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UNLOCKING THE LINK: ELECTROLYTES, LIPID PEROXIDATION, INFLAMMATORY MARKERS, METABOLITES, DEMOGRAPHIC FACTORS, AND HEAVY METALS, IN HYPERTENSION-RELATED CORONARY ARTERY DISEASE

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Abstract

Background: Hypertension (HTN) is a major cause of cardiovascular illnesses like as atherosclerosis and coronary artery disease (CAD), which is among top ten diseases causing death especially in KSA. This study examines the complex relationship between inflammatory indicators, heavy metals, electrolytes, lipid profiles, oxidized low-density lipoprotein (ox-LDL), Malondialdehyde (MDA), and cardiovascular risk in individuals with hypertension.

Method: A total of ninety Saudi patients, ranging in age from 20 to 70, were included in this study. They were asked to complete questionnaires that gathered detailed information on their disease status, lifestyle variables, age, sex, and medication. After a period of fasting for 12 hours, blood samples were taken from the veins to analyze the levels of lipids, heavy metals, malondialdehyde, uric acid, vitamin D, and electrolytes. The participants were classified into three groups: negative control (NTC), hypertensive patients (HTN), and cardiac patients (HTN + CAD). The study received ethical approval from the Ethics Committee of King Abdulaziz University, and all participants provided signed informed permission.

Results: The analysis showed interesting connections, where high-density lipoprotein (HDL) levels were found to have a positive correlation with cholesterol levels. Additionally, patients with coronary artery disease (CAD) had lower levels of HDL. Hypertensive (HTN) patients exhibited higher levels of sodium, potassium, calcium, and vitamin D3 in comparison to the control group. However, there were no significant changes observed between the HTN group and the HTN + CAD (coronary artery disease) group. While the levels of C-reactive protein (CRP) increased in both groups, there were no significant differences observed between them. Both blood pressure and cholesterol levels increased, although there were no significant differences between the groups.

Conclusion: This investigation reveals significant associations between several biomarkers and the interaction of hypertension and CAD risk. While providing information on these connections, additional research is necessary to clarify the underlying mechanisms, which could potentially transform the way these common diseases are diagnosed and treated. This study aims to enhance our comprehension of the intricate pathophysiology, with the goal of facilitating targeted therapies and enhancing patient outcomes in the field of cardiovascular health.

Keywords: Hypertension, Coronary artery disease, Lipid profile, inflammatory markers, Malonaldehyde, CRP, Electrolytes, Heavy metals.

Introduction

One of the most significant topics of inquiry and concern in the field of cardiovascular health is the intricate relationship that exists between CAD and hypertension (1). In a large national study conducted in 2014, it was found that 15.2 to 25.5% of Saudi adults had high blood pressure (2). In light of the fact that high blood pressure affects a lot of people around the world, it is very important to fully understand how it raises the chance of CAD (3). New cardiovascular research has shown how important biochemical markers are for figuring out how CAD will progress (4). People used to think that high blood pressure and other common risk factors were the most important ones, but these changes go beyond those (5). A long time ago, heavy metal intake was mostly seen as a problem related to work-related risks (1). However, it is now generally accepted that it may also play a role in heart disease (6). Some heavy metals, like lead, cadmium, and mercury, can damage endothelial function, cause inflammation, and cause oxidative stress (7). All these factors are important in the pathogenesis of CAD (8).

Antioxidants, which are known to protect against oxidative stress, play a big role in how CAD and high blood pressure affect each other (9). People with high blood pressure usually have less antioxidant power, which leaves them open to oxidative damage and, as a result, changes in how well endothelium cells work (10). It is important to look into the current state of antioxidants in people with high blood pressure in order to learn more about possible treatments for lowering the chance of CAD (11).

A receptor for 1,25-dihydroxyvitamin D has been identified in smooth muscle tissue, indicating that Vitamin D may have a role in regulating smooth muscle contraction and blood pressure(12) . Observational studies on the dietary intake of Vitamin D revealed that both the measured 25(OH)D and estimated 25(OH)D were shown to have a negative correlation with the risk of developing hypertension in both males and females (13). This conclusion is backed by a recent study published in NHANES III, which discovered a negative correlation between serum 25(OH)D levels and both systolic blood pressure and pulse pressure (14). There are multiple pathways that potentially account for the preventative benefits of Vitamin D on hypertension (15). Asymptomatic hyperuricemia without comorbidities is a predictive factor for the development of hypertension as been found in a longitudinal cohort study. Furthermore, hyperuricemia also plays a role in the progression of hypertension from prehypertension (16).

Researchers have extensively studied inflammatory biomarkers, with greater evidence supporting the role of C-reactive protein (CRP) in CAD (17). Epidemiological findings using high sensitivity (hs)

assays indicate a correlation between hs-CRP and the likelihood of future cardiovascular morbidity and mortality in individuals at high risk or with confirmed CAD (18)

LDL particles that have been oxidized are being studied as a metabolic marker and CAD, which is one of the most common heart diseases (19). Atherosclerosis is characterized by high levels of oxidized LDL in people who have high blood pressure (20). This makes it even worse for CAD to get worse (21). Controlling oxidized LDL in people with high blood pressure by making changes to their lifestyle or taking drugs may lower their chance of CAD (22).

Oxidative and antioxidative parameters are significant factors in the pathogenesis of atherosclerosis and CAD caused by atherosclerosis. MDA is a crucial indicator of lipid peroxidation. The development of CAD is associated with a rise in oxidative stress, which is directly correlated with elevated levels of malondialdehyde MDA (23).

CAD is a big health problem around the world that is affected by age, gender, race (24). Being older is a big risk factor because it makes CAD more likely and raises the risk of problems like myocardial infarction and heart failure (25). The onset of CAD is different for men and women. Men get CAD earlier in life than women do (26). Epidemiological studies have shown physical inactivity as a significant risk factor for the development of CAD (26).

The connection between high blood pressure, metabolic factors, and CAD is a major area of study and care in both research and clinical settings (6). Because cardiovascular diseases, like CAD, are the top cause of death in the world, it is very important to understand their complicated causes (6, 27). High blood pressure, which is a very common risk factor for CAD, is a big reason why people are taking steps to avoid getting cardiovascular disease and lower the number of people who get sick and die from it (28). This study aims to find correlation between these markers, demographic factors and cardiovascular disease in hypertensive patients.

Method

Study design

A cross-sectional study was conducted on 90 Saudi patients who answered questionnaires covering previous and current disease status, lifestyle factors, age, sex, and medication were completed by the participants at the time of sample collection. An age- and sex-matched strategy were not considered in the selection criteria. All participants fastened for 12 hours, after that a venous blood samples (5ml) were collected from all participants. The serum was obtained by centrifuging the blood samples at 3000 rpm for 5 min. The following tests were performed, Lipid profile including cholesterol, triglyceride, HDL-Cholesterol, LDL-Cholesterol. Serum heavy metals including Cadmium (Cd), Cobalt (Co), Chromium (Cr), Cupper (Cu), and Lead (Pb). In addition; Malondialdehyde (MDA) was measured using thiobarbituric acid reactive substance (TBARS). ESR, Vitamin D, Serum Calcium level, and uric acid were performed for all patients.

Participants

The study included 90 participants with ages ranging from 20-70 years, who were categorized into three groups (n= 30) as follows: the negative control (NTC), the hypertensive patients (HTN), and the cardiac patients (HTN + CAD). HTN is diagnosed when blood pressures >140/90 mmHg, according to The World Health Organization.

Ethical approval

The study was performed on Saudi participants, and written informed consent was obtained from all participants. The study protocol has been approved by the Ethics Committee of the King Abdulaziz University (Ref. No. 356-14).

Statistical analysis

The study used SPSS version 25 to analyze qualitative and continuous quantitative data. Qualitative data was expressed as frequency and percentage, while continuous quantitative data was expressed as

mean ± standard deviation. The mean represents the central value of a discrete set of numbers, while standard deviation measures the dispersion of a set of values. A low standard deviation indicates values are close to the mean, while a high standard deviation indicates values are spread out over a wider range. A P-value of <0.05 was considered significant, 0.001 highly significant, and >0.05 insignificant. Tests used included Chi-square test for qualitative data comparison, Independent sample T test for continuous quantitative data comparison, logistic regression analysis for binary outcomes, and Pearson's correlation coefficient test for data correlation.

Results

The study found a significant increase in the mean age of patients with heart disease (HTN) (48 **± 7.6)** compared to the control group (34 ± 7.2), with a higher increase in HTN with CAD patients (54 ± 6). However, no significant differences were found between hypertensive groups. Smoking was also higher in the HTN group (13 patients, 43.3%) and the HTN with CAD group (11 patients, 36.7%). No significant differences were found between the hypertensive groups.

Residence was not significantly different between the groups. There was no significant difference in education level between hypertensive groups. However, there was a significant difference in the number of non-educated patients (26.7%), intermediate and secondary educated patients (26.7%), and university educated patients (26.7%) compared to the control group (3.3%).

In terms of income, there were no significant differences between the groups. Physical activity varied among the groups. In the control group, 20 patients (20%) had low physical activity, 19 patients (63.3%) had medium activity, and 5 patients (16.7%) had high physical activity. In the HTN group, 86.7% had low physical activity, 4 patients had medium activity, and 18 patients (60%) had low physical activity.

Table 1: comparison of all studied groups as regard demographic data

Demographic Data		Groups						P-Value
		Control (N=30)		HTN (N=30)		HTN & CAD (N=30)		
Age	(M±SD)	34 ± 7.2		48 ± **7.6**		54 ± **6**		P1< 0.001** P2< 0.001** P3= 0.03*
Gender	Male	15	50%	15	50%	15	50%	P1= 1 P2= 1 P3= 1
	Female	15	50%	15	50%	15	50%	
Smoking		0	0%	13	43.3%	11	36.7%	P1< 0.001** P1< 0.001** P3= 0.6
Residence	Rural	13	43.3%	8	26.7%	12	40%	P1= 0.18 P2= 0.8 P3= 0.27
	Urban	17	56.7%	22	73.3%	18	60%	
Education level	None	1	3.3%	4	13.3%	8	26.7%	P1= 0.3 P2= 0.01 * P3= 0.2
	Intermediate	4	13.3%	4	13.3%	8	26.7%	
	Secondary	9	30%	12	40%	8	26.7%	
	University	16	53.3%	10	33.3%	6	20%	
Income	Low	5	16.7%	8	26.7%	11	36.7%	P1= 0.4 P2= 0.16 P3= 0.7
	Medium	22	73.3%	17	56.7%	15	50%	
	High	3	10%	5	16.7%	4	13.3%	
Physical Activity	Low	6	20%	26	86.7%	18	60%	P1< 0.001** P2= 0.002* P3= 0.06
	Medium	19	63.3%	4	13.3%	12	40%	
	High	5	16.7%	0	0%	0	0%	

***: P-value< 0.05 is considered significant.**
M: mean, SD: standard deviation
****: P-value< 0.001 is considered highly significant**
P1= Statistical difference between (HTN Vs control) groups.
P2= Statistical difference between (HTN & CAD Vs control) groups.
P3= Statistical difference between (HTN Vs HTN & CAD) groups.

The study found that patients in the HTN group had significantly higher cholesterol levels (210 ± 42.5) and a higher cholesterol level (190 ± 36.4) compared to the control group (160 ± 28.9). There was no significant difference between the HTN and HTN with CAD groups. The HTN group had significantly higher levels of TGs (186 ± 81.5) and a higher level of TGs (153 ± 42.8) compared to the control group (125 ± 27.7). The HTN group had significantly lower levels of high-density lipoprotein (HDL) and low-density lipoprotein (LDL) compared to the control group (92 ± 30.6) And higher level of low-density lipoprotein (LDL) (136+40.9) compared to the control group (43+-5) & (92 ± 30.6) respectively (Table 2)

Table 2: comparison of all studied groups as regard Lipid profile

Lipids Profile	Groups			P-Value
	Control (N=30)	HTN (N=30)	HTN & CAD (N=30)	
Cholesterol	160±28.9	210±42.5	190±36.4	P1< 0.001** P2= 0.01* P3= 0.056
TGs	125±27.7	186±81.5	153±42.8	P1< 0.001** P2= 0.003* P3= 0.055
HDL	43±5	37±6.3	40±5.7	P1< 0.001** P2= 0.35 P3= 0.08
LDL	92±30.6	136±40.9	120±39.1	P1< 0.001** P2= 0.003* P3=0.12

***: P-value< 0.05 is considered significant.**
M: mean, SD: standard deviation
****: P-value< 0.001 is considered highly significant**
P1= Statistical difference between (HTN Vs control) groups.
P2= Statistical difference between (HTN & CAD Vs control) groups.
P3= Statistical difference between (HTN Vs HTN & CAD) groups.

The study found that patients with (HTN) had significantly higher levels of sodium (Na) compared to the control group (139 ± 3.5), potassium (K) compared to the control group (3.8 ± 0.3). However, there was no significant difference (P= 0.8) between HTN and HTN with CAD groups. In terms of calcium, there was a significant increase (P= 0.02) in HTN patients compared to the control group (9.4 ± 0.3), but no significant difference (P= 0.08) between HTN with CAD and control groups. In terms of vitamin D3, there was no significant difference (P= 0.07) between HTN and control groups, however, there was a significant decrease (P< 0.001) in HTN patients with CAD group (30 ± 16.6) compared to the control group (46 ± 15.3).In terms of CRP, there was a significant increase in HTN patients (8.3 ± 7) compared to the control group (4.5 ± 2.3), and a significant increase in HTN patients with CAD (13.6 ± 9.6) compared to the control group. In terms of ESR, there was no significant difference (P= 0.58) between HTN and control groups. However, there was a significant increase in HTN patients with CAD (41.6 ± 13.7) compared to the control group (7.3 ± 3.7). In terms of uric acid, there was a significant increase in HTN patients (6 ± 1.5) compared to the control group

(4.2 ± 1.4), but no significant difference (P= 0.1) between HTN with CAD and control groups. (Table 3).

Table 3: comparison of all studied groups as regard electrolytes and inflammatory markers.

	Groups			P-Value
	Control (N=30)	HTN (N=30)	HTN & CAD (N=30)	
Na	139±3.5	144±4	142±3.3	P1< 0.001** P2< 0.001** P3= 0.06
K	3.8±0.3	4.44±0.4	4.42±0.4	P1< 0.001** P2< 0.001** P3= 0.8
Ca	9.4±0.3	9.7±0.4	9.6±0.4	P1= 0.02* P2=0.08 P3= 0.48
Vit. D3	46±15.3	39±16.9	30±16.6	P1= 0.07 P2< 0.001** P3= 0.06
CRP	4.5±2.3	8.3±7	13.6±9.6	P1= 0.007* P2< 0.001** P3= 0.02*
ESR	7.3±3.7	7.9±4.2	41.6±13.7	P1= 0.58 P2< 0.001** P3< 0.001**
Uric Acid	4.2±1.4	6±1.5	4.9±1.8	P1< 0.001** P2= 0.1 P3= 0.01*

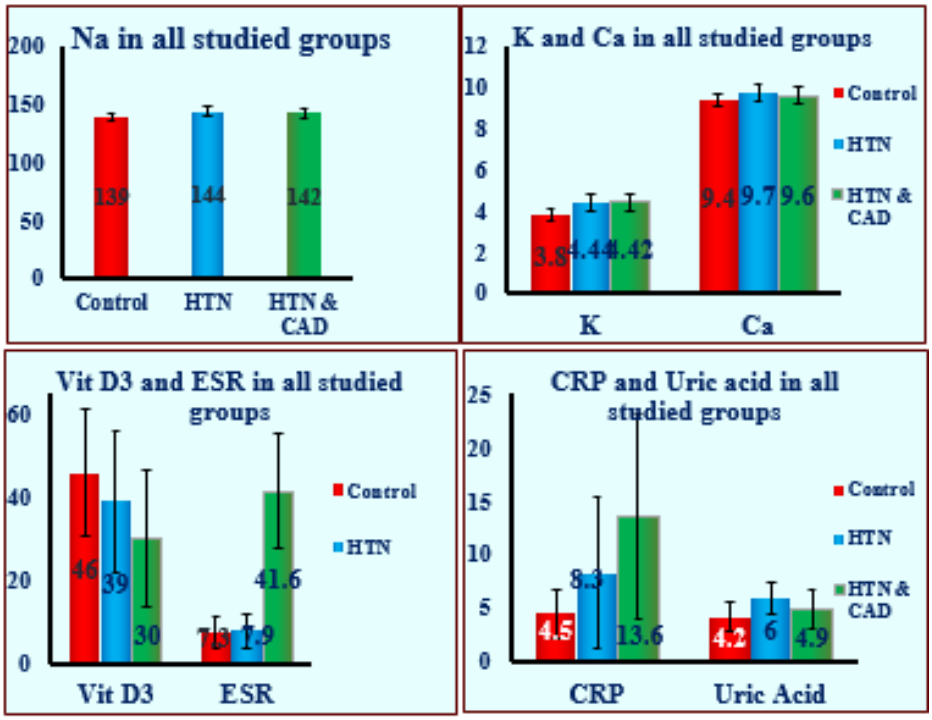

Figure 1: comparison of all studied groups as regard Na, K, Ca, Vit D3, ESR, CRP and Uric acid

Table 4: comparison of all studied groups as regard heavy metals.

Heavy metals	Groups			P-Value
	Control (N=30)	HTN (N=30)	HTN & CAD (N=30)	
Cd	0.0094±0.0021	0.0099±0.0031	0.0096±0.0002	P1= 0.42 P2= 0.58 P3= 0.55
Co	0.0281±0.0019	0.0304±0.0044	0.0307±0.0005	P1= 0.009* P2< 0.001** P3= 0.7
Cr	0.025±0.0018	0.0273±0.0042	0.0276±0.0004	P1= 0.008* P2< 0.001** P3= 0.7
Cu	0.0514±0.0037	0.055±0.0068	0.0557±0.0013	P1= 0.014* P2< 0.001** P3= 0.55
Pb	0.1491±0.0039	0.1606±0.016	0.1632±0.0026	P1< 0.001** P2< 0.001** P3= 0.4
Fe	0.0381±0.0033	0.0416±0.0062	0.043±0.0032	P1= 0.009* P2< 0.001** P3= 0.27
Ni	0.027±0.002	0.0295±0.0045	0.0299±0.0005	P1= 0.007* P2< 0.001** P3= 0.62
Zn	0.0116±0.0023	0.013±0.0035	0.0136±0.0026	P1= 0.077 P2= 0.002* P3= 0.41

***: P-value< 0.05 is considered significant.**
M: mean, SD: standard deviation
****: P-value< 0.001 is considered highly significant**
P1= Statistical difference between (HTN Vs control) groups.
P2= Statistical difference between (HTN & CAD Vs control) groups.
P3= Statistical difference between (HTN Vs HTN & CAD) groups.

The study found no statistically significant differences in Cd levels between the HTN and control groups, HTN with CAD, and control groups. However, there were significant increases in the levels of Co, Cr, Cu, Pb, Fe, Ni, Ni, Zn, and Zn in the HTN group compared to the control group. The HTN group showed a statistically significant increase in Co (0.0304±0.0044) compared to the control group. No significant difference was found between the HTN and HTN with CAD groups. In terms of Cr, there was a significant increase in HTN group (0.0273±0.0042) and a high increase in HTN with CAD group (0.0276±0.0004). No significant difference was found between HTN and HTN with CAD groups. In Cu, there was a significant increase in HTN group (0.055±0.0068) and a high increase in HTN with CAD group (0.0557±0.0013). In terms of Fe, there was a significant increase in HTN group (0.0416±0.0062) and a high increase in HTN with CAD group (0.043±0.0032). No significant difference was found between HTN and HTN with CAD groups. No significant difference was found between HTN and control groups.

Table 5: comparison of all studied groups as regard Oxidized LDL, MDA

	Groups			P-Value
	Control (N=30)	HTN (N=30)	HTN & CAD (N=30)	
MDA	0.58±0.15	0.88±0.44	0.65±0.77	P1= 0.001* P2< 0.001** P3= 0.17
Ox-LDL	1.02±0.97	1.66±0.39	1.67±0.5	P1= 0.001* P2= 0.36 P3= 0.94

***: P-value< 0.05 is considered significant.**
M: mean, SD: standard deviation
****: P-value< 0.001 is considered highly significant**
P1= Statistical difference between (HTN Vs control) groups.
P2= Statistical difference between (HTN & CAD Vs control) groups.
P3= Statistical difference between (HTN Vs HTN & CAD) groups.

The table shows a significant increase in Ox-LDL levels in patients with HTN compared to the control group. No significant difference was found between HTN with CAD and control groups. MDA levels also showed an increase in HTN patients, and a high increase in HTN with CAD patients Compared to control group No significant difference was found between HTN and HTN with CAD groups.

Table 6: Multivariate logistic regression analysis for demographic data, lipids profile and electrolytes as a predictive risk factor of CAD.

	B	SE	p-value	Odds	95% CI	
Age	0.174	0.04	**<0.001****	1.19	1.1	1.29
Gender	0	0.447	1	1.000	0.416	2.403
smoking	0.739	0.492	0.13	2.093	0.799	5.487
Residence	-0.214	0.461	0.64	0.808	0.327	1.992
Education Level (Intermediate)	-0.470	0.758	0.54	0.625	0.141	2.763
Education Level (secondary)	-1.435	0.705	**0.042***	0.238	0.060	0.949
Education Level (university)	-1.936	0.728	**0.008***	0.144	0.035	0.601
Income	-0.398	0.369	0.28	0.671	0.326	1.385
Physical activity	-0.435	0.392	0.27	0.647	0.300	1.396
Cholesterol	0.003	0.005	0.56	1.003	0.993	1.014
TGs	-0.001	0.004	0.87	0.999	0.992	1.007
HDL	-0.003	0.037	0.93	0.997	0.928	1.071
LDL	0.004	0.005	0.51	1.004	0.993	1.014
Na	0.043	0.054	0.43	1.044	0.938	1.161
K	1.274	0.499	**0.01***	3.574	1.345	9.500
Ca	0.288	0.565	0.61	1.333	0.441	4.032

B: Regression coefficient, SE: Standard error, CI: Confidence interval.
Using Multivariate logistic regression analysis, this table demonstrates that the following factors were predictive for CAD:

- Age (B= 0.174, SE= 0.04, P < 0.001, Odds= 1.19, CI= 1.1 – 1.29).
- Education Level (secondary) (B= -1.435, SE= 0.705, P= 0.042, Odds= 0.238, CI= 0.06 – 0.949).

- Education Level (university) (B= -1.936, SE= 0.728, P= 0.008, Odds= 0.144, CI= 0.035 – 0.601).
- K (B= 1.274, SE= 0.499, P= 0.01, Odds= 3.574, CI= 1.345 – 9.5).

Table 7: Multivariate logistic regression analysis for inflammatory markers, heavy metals, Ox LDL and MDA as a predictive risk factor of CAD.

	B	SE	p-value	Odds	95% CI	
VD3	-0.046	0.015	**0.002***	0.955	0.927	0.984
CRP	0.148	0.042	**<0.001****	1.16	1.068	1.259
ESR	0.526	0.193	**0.007***	1.693	1.159	2.473
Uric Acid	-0.07	0.130	0.597	0.934	0.724	1.204
Cd	-15	107.7	0.89	0	0	1.450
Co	185.2	92.6	**0.046***	2.58	40	1.670
Cr	203.2	101	**0.044***	1.7	174	1.670
Cu	114.4	51.7	**0.027***	4.68	442712	4.950
Pb	70	22.6	**0.002***	2.4	139596964203	4.120
Fe	150.8	55.8	**0.007***	3.1	929382814587732000	1.040
Ni	203.9	93.9	**0.03***	3.5	389318527	3.190
Zn	162.4	87.1	0.062	3.36	0	4.340
Ox LDL	0.67	0.36	0.063	1.95	0.965	3.941
MDA	-0.29	0.45	0.52	0.748	0.311	1.798

B: Regression coefficient, SE: Standard error, CI: Confidence interval.

Using Multivariate logistic regression analysis, this table demonstrates that the following factors were predictive for CAD:

- VD3 (B= -0.046, SE= 0.015, P= 0.002, Odds= 0.955, CI= 0.927 – 0.984).
- CRP (B= 0.148, SE= 0.042, P <0.001, Odds= 1.16, CI= 1.068 – 1.259).
- ESR (B= 0.526, SE= 0.193, P= 0.007, Odds= 1.693, CI= 1.159 – 2.473).
- Co (B= 185.2, SE= 92.6, P= 0.046, Odds= 2.58, CI= 40 – 1.67).
- Cr (B= 203.2, SE= 101, P= 0.044, Odds= 1.7, CI= 174 – 1.67).
- Cu (B= 114.4, SE= 51.7, P= 0.027, Odds= 4.68, CI= 442712 – 4.95).
- Pb (B= 70, SE= 22.6, P= 0.002, Odds= 2.4, CI= 139596964203 – 4.12).
- Fe (B= 150.8, SE= 55.8, P= 0.007, Odds= 3.1, CI= 929382814587732000 – 1.04).
- Ni (B= 203.9, SE= 93.9, P= 0.03, Odds= 3.5, CI= 389318527 – 3.19).

Table 8: comparison of smokers and non-smokers patients as regard heavy metals in HTN without CAD and HTN with CAD groups.

		Smokers M±SD	Non-smokers M±SD	P-Value
Co	**HTN**	0.0286±0.0027	0.0319±0.005	**0.043***
	HTN and CAD	0.03104±0.0003	0.03057±0.0004	**0.005***
Cr	**HTN**	0.0256±0.0025	0.0287±0.0049	**0.049***
	HTN and CAD	0.0279±0.000298	0.0275±0.00037	**0.013***
Cu	**HTN**	0.0517±0.0048	0.0574±0.0072	**0.021***
	HTN and CAD	0.056±0.001	0.0556±0.0013	0.415
Pb	**HTN**	0.1531±0.0136	0.1664±0.0155	**0.02***
	HTN and CAD	0.1647±0.002	0.1622±0.002	**0.009***
Ni	**HTN**	0.0276±0.0026	0.0309±0.0052	**0.047***
	HTN and CAD	0.0302±0.00056	0.02978±0.00047	**0.048***
Zn	**HTN**	0.0127±0.0026	0.0132±0.0042	0.71
	HTN and CAD	0.0129±0.001	0.0141±0.003	0.23

- ***: P-value< 0.05 is considered significant.**
- **M: mean, SD: standard deviation**
- ****: P-value< 0.001 is considered highly significant**

The findings indicate that smoking could impact the concentrations of specific heavy metals in individuals with hypertension. Smokers exhibit decreased levels of cobalt, chromium, copper, lead, and nickel in comparison to non-smokers, suggesting a possible impact of smoking on the metabolism or elimination of heavy metals. Nevertheless, the impact of smoking on zinc levels seems to be negligible in both the HTN and HTN with CAD groups. Additional investigation is necessary to clarify the processes that explain these connections and to examine the practical consequences of changed levels of heavy metals in individuals with hypertension, especially those who also have coronary artery disease.

Table 9: correlation study between MDA and heavy metals in HTN with CAD group.

Heavy metals in HTN with CAD group	MDA in HTN with CAD group	
	r	P-Value
Co	-0.508	**0.004***
Cr	-0.52	**0.003***
Cu	-0.387	**0.034***
Pb	-0.507	**0.004***
Ni	-0.255	0.173

***: P-value< 0.05 is considered significant.(r): Pearson correlation coefficient**

This table shows:

- **In patients of HTN with CAD group there were:**

- Statistically significant **(p-value = 0.004)** negative correlation **(r = -0.508)** between MDA and Co.
- Statistically significant **(p-value = 0.003)** negative correlation **(r = -0.52)** between MDA and Cr.
- Statistically significant **(p-value = 0.034)** negative correlation **(r = -0.387)** between MDA and Cu.
- Statistically significant **(p-value = 0.004)** negative correlation **(r = -0.507)** between MDA and Pb.
- No statistically significant **(p-value > 0.05)** correlation between MDA and Ni.

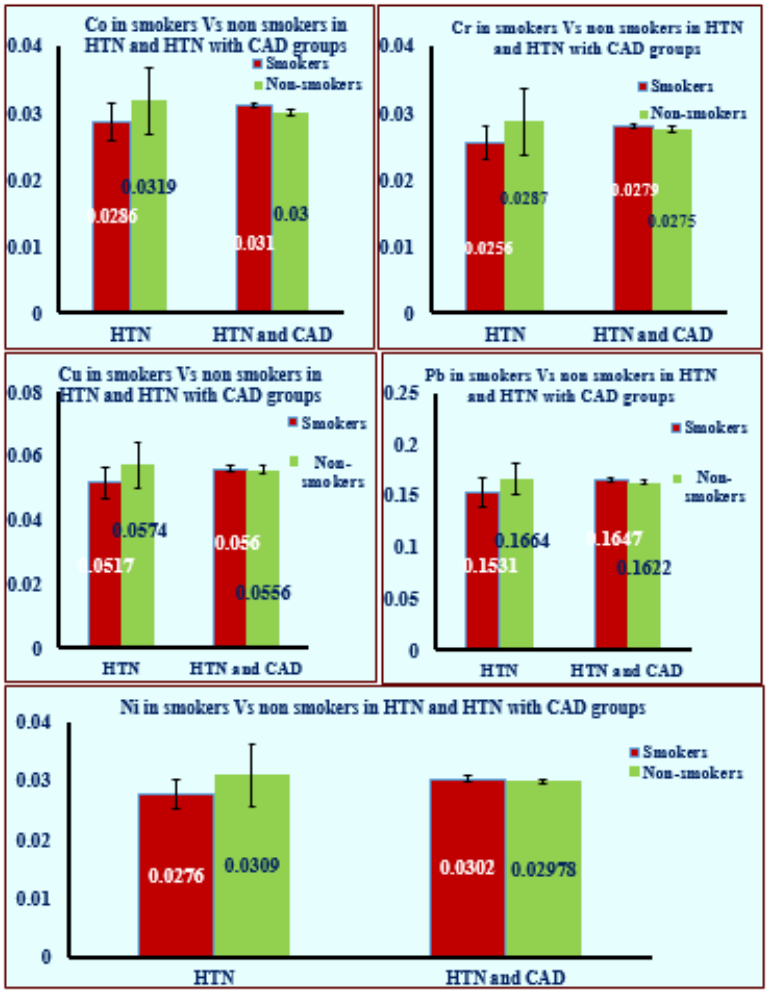

Figure 2: comparison of smokers and non-smokers as regard heavy metals in HTN and HTN with CAD groups.

Table 10: correlation study between CRP and heavy metals in HTN with CAD group and HTN group

Heavy metals in HTN group	**CRP in HTN group**	
	r	**P-Value**
Co	0.452	**0.012***
Cr	0.45	**0.013***
Cu	0.36	0.051
Pb	0.362	**0.049***
Ni	0.437	**0.016***
Heavy metals in HTN with CAD group	**CRP in HTN with CAD group**	
	r	**P-Value**
Co	-0.025	0.897
Cr	-0.081	0.672
Cu	-0.136	0.475
Pb	-0.034	0.858
Ni	-0.222	0.239

*P-value< 0.05 is considered significant. (r): Pearson correlation coefficient.

Heavy metals such as cobalt, chromium, lead, and nickel may cause inflammation in hypertensive patients who do not have coronary artery disease (CAD). This is supported by the fact that these metals have been found to have positive associations with levels of C-reactive protein (CRP).

Nevertheless, among individuals with hypertension and coronary artery disease (CAD), this correlation seems to be non-existent, indicating that causes unrelated to heavy metals may be responsible for the inflammation observed in this group.Additional research is required to clarify the fundamental mechanisms and clinical significance of these findings, especially in relation to the advancement and treatment of cardiovascular disease.

Table 11: correlation between lipid profile and electrolytes in HTN group and HTN with CAD group

Lipids profile	Na in HTN group		Na in HTN with CAD group	
	r	**P-Value**	**r**	**P-Value**
Cholesterol	0.266	0.155	-0.121	0.526
TGs	0.06	0.753	-0.255	0.174
HDL	-0.018	0.924	0.03	0.875
LDL	0.258	0.169	-0.061	0.751
	K in HTN group		**K in HTN with CAD group**	
	r	**P-Value**	**r**	**P-Value**
Cholesterol	-0.142	0.455	-0.103	0.589
TGs	0.001	0.996	-0.175	0.354
HDL	0.092	0.628	0.214	0.256
LDL	-0.161	0.395	-0.089	0.64
	Ca in HTN group		**Ca in HTN with CAD group**	
	r	**P-Value**	**r**	**P-Value**
Cholesterol	0.275	0.142	-0.145	0.445
TGs	0.387	**0.035***	-0.111	0.558
HDL	-0.341	0.065	0.170	0.368
LDL	0.185	0.329	-0.134	0.48

***: P-value< 0.05 is considered significant. (r): Pearson correlation coefficient**

In patients of HTN group there was no statistically significant (P> 0.05) correlation between K and lipids profile (Cholesterol – TGs – HDL – LDL). In patients of HTN with CAD group there was no statistically significant (P> 0.05) correlation between K and lipids profile (Cholesterol – TGs – HDL – LDL). In patients of HTN group there were: A statistically significant (P= 0.035) positive correlation (r=0.387) between Ca and TGs. No statistically significant (P> 0.05) correlation between K and other lipids profile parameters (Cholesterol – HDL – LDL). In patients of HTN with CAD group there was no statistically significant (P> 0.05) correlation between Ca and lipids profile (Cholesterol – TGs – HDL – LDL).

Discussion

CAD is a multifaceted condition that is influenced by various risk factors, such as nutritional, genetic, behavioral, and environmental factors (29). Furthermore, it can be triggered by hypertension, dyslipidemia, diabetes, obesity, Mellitus, high-fat intake, lack of physical activity, a diet high in cholesterol, and cigarette smoking (30).

The study did a full analysis to see how different demographic factors, lipid profiles, electrolytes, inflammatory markers, heavy metals, oxidized LDL (Ox-LDL) levels, and malondialdehyde (MDA) levels were related in hypertensive people with and without CAD with the aim of finding correlations between these markers and cardiovascular disease in hypertensive patients.

HTN is a common risk factor for cardiovascular disease that can be modified. It is closely linked to a higher risk of cardiovascular disorders such as stroke, renal disease, and heart attack, as well as an increased chance of death (31). Hypertension is diagnosed when the mean of two or more diastolic or systolic blood pressure readings, obtained during at least two separate visits, is equal to or above 90

mmHg or 140 mmHg, respectively (32). Primary hypertension is defined as high blood pressure without any underlying causes such as kidney failure, renal artery disease, excessive aldosterone production, or a tumor called pheochromocytoma (33). Research has demonstrated that factors such as the process of becoming older and being overweight can lead to the development of hypertension (34)

In our study, an important set of relationships were found, especially when looking at demographic information. Age was found to be a strong predictor of CAD risk, which is in line with earlier research that linked getting older to a higher risk of cardiovascular disease.

In the cohort study conducted by Mortensen, M. B (35), the study utilized data from the Western Denmark Heart Registry and had a median follow-up duration of 4.3 years. The study included individuals who were 18 years of age or older and had undergone computed tomography angiography (CTA) between January 1, 2008, and December 31, 2017, due to symptoms that indicated CAD. The study found correlation between age and CAD.

Additionally, we found that there was a strong link between education level and CAD risk. People with secondary and university education had lower chances of developing CAD compared to people who were not educated. This shows how education might help improve heart health and keep people from getting heart disease. The same findings were obtained by Tillmann, T., et al. (36) as he found that This study on mendelian randomization provides evidence supporting the idea that inadequate education is a causative risk factor for the development of coronary heart disease. Possible pathways may involve factors such as smoking, body mass index, and blood lipids. These findings, when combined with data from studies using different methods, indicate that increasing education could lead to significant improvements in health (37).

According to our multivariate logistic regression, there was a significant correlation between vitamin D3 (P=0.002*) and CAD and HTN. There is accumulating evidence that low Vitamin D status adversely affects cardiac function (38). A receptor to the active metabolite 1,25-dihyroxyvitamin D_3 has been identified in the rat heart (39). Vitamin D deficiency results in increased cardiac contractility, hypertrophy, and fibrous in rats (39). Vitamin D supplementation lowers blood levels of MMP-9 and MMP-2 (40). Similarly, reversal of cardiomegaly by calcium and Vitamin D supplementation has been described in children with rickets and in an adult with congestive heart failure (41).

Our finding regard lipid profiles shows that people with high blood pressure had higher amounts of cholesterol, triglycerides, and LDL compared to the control group. This shows that dyslipidemia is common in this group of people. However, there were no significant differences found between hypertensive people with and without CAD. This suggests that hypertension may have a big effect on lipid metabolism and cardiovascular risk (42).

Our findings didn't find positive correlation between uric acid and CAD and HTN. On the other hand; hyperuricemia is prevalent in individuals with primary hypertension (43), particularly in those with accelerated (or malignant) hypertension(44).

High blood pressure has a big effect on lipid metabolism, which can cause dyslipidemia and raise the chance of heart disease in people with high blood pressure (42). People with high blood pressure often have dyslipidemia, which is when their amounts of lipids like total cholesterol, LDL-C, HDL-C, and TGs are not normal (45).

Atherosclerotic plaques are made when LDL-C levels are high (46). These plaques narrow the walls of arteries and raise the chance of CAD (47). High levels of TG are linked to insulin resistance, fat, and metabolic syndrome, while low levels of HDL-C are linked to high blood pressure (48). Oxidative stress, inflammation, insulin resistance, and endothelial failure are some of the ways that high blood pressure can mess up lipid metabolism(49). This mix speeds up the development of atherosclerosis, which causes plaques to form in the arteries and heart problems. Medications, lifestyle changes, and checking for and treating cholesterol should all be part of managing high blood pressure (50).

People with high blood pressure were found to have electrolyte imbalances, especially high amounts of sodium and potassium (51). Potassium was found to have a strong link with the risk of CAD (52). These results show how important it is for people with high blood pressure to keep their electrolyte levels balanced, since changes can lead to heart problems (53).
Our study found no significant correlation between K and lipids profile in patients with HTN, CAD, or between K and TGs (Cholesterol - TGs - HDL - LDL), and no significant correlation between K and other lipid profile parameters in HTN and CAD patients. Electrolytes like sodium, potassium, calcium, and magnesium all play a role in how people with high blood pressure feel (54). Sodium controls blood pressure by controlling the amount of fluid outside of cells (55). Potassium, on the other hand, controls the tone of blood vessels and the balance of sodium(56). Low potassium levels, or hypokalemia, and high potassium levels are both linked to high blood pressure (57). Calcium affects how blood pressure is controlled by changing the tone of smooth muscle in arteries and the heart's ability to beat (58).

Regarding inflammatory markers multiple regression analysis showed statistically significant differences between groups regarding CRP and ESR where the *P*-value were <0.001, and 0.007 respectively. Several inflammatory markers, including CRP and ESR, were significantly higher in people with high blood pressure, especially those who had CAD (59). This showed that there was widespread inflammation and possible endothelial dysfunction. These results show that inflammation is a major factor in the development of CAD and suggest that targeting inflammation may be a useful treatment for people with high blood pressure.

Our findings found significant correlation between the heavy metal concentration associated with smoking and CRP. The presence of heavy metal was investigated by Nguyen, H. D., et al., (60) who indicated a notable correlation between the rise in cadmium, lead, mercury, and hs-CRP levels, and the 10-year risk of cardiovascular disease (CVD). These findings agree with our findings in the presence of correlation between heavy metals and the hs-CRP in CAD patients.

Researchers also looked at heavy metal intake and found strong links between some metals (like cobalt, chromium, copper, lead, iron) and CAD risk. It's interesting that smokers had higher amounts of these metals, which suggests that heavy metal exposure, smoking, and heart disease risk may be linked (61, 62). Also, there was a negative relationship found between MDA levels and some heavy metals in people with CAD who also had high blood pressure. This suggests that MDA may have a beneficial effect against oxidative stress (63). MDA makes cells' antioxidant defense systems work better by activating antioxidant enzyme systems (64). It may also work as a signaling molecule, starting up cellular processes that help protect against free radicals, fix DNA, and deal with stress (65). It's also possible that MDA can protect mitochondria, making them more resistant to oxidative damage (65). Exposure to low amounts of oxidative stress can cause adaptive responses, like hormesis, which make cells more resistant to stress and help them last longer (66). MDA can also control the signaling pathways in cells, helping them react to damage caused by oxidative stress (67)

Our results show a significant increase in Ox-LDL levels in patients with HTN compared to the control group with no significant difference between HTN group and CAD group. ox-LDL plays a major role in the development of atherosclerosis and CAD, especially in patients with hypertension and diabetes (68). It induces inflammation, facilitates fat accumulation, and contributes to the formation of plaque in arteries (69). Chronic inflammatory disorders and aberrant lipoprotein metabolism are additional factors that might contribute to elevated levels of ox-LDL (70)

Conclusion

People with high blood pressure are more likely to get heart disease, which is one of the most common

and dangerous illnesses in the world. Several important links were found between different factors and the chance of getting heart disease and high blood pressure in this study. Age was found to be one of the most important things that raises the risk of heart disease. Education was also found to be an important way to lower this risk. Another link has been found between not getting enough vitamin D and a higher chance of heart disease and high blood pressure. Also, changes in the body's mineral and acid levels may raise the risk of heart disease. In conclusion, this study shows how important it is to keep an eye on these numbers and do what you need to do to keep your heart healthy, whether that's eating right, working out, or getting the right medical care.

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