ability of SC level and both HOMA-IR and McA index to predict hypertension occurrence thru Systolic Blood Pressure. Table 6 presents the analysis results. The results suggested that hypertension prediction had a strong significance in NHW compared to other groups. Moreover, within the NHW, McA prediction of hypertension was more significant with the regression equation found ($F(0.45) = 12.96$, $p < 0.00001$) for adjustment 1 (age and gender adjustment), and R^2 of 56.3 ($p < 0.001$) in the adjustment 2 (multivariate adjustment). NHW mean systolic blood pressure varies for each unit of McA.

Table 7 shows HOMA-IR, McA, and SC analysis of hypertension in our present study population. We

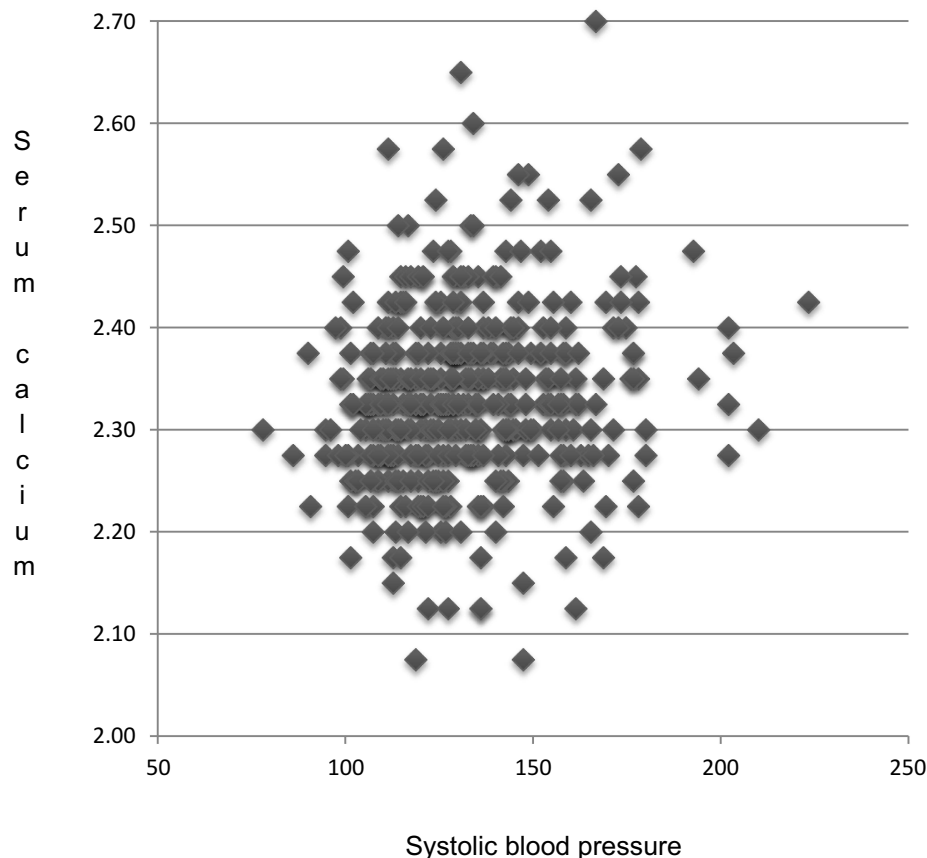


Figure 1 Serum calcium and systolic blood pressure correlation.

Table 5 Hypertension Likelihood Within Race Groups

	Mexican-Americans	Other Hispanics	Non-Hispanic Whites	Non-Hispanic Blacks
Mean (SD)				
OR (95% CI)	1	1.29 (0.71–2.32)	0.9 (0.43–1.02)	2.68 (0.45–1.02)

Table 6 Hypertension Occurrence, Serum Calcium, and Insulin Resistance Within Race Groups

	Mexican-Americans	Other Hispanics	Non-Hispanic Whites	Non-Hispanic Blacks
Serum Calcium				
Adjustment 1 p-value (R ²)	δ	0.006* (24.4)	0.001** (10.1)	< 0.03* (7.5)
Adjustment 2 p-value (R ²)	< 0.001** (61.6)	< 0.001** (69.4)	< 0.001** (57.2)	< 0.001** (57.8)
HOMA-IR				
Adjustment 1	< 0.001** (33.2)	< 0.0001*** (31.9)	< 0.0001*** (16.5)	< 0.001** (10.8)
Adjustment 2	< 0.001** (62.5)	< 0.001** (67.7)	< 0.001** (55.7)	< 0.001** (54.6)
Mc Auley				
Adjustment 1	0.004 (25.7)	0.007** (24.5)	< 0.00001*** (20.7)	δ
Adjustment 2	< 0.001** (61.7)	< 0.001** (65.1)	< 0.001** (56.3)	< 0.001** (50.4)

Notes: ***Less than 0.0001 Significant correlation. **Less than 0.01 Significant correlation. *Less than 0.05 Significant correlation. δ Nonsignificant P-value. Adjustment 1, adjustment for Age and Gender. Adjustment 2, adjustment for Age, Gender, BMI, Smoking status, Drinking status, Glycohemoglobin percentages, Total cholesterol.

evaluated the HTN risk in the lowest and highest ranges of SC, Mc Auley index, and HOMA-IR. Risk of cross-tabs and logistic regressions was performed on the quartiles and 4 cut-off points. The following results showed the quartile analysis, with the first quartiles as reference. As outcome, OR in highest quartiles of HOMA-IR, OR = 0.54, 95% CI = [0.36–0.8] and McA, OR = 1.23, 95% CI = [0.78–2.80], increased significantly when adjusted with age and gender, OR = 0.55, 95% CI = [0.34–0.8] and OR = 1.25, 95% CI = [0.62–0.47], respectively. These results infer that 1 unit increase of HOMA or McA in people with the highest values of HOMA could tend to an increase in hypertension compared to those with low values of HOMA and McA.

Analyzing Insulin Resistance on to SC - HTN: Mediation and Moderation Effects

We analyzed insulin resistance mediations in each race group thru linear regression, to find out the effects of HOMA-IR and Mc Auley index on SC to hypertension. As results of this model 4 mediation model analysis, there was no significant mediation occurring within SC and

HTN in all race groups, with HOMA as mediator. Thus, the group that responded to a significant mediation of insulin resistance mediation on to hypertension occurrence was that of non-Hispanic Whites. SC direct effects path c coefficient $coef_{DE} = 63.1 (0.002)$ and path c' $coef_{DE} = 49.83 (0.01)$ stayed significant in the presence of the mediator. There was also a significant total indirect effect $Coef_{IE} = 13.25 (21\% \text{ mediation})$ of Mc Auley in that was found to be greatly significant (Figure 2). These results suggested a partial mediation of the Mc Auley index occurring in the SC direct effect on hypertension (CI), 1.42–32.13. These results meant that the serum calcium effect on hypertension could reduce of 21% in the presence of Mc Auley-IR. The significance mentioned above appeared to be unchanged when the model was adjusted for gender, age, current smoking, current drinking, regular exercise, caloric intake.

Moreover, hypertension variations under SC and McA moderation effect are shown in a scatterplot (Figure 3). The scatterplot outcomes show a continuous increase in R² linear with the Mc Auley value variations from low to high.

Table 7 Hypertension Incidence Risk Analysis by IR and SC Quartiles Within the CS Population

	Fst Quartile	Sec. Quartile	Trd Quartile	Fth Quartile 4
HOMA-IR				
Total Number of cases (a)	416			
Mean (SD)	2.33			
Unadjusted OR (95%, CI)	1.00	2.97 (0.33–26.8)	0.36 (0.06 –1.99)	0.54 (0.36–0.8)
Adjustment with Age and Gender OR (95%, CI)	1.00	0.29 (0.03–2.95)	0.77 (0.13–4.49)	0.55 (0.34–0.8)
Mc_Auley				
Total Number of cases	416			
Mean (SD)	3.29			
Unadjusted OR (95% CI)	1.00	2.46 (0.79–7.7)	1.48 (0.29 –5.2)	1.23 (0.78–2.80)
Adjustment with Age and Gender OR (95%, CI)	1.00	2.91 (0.879–8)	0.86 (0.18–4.04)	1.25 (0.62–2.47)
Serum Calcium				
Number of cases	416			
Means	1.97			
Unadjusted OR (95% CI)	1.00	1.3 (0.82–2.05)	1.05 (0.67–1.68)	0.74 (0.47–1.18)
Adjustment with Age and Gender OR (95%, CI)		1.48 (0.91–2.41)	0.9 (0.55–1.49)	0.89 (0.54 –1.46)

Abbreviation: OR, odd ratio.

The model 1 moderation was performed to find out any moderation effect of IR on SC to Hypertension in each race group. The below [Table 8](#) presents the analysis results. We calculated the interaction coefficients after multiplying standardized McA index and SC (Z-transformation) and crossing the moderator variable with systolic blood pressure values. The analysis sorted out that there was a non-significant moderation effect of HOMA-IR on to the SC concentrations-HTN occurrence in all race groups. However, the same targeted effect was significant with the McA as a moderator in OH group (Interaction (0.04) = 0.027) and in NHW group (Interaction (0.001) = 0.28). [Table 8](#) displays the analysis coefficient and P-values. [Table 9](#) states both baseline study and current study outcomes

Discussion

The present study's results were in agreement with our hypothesis in some ways but also revealed interesting outcomes that are going to be discussed in subsequent paragraphs.

Race and Hypertension

Our analysis was conducted on Americans national civilians, in which results were appended to a previous study on a native Chinese population. Race and ethnicity related to disease, and precisely with hypertension is now an evidence.^{22,23} In the present study population, incident hypertension rate was higher in NHB than in other groups; Lackland showed same evidence concerning incident hypertension among Whites and Blacks in the National Health and Nutrition Examination Survey (NHANES) from 1988–1994 period to 2009–2010.²⁴ Similarly, Holmes et al²⁵ and Laidley et al²⁶ found a significant association between blacks or darker skin tone and self-reported hypertension. Disparities among racial groups in national Americans are becoming indubitable evidence thru studies. The dependence between race and hypertension incidence found in this study is also not far from the evidence from Ford²⁷ who underlined race as one of the predisposing factor for cardiovascular diseases among adult Americans high blood pressure. Also, Berenson et al²⁸ in the Bogalusa

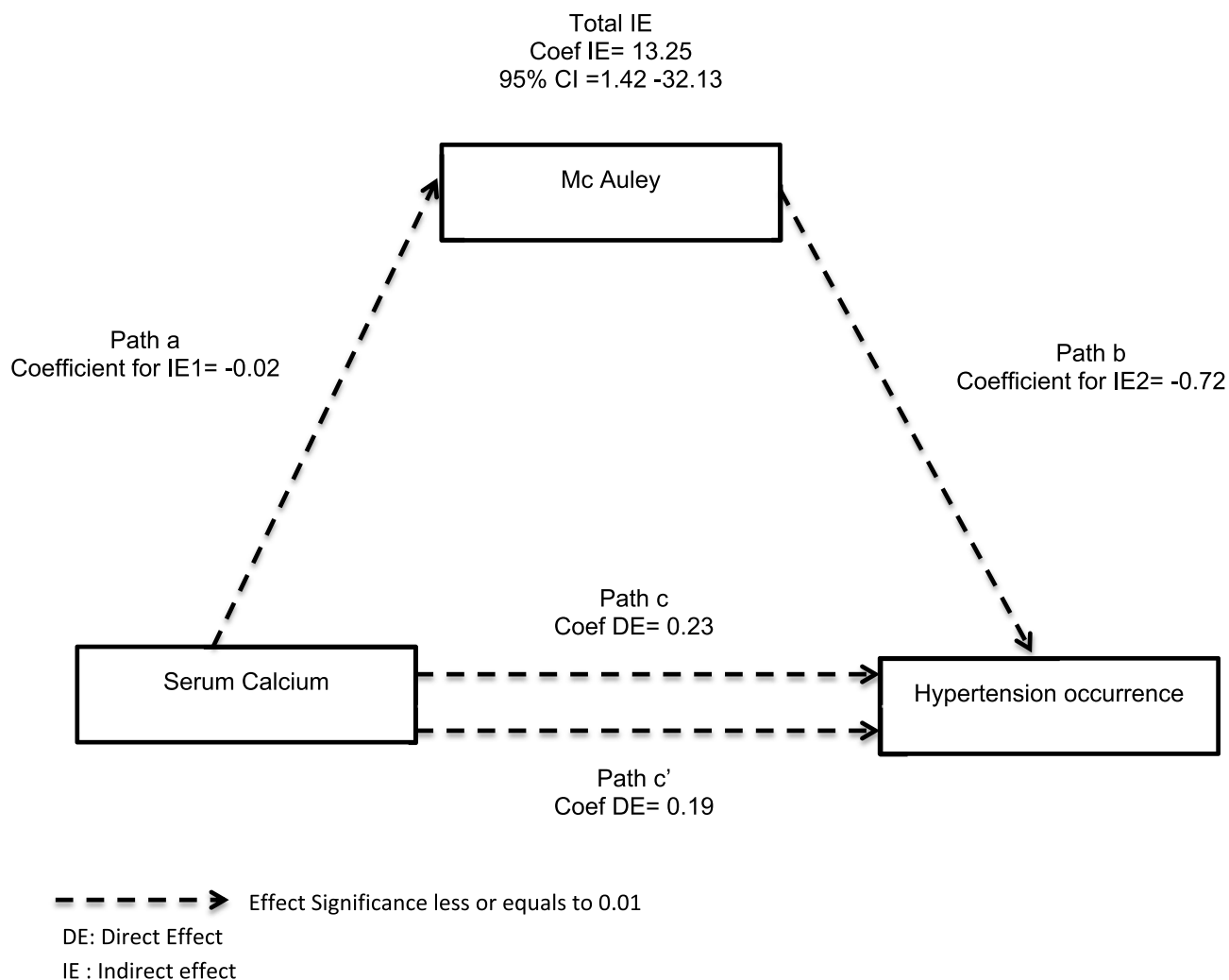


Figure 2 Mc Auley mediation effect occurring in non-Hispanic Whites.

study found a significant racial disparity among adults, after induced hypertension during their youth period. The racial factor is not clearly elucidated, but Klimentidis et al²⁹ evoked genetic and ancestral factors as being associated with blood pressure differences among racial and ethnic.

Serum Calcium Associated with Insulin Resistance and Hypertension Incidence

SC undergoes various physiological functioning.³⁰ One of a probably resultant of the SC physiological functions was assessed in our study and appeared to be associated with hypertension incidence and also with IR. We found in our study an association between SC and IR, similarly as Hagström et al,³¹ whose study suggested an association between SC and IR in older adults. This association in the present study was the same in the reference study, where a

significant association was found between increasing SC and HTN incidence. The association was persistent when adjusted by gender and age, stipulating a significant direct effect of serum calcium on HTN. Di et al³² obtained similar results in their study inferring that high serum calcium was associated with hypertension risk in a Chinese population and by Behradmanesh et al³³ in patients living with type 2 diabetes; on the other hand, Prada et al³⁴ found an increased blood pressure in ewes with low serum calcium level after a low dietary calcium intake. However, there were some differences in the above-cited association after adjustments in the baseline study. Adjustment with Race and increased OR in SC increased the CI as well, while the OR became refined in McA and HOMA-IR index. We suggest again that, this discrepancy might be due to the racial factor, in which has been involved several times in the disparities in the incidence of diseases observed among population groups.

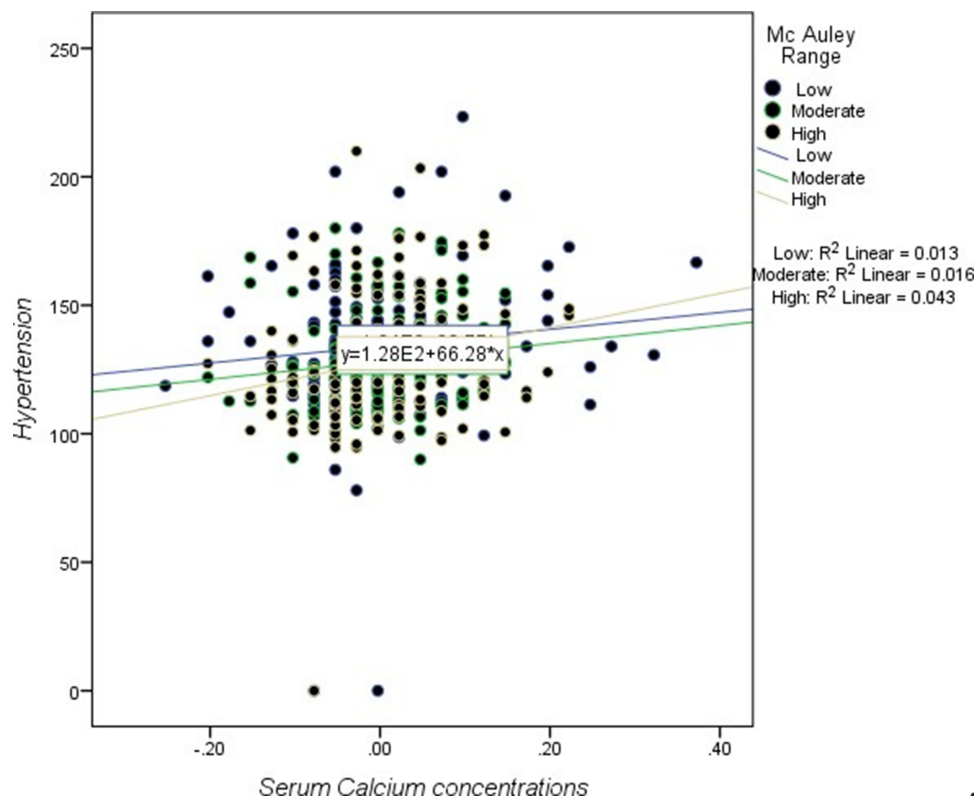


Figure 3 McA moderation in the SC effect on hypertension in all race groups.

Disparities in the Association Between SC, Insulin Resistance and Hypertension

Insulin resistance inducing chronic diseases and its expression could vary depending on the environment in which each person is involved.³⁵ While SC was associated with HTN in all groups of the present study, IR was not. The results of our study revealed a significant correlation

between HOMA-IR and McA in all races, but these results remained significant after multivariate adjustment only in NHW ($p < 0.0001$ and $p = 0.03$), respectively, before and after adjustments. McA was negatively correlated with hypertension in all race groups, suggesting that McA effects reduce hypertension risk. However, this correlation persisted only in the NHW group after adjustment. Lu

Table 8 IR Moderation Analysis per Race Group

	Mexican Americans	Other Hispanics	Non-Hispanic Whites	Non-Hispanic Blacks
Adjusted with covariates and confounders				
Hypertension Interaction with Serum Calcium and McA				
Interaction (<i>I</i>)	δ	0.27	0.28	δ
P-value		0.04	0.001	
Hypertension Interaction with Serum Calcium and HOMA-IR				
Interaction	δ			
P-value				

Note: Confounders: age, gender, BMI, alcohol drinking status, smoking status, exercise and fitness status, glycohemoglobin.
Abbreviations: δ, non-significant moderation.

Table 9 Results Summary of the Baseline Study and Current Study Outcomes

Results	Baseline Study	Current Study
Correlations with the incidence of hypertension	/	Significant correlation between Race and hypertension incident
SC/IR and Hypertension	Significant incident hypertension increasing the trend in SC and HOMA-IR (P-trend<0.0001 and P-trend < 0.0001p-, respectively) SC associated with HOMA-IR and Gutt index in hypertension incidence interactions = 0.0290.009 and respectively	Higher HTN occurrence risk in NHB compared to other Race groups 2.68 (0.45–1.02) Significant Hypertension risk found in High levels of HOMA-IR and McA, OR =0.55 (0.34–0.8) and 1.25 (0.42–2.67) respectively.
IR indirect effects hypertension	Significant mediation effect of Gutt index as a mediator of SC to HTN	No mediation effect of HOMA in all race groups Significant mediation of Mc Auley index in Whites CI[1.42–32.13] Significant moderation effect of Mc Auley in other Hispanics (0.27, p = 0.001p =) and in non-Hispanic Whites (0.28, 0.0008)
Temporal relation between SC and HT	SC preceding HTN	McA moderation effect suggests that IR could precede the effect of SC to HTN

et al³⁶ observed similar results in African Americans and Whites, while Saad et al³⁷ found opposite results, no correlation of IR or SC with hypertension in three ethnic groups, Lu et al found out that Whites experienced higher mortality associated with high SC levels compared to African Americans. In this study, the race factor was highly associated with hypertension compared to other cardiovascular and cerebrovascular events such as strokes.

IR Mediation and Moderation on Serum Calcium to Hypertension

Insulin resistance has an early action on the installation of diabetes and also cardiovascular disease.³⁸ In the present study, hypertension McA-IR played a mediator role in the effect of SC on HTN in NHW and a moderator role in OH and NHW. Similarly, the baseline study mediator on the effect of SC on HTN was found to be Gutt index but not as HOMA-IR. In this part of our study, we underlined once again a disparity in the results within race groups. McA mediation effect in our population, combined with its moderator effect and its negative correlation with hypertension suggests that this component contributed to lower down the effect of serum calcium on HTN (SC-HTN direct effect in and out of mediation equal to 0.23 and 0.19 respectively, 95% CI = [1.42–32.13]). Except in the baseline study where a mediation effect of the insulin

resistance on hypertension incidence was assessed and suggested, we did not found background underlying a mediation or a moderation effect of insulin resistance mediation or moderation effect on the hypertension risk.

Insulin Resistance Indexes and Hypertension

In the baseline study, HOMA-IR was not a mediator, while Gutt index was a mediator while in the present study, HOMA-IR was not a mediator, while Mc Auley was a mediator only in NHW, and Mc Auley was a moderator in OH and NHW. Kunicki et al³⁹ similarly in a study where measuring IR in women with premature ovarian sufficiency using different indexes found different results with different indexes of IR. This highlights the validity of the insulin resistance index measures, which might explain the differences in our results. The difference in the computed variables for these index calculations might also explain our results. HOMA-IR is calculated by using patients fasting insulin and fasting glucose, while Mc Auley index is calculated by using fasting triglyceride and fasting insulin.

Strength and Limitation

Our study has the advantage of having explored a newly suggested risk factor of hypertension. Moreover, this study

was made on a different population in terms of race and socio-demographic location, compared to that of the baseline study. Also, we took into account a higher number of confounders, including the lipid profile of patients. However, our study also has limitations. The size of the sample, although significant for our type of analysis, was much smaller than that of the reference study. Indeed, a similar sample size would have been more accurate in the comparison. Moreover, our study did not provide an explanation of the effect of insulin on the existence or absence of hypertension in participants, neither an explanation of the racial factor. However, it was noted that our goal was not to demonstrate the action of the mechanism of serum calcium or insulin resistance, but rather to compare the association of the above-cited factors with the risk of hypertension, in a population with different racial characteristics.

In conclusion, there was an ethnic disparity in the risk factors and hypertension occurrence. There were several differences in insulin resistance expression on the effect of serum calcium on hypertension. The relation between hypertension occurrence and the racial factor was found to be more accurate in some race groups than in others as well as the risk factors. Although serum calcium had an effect on hypertension in all race groups, the expressions were higher in non-Hispanic Whites. McA-IR was a mediator between SC and in non-Hispanic Whites, while it was stated as a moderator on SC-HTN in other Hispanics. Mc Auley, as well as HOMA-IR, had no mediation or moderator effect in Mexican-Americans and in non-Hispanic Blacks. HOMA-IR also had no mediation effect on NHW and OH. These may relate to a proper racial or ethnic effect. Insulin resistance effects were found to be different on the same targets in both baseline study and present study. These conclusions suggest the need for further researches to take into account geolocalisation and proper racial factors to explain more the reasons for these observed disparities. Also, a temporal association of IR and Hypertension risk could be assessed by using several insulin resistance indexes in the same population, to explain more the differences observed in the IR outcomes on same target effects in the same population.

Data Sharing Statement

The current study results were based on quantitative data, which are available under the DOI: 10.21227/50x7-xh53. However, these data will be available to other researches upon request.

Equations

Equations 1 and 2 detailed in the [Supplementary file](#).

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Disclosure

The authors declare that they have no conflict of interest in this study.

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