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Serum Analysis of Hypertensive Patients Reveals High Levels of Lead, Cadmium and Copper but Not Zinc.

(*El análisis del suero de pacientes hipertensos revela altos niveles de plomo, cadmio y cobre, pero no de zinc*)

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Abstract(english)

Heavy metal exposure through environmental contamination such as water and diet can cause severe health problems. Present investigation was conducted to analyze the electrolytes and metals in the blood serum of cardiovascular hypertensive patients. A convenient sample of 50 diagnosed hypertensive patients were selected from Cardiology Cell of DHQ Hospital, Sargodha. Patients aged 26-70 (years), irrespective of their genders with confirmed diagnosis of hypertension and current blood pressure ≥ 140/90 mmHg were included in the study. Statistically significant difference was found in mean concentration of lead among hypertensive patients and normotensives as 2.143 ± 0.7753mg/L and 1.455± 0.01749mg/L respectively. Significant (P= <0.0001) variations were found in the cadmium level in hypertensives 0.902± 0.3mg/L compared with its levels in normotensives 0.1817 ± 0.021mg/L. Elevated concentration of copper 2.125± 0.909 mg/L is found in patients suffering from hypertension compared with its normal counterparts 0.218 ± 0.021mg/L. This variation is highly significant (P= <0.0001). Serum zinc concentration in hypertensive patients and normal persons remained as 6.678±2.634mg/L and 21.619±10.432mg/L respectively. The statistically non-significant (P = 0.56) difference was found for calcium among both hypertensive and control groups, with 870.319±847.11mg/L and 953.258±548.24mg/L in normotensive and hypertensive patients. Higher concentration of blood lead, cadmium and copper but lower zinc concentration were found in hypertensives.

Keywords(english)

Hypertension, metal elements, systolic blood pressure, diastolic blood pressure.

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Resumen(español)

La exposición a metales pesados a través de la contaminación ambiental, como el agua y la dieta, puede causar graves problemas de salud. La presente investigación se realizó para analizar los electrolitos y metales en el suero sanguíneo de pacientes hipertensos cardiovasculares. Se seleccionó una muestra conveniente de 50 pacientes hipertensos diagnosticados de la Célula de Cardiología del Hospital DHQ, Sargodha. Se incluyeron en el estudio pacientes de 26 a 70 (años), independientemente de su sexo, con diagnóstico confirmado de hipertensión y presión arterial actual ≥ 140/90 mmHg. Se encontró una diferencia estadísticamente significativa en la concentración media de plomo entre pacientes hipertensos y normotensos de 2,143 ± 0,7753 mg/L y 1,455 ± 0,01749 mg/L, respectivamente. Se encontraron variaciones significativas (P= <0.0001) en el nivel de cadmio en hipertensos 0.902± 0.3mg/L comparado con sus niveles en normotensos 0.1817± 0.021mg/L. Se evidencio una concentración elevada de cobre de 2,125 ± 0,909 mg/L en pacientes que padecen hipertensión en comparación con sus homólogos normales de 0,218 ± 0,021 mg/L. Esta variación es altamente significativa (P= <0.0001). La concentración sérica de zinc en pacientes hipertensos y personas normales se mantuvo en 6.678±2.634mg/L y 21.619±10.432mg/L respectivamente. Se observo además una diferencia estadísticamente no significativa (P = 0,56) entre los grupos de hipertensos y control, con 870,319±847,11mg/L y 953,258±548,24mg/L en normotensos e hipertensos. Finalmente, evidenciamos una mayor concentración de plomo, cadmio y cobre en sangre, pero menor concentración de zinc en los individuos hipertensos.

Palabrasclave(español)

Hipertensión, elementos metálicos, presión arterial sistólica, presión arterial diastólica

Introduction

It is estimated that nearly one billion people are affected by hypertension worldwide, and this figure is predicted to increase to 1.5 billion by 2025 (1). Because of the complex etiology, traditional markers of the prevalence of hypertension in the general population, such as age, smoking, alcohol consumption, and obesity, cannot accurately reflect this prevalence. The previous study has linked pollution and environmental metal intake to hypertension (2). Recent studies have shown an intriguing role for stress in the release of low testosterone which can lead to diabetes. Regarding this sentence, it is possible that due to hypertension the level of hormones goes up or down and may cause alteration in metal elements. Future research will take an interesting tack by trying to understand this idea (3, 4, 5). Hypertension is classified into two stages. Stage I has a systolic blood pressure of 140-159 mmHg and diastolic blood pressure of 90-99 mmHg, whereas stage II has a systolic blood pressure of 160 mmHg and diastolic blood pressure of 100 mmHg (6). Lead toxicity is a serious health concern due to pollution and miseducation. It affects almost all of the organ systems throughout the body. Hypertension is caused by high cadmium (Cd) exposure. Cd is present in the human body from birth but builds over time. Study from Korea found that Cd values were linked to an increased risk of hypertension in persons over the age of 20 (7). Copper, an essential trace metal, possesses antioxidant properties maintained by various redox enzymes. Previous studies on the link between serum copper and blood pressure (B.P.) were unclear or conflicting (8). Copper has been shown to block the angiotensin-converting enzyme, a key enzyme in blood pressure regulation (9). Following a randomized trial conducted in the United States of America (U.S.), low-to-moderate urine Cd levels were associated with hypertension in the general public (10).

On the other hand, a cross-sectional study of Canadian adults discovered an inverse connection between urine Cd and B.P. (11). When different metals are evaluated, a study found a stronger bond between urine zinc (Zn) and hypertension (12). Other studies have found that hypertensive patients have lower serum zinc values (13). Zinc is an antioxidant, and a lack of it promotes hypertension due to oxidative stress (14). Metals accumulate in body parts as people ingest polluted rice. This study aimed to determine the concentrations of Pb, Cd, Cu, and Zn in Pakistan's Sargodha district. The study's purpose was to see how dangerous heavy metals were in the serum of hypertensive patients. In addition, accumulations of hazardous elements in hypertensive individuals' serum were evaluated to analyze the connection between electrolytes, metal elements, and hypertension. This study's main contribution is the finding that the hypertension rate in the area is higher than that of the neighborhoods nearby. We group the hypertension values according to electrolyte concentration before comparing them to the concentration. This is Pakistan's first submission with the characteristics listed above.

Materials and Methods

Study design. A cross-sectional study was designed to collect data from all participants. The present study was conducted at District Head Quarter (D.H.Q.) Hospital (Sargodha, Pakistan) and Pharmacy Lab, Pharmacy Department University of Sargodha, Sargodha, Pakistan. The target population was all hypertensive patients who had been diagnosed with hypertension. A convenient sample of 50 Diagnosed hypertensive patients was selected from the Cardiology Cell of D.H.Q. Hospital, Sargodha. An approval from the ethical committee of D.H.Q. Hospital, Sargodha was taken for collection of blood samples and relative information from patients. Patients aged 26-70 (years), irrespective of their genders, with a confirmed diagnosis of hypertension and current blood pressure ≥ 140/90 mmHg were included in the study. Hypertensive patients with diabetes, kidney stone, and other kidney diseases were excluded.

Data and sample collection and processing. Cases of hypertension were selected based on blood pressure screening at D.H.Q. Hospital or their current blood pressure status and recommended by the doctor. Fifty average healthy persons were also chosen as a control based on blood pressure screening. Blood samples were drawn by venipuncture of the cubital vein from each individual. Blood was poured into anticoagulant-free tubes. Representatives were allowed to clot and were centrifuged at 10,000 rpm for serum separation. The serum was separated with the help of a micropipette and put into marked aphon drops, and stored below 4 °C before further processing. The serum was digested with nitric acid and hydrogen peroxide by the process of wet acid digestion after wet acid digestion standards were prepared for copper, zinc, lead, cadmium, and calcium.

Laboratory analysis. The concentrations of calcium electrolytes and metals (lead, cadmium, copper, zinc) were analyzed by atomic absorption spectrophotometer (AA 6600 Shimadzu), which allows for the measurement of a wide range of concentrations of metals in biological samples. In addition, concentrations of sodium and potassium electrolytes were analyzed by using an Automated electrolyte analyzer (Fp 20 SEAC), which gives electrolyte measurement by using the technique of flame photometry.

Statistical analysis. Statistical analysis was carried out using SPSS 20th version and graph Instant 3. Data collected for lead, cadmium, copper, zinc, and calcium were analyzed by unpaired t-test, while one sample t-test was applied to the data regarding sodium and potassium levels. In addition, a one-sample t-test was used for comparison with the reference range of data regarding blood pressure. A P-value of ≤ 0.05 was considered statistically significant.

Results

Hypertensive patients had higher levels of lead cadmium and copper. According to the findings, hypertensive patients have higher blood lead levels (2.143µg/L) than normal healthy people (1.455µg/L). This difference is statistically significant (*p*=0.00). This experiment's results also revealed substantial differences in hypertensive cadmium levels (0.902µg/L) compared to normotensives (0.1817µg/L). This difference is judged significant (*p*=0.00). Copper concentrations (2.125 µg/L) were significantly higher in hypertensive patients than in the general population (0.218 µg/L). This difference is highly significant (P=0.00). In patients, Zinc levels in hypertension were lower (6.678µg/L) than in normal healthy people (21.619µg/L). This difference is statistically significant (P=0.00). Data on calcium concentration revealed a non-significant difference between hypertensive patients (953.258µg/L) and normotensive individuals (870.319µg/L). This difference is statistically insignificant (*p*= 0.56). All of the appropriate values are depicted in Figure 1 and Table 1.

Systolic vs. diastolic blood pressure. To assess the stage 1 and 2 hypertension in hypertensive patients with metal poisoning in their blood, systolic and diastolic blood pressure readings of already diagnosed hypertensive patients were taken. The findings revealed that 80% of hypertensive individuals had B.P. readings at stage 2 (160/100mmHg and above), while the remaining 20% had hypertension at stage 1 (140/90mmHg and above). For hypertensive patients with metal poisoning in their blood, the mean blood pressure was 170/100mmHg. All of the appropriate values are depicted in Figure 2 and Table 1.

K and Na levels decrease in Hypertensive patients. The findings of this study show that blood potassium levels in hypertensive patients are low (4.250mEq/L) compared to the reference value (4.5mEq/L). This difference is statistically significant (P=0.00). Sodium levels in hypertensive individuals are

Table 1. All relevant values between normal and patients for metal elements, electrolytes and blood pressure.

Metals (µg/L)	Mean	Standard deviation	Standard error of mean	
				*p**
Lead normotensives	1.455784655	0.01749	0.002474	
Lead hypertensives	2.14347957	0.7753	0.1096	< 0.00
Cadmium normotensives	0.181721853	0.02188	0.003095	
Cadmium hypertensives	0.902103965	0.3	0.04243	< 0.00
Copper normotensives	0.218217644	0.04744	0.006709	
Copper hypertensives	2.125114454	0.9091	0.1286	< 0.00
Zinc normotensives	21.61926206	10.432	1.475	
Zinc hypertensives	6.678332844	2.634	0.3725	< 0.00
Values for K and Na electrolytes in hypertensive patients				
Electrolytes	Mean	Reference value	SD	*p*-value
Calcium hypertensives	953.2581	10.2 mg/dL	77.533	0.56
Potassium in hypertensive patients	4.250	5.2 mEq/L	0.2742	<0.00
Sodium in hypertensive patients	135.12	145 mEq/L	0.40457	0.01
Values for Systolic and Diastolic blood pressure in hypertensive patients				
	Test Value = 120 mmHg/80mmHg			
	T	P*	Mean Difference	Mean value(mmHg)
S.B.P	33.161	0.00	1.82000	170.7
D.B.P	33.161	0.00	1.82000	100.4

also lower (135.12mEq/L) than the reference value of (140.5mEq/L). Again, the difference is statistically significant (p= 0.01). All of the appropriate values are shown in Table 1

Discussion

The current study collects information on copper, lead, cadmium, and zinc in patients suffering from hypertension. Cigarette smoke, obesity, food with low nutritional value, scarcity of cold-water fish, fresh fruits and vegetables, poor sleep, heredity, stress, and insomnia are all causes of high blood pressure. Zinc is essential for regular metabolism and aids in over 200 enzymatic processes (15). Earlier observational research discovered that Zn insufficiency is associated with higher cardiovascular disease risk and hypertension (16).

In our investigation, cardiovascular hypertensive patients had elevated serum copper, lead, and cadmium levels, whereas hypertensive individuals had lower serum zinc levels. Increased lead levels are similar to the results of Rahman et al. (17). In observational studies, elevated blood lead levels are related to a higher risk of hypertension (18). Our findings contribute to the growing body of research linking lead to elevated blood pressure in populations (19). Our findings imply that lowering current levels of lead exposure in the environment may benefit individuals by reducing blood pressure and the associated disease risk. Lead poisoning is most

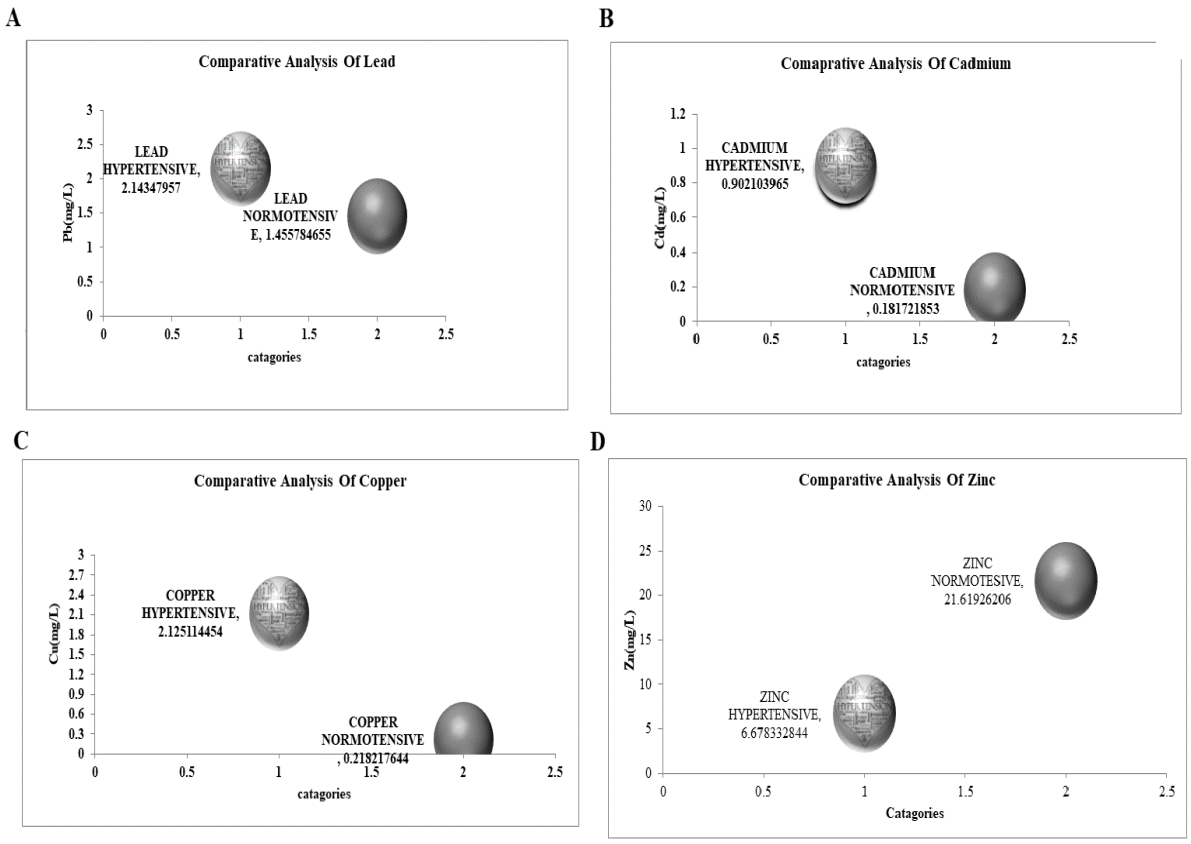

Figure 1. Concentration of Lead, Cadmium, Copper and Zinc (µg/L) in serum samples of normotensive and hypertensive patients

commonly caused by consuming contaminated food or beverages. Unexpected intake of polluted soils, dirt, or spur paint, on the other hand, can outcome in toxicity.

There is a clear link between ambient Cd contamination and adverse health effects such as hypertension (20). Higher cadmium concentrations was linked with hypertensive individuals (21).

Because Cd is a constituent of cigarettes and can remain in the arterial wall for decades, it may cause endothelial dysfunction and prolong the inflammatory mediators and thrombogenic processes required to speed up the atherosclerosis cycle. To summarize, smoking prevalence significantly complicates assessing the connection between Cd exposure and blood pressure. Furthermore, the methods through which Cd causes hypertension are still unknown. Study reported a rise in plasma copper levels in hypertension patients (22). According to Bastola et al. hypertensives have greater serum copper levels (23). The current investigation found that serum zinc levels were significantly lower in hypertension patients compared to non-hypertensive individuals; in contrast to previous findings (23).

Just plasma calcium was determined to be non-significant (p=0.5) between the two groups in our investigation; the same conclusion was reported by (24). Reduced serum potassium levels were discovered in cardiovascular hypertension patients, consistent with (25, 26). In our investigation, sodium electrolyte levels remained considerably lower in hypertension patients. As a result, the mean systolic (170.7mmHg) and diastolic blood pressure (100.4mmHg) among cardiovascular patients were higher than the normal blood pressure (Table 1). Just 18% of patients were in stage-I hypertension, while 82% were in stage-II hypertension (Fig 2).

Limitations and strengths. Because the current study was cross-sectional and did not take into account the temporal relationship between exposure and outcome, we are unable to draw any conclusions

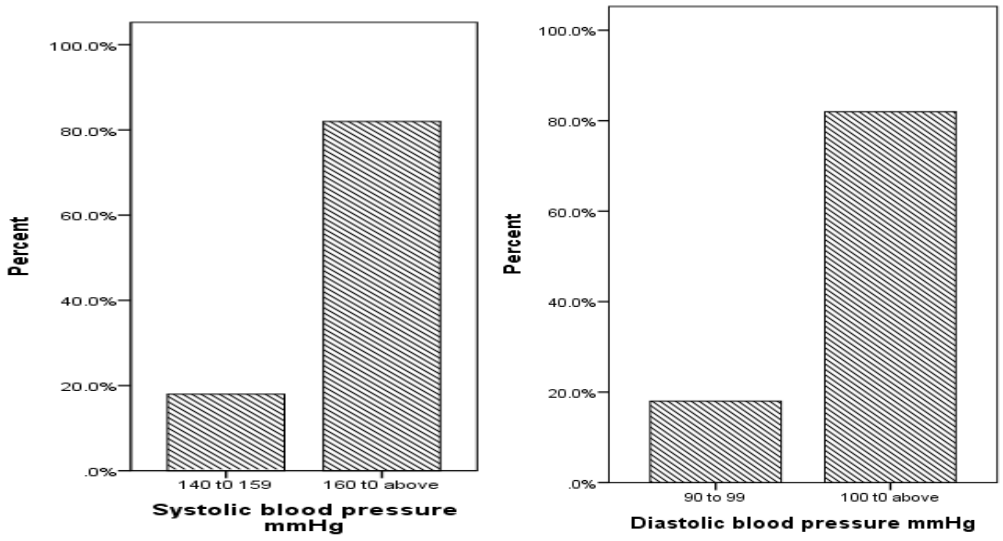

Figure 2: Systolic and diastolic blood pressure (mmHg) in hypertensive patients

about a causal connection. Our study's reliance on a volunteer cohort with particulars that might restrict generalizability is yet another drawback. Participants had a higher than average risk of developing cardiovascular diseases, which could share risk factors with hypertension and have an impact on the metals level. The eligible participants did not take into account a background of heart disease, and we did not make any modifications for this in the assessment. Furthermore, instead of using attendees' personal levels of exposure, we used airborne metal levels based on census-tract level exposures. The prediction of metal exposure premised on census-tract level did not take into account the possibility that an individual could experience various metal concentrations depending on their behavior and activity pattern.

We measured participants' height, weight, and blood pressure by trained examiners at enrollment rather than by self-report is a research strength because it allows us to evaluate hypertension and obesity more precisely than other studies. Another advantage is that we took into account the combined and individual effects of the total metal mixture on hypertension. To the best of our knowledge, this study is the first to investigate the link between metal levels, electrolytes, and hypertension in our local population.

In conclusion and according to the findings of this study, hypertension was associated with considerably more significant levels of lead, cadmium, and copper metals, as well as lower levels of zinc, potassium, and sodium electrolytes in blood serum. In contrast, there was no significant calcium involvement in patients with hypertension. In addition, this study found that several metals contribute to hypertension. As a result, early alteration of this characteristic will aid us in lowering the likelihood of prevailing hypertension.

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