Proceedings of the 4th International Conference on Biological Engineering and Medical Science
DOI: 10.54254/2753-8818/70/2024.18203

The role of plasma trace elements in hypertension among elderly populations in China: A cross-sectional analysis using CLHLS data

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Abstract. Nearly half of adults aged 60 and above in China suffer from hypertension, a critical public health issue. Emerging evidence suggests that trace elements in plasma, such as copper and selenium, may play significant roles in the development of hypertension. This study examines the relationship between plasma concentrations of these elements and hypertension risk among elderly Chinese populations. A cross-sectional analysis was conducted using data from the China Health and Longevity Survey (CLHLS), which included a nationally representative sample of older adults aged 60 and above. The study analyzed data from 452 participants, focusing on plasma concentrations of copper and selenium measured in 2009 and their association with hypertension outcomes in subsequent years. Statistical analyses, including logistic regression models, were used to assess the relationships while controlling for confounding factors such as age, sex, and comorbidities. The results revealed that higher plasma copper levels are associated with a reduced risk of hypertension, particularly in rural areas of Hubei and Guangxi provinces. The association between selenium and hypertension was statistically significant but had a negligible effect size. These findings suggest that copper may play a protective role against hypertension, with potential implications for public health interventions targeting the elderly population in China.

Keywords: Hypertension, Elderly, Trace Elements, Copper, Selenium, CLHLS.

1. Introduction

Hypertension is a significant global public health issue, with the World Health Organization (WHO) estimating that approximately 1.28 billion adults worldwide are affected, contributing substantially to the global burden of cardiovascular diseases, stroke, and mortality, particularly among the elderly [1]. In China, the prevalence of hypertension is even more concerning, with nearly 50% of adults aged 60 and above affected [2]. As life expectancy continues to rise, understanding the risk factors associated with hypertension in the elderly becomes increasingly important. Emerging evidence suggests that plasma metal elements may also play a significant role in the development of hypertension[3].

Copper (Cu), selenium (Se), manganese (Mn), magnesium (Mg), calcium (Ca), iron (Fe), and zinc (Zn) are essential trace elements involved in various physiological processes [4], including the regulation of oxidative stress, immune function, and the activation of enzymes crucial for vascular health

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[5-7]. The balance of these elements is critical [8] because both deficiencies and excesses can adversely impact cardiovascular health.

This research investigates the relationship between the plasma concentrations of these metal elements and the risk of hypertension among the elderly in China, with particular attention to how these associations vary by province of residence, urban-rural status, age, and gender. Additionally, the study will explore whether comorbidities such as diabetes and cardiovascular diseases modify the relationship between these trace elements and hypertension risk. Understanding these associations can provide valuable insights into the role of trace elements in hypertension and inform targeted interventions for the prevention and management of hypertension in the elderly.

The findings of this study may contribute to a more nuanced understanding of the roles of multiple trace elements in hypertension and could have significant public health implications, particularly in the development of dietary recommendations and strategies for preventing hypertension in the elderly. By leveraging the rich dataset of the CLHLS, this study aims to fill a critical gap in the literature and advance our understanding of the multifaceted factors influencing hypertension in the elderly.

2. Method

2.1. Key Variables Explanation

The primary outcome variable in this study was the presence of hypertension, defined as a self-reported diagnosis of hypertension or use of antihypertensive drugs, consistent with the CLHLS survey protocol. The key exposure variable is the concentration of metal elements in the plasma, measured in micrograms per deciliter (μg/dL). These measurements are obtained by standardized blood sampling and laboratory procedures described in the CLHLS protocol. The covariates included in the analysis included demographic variables, such as age (continuous), sex (male/female), province of residence (classification), urban/rural status (urban/rural), etc. Also of concern were the participants' comorbidities: self-reported history of diabetes, cardiovascular disease, and stroke and CVD (yes/no).

2.2. Statistical Analysis

Statistical analysis was performed using SAS. Descriptive statistics were first calculated to summarize the characteristics of the study population, including the distribution of plasma concentrations of copper, selenium, and iron, and the prevalence of hypertension in different demographic and health-related subgroups.

To explore the relationship between trace element concentrations in plasma and hypertension, this paper used a univariate logistic regression model, a multivariate logistic regression model, and a stepwise regression analysis model. The models were adjusted for potential confounders, including age, sex, BMI, smoking status, alcohol consumption status, physical activity, comorbidities, and regional factors (provincial and urban/rural). Interaction terms were included to explore the influence of age, sex, rural-urban status, and the presence of comorbidities on potential effects. Cross-tabulation and Chi-square test were also used to analyze the interaction between different factors, and cross-action analysis was used to study the interaction.

The strength of the association was expressed by the odds ratio (or) and 95% confidence interval (ci). $p < 0.05$ was considered statistically significant. Sensitivity analyses were performed to test the robustness of the results, including analysis stratified by sex, age group, and urban/rural status, as well as excluding participants with micronutrient extremes or comorbidities. All statistical analyses follow the assumptions of their respective statistical tests and perform appropriate diagnostic tests to validate the model.

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3. Results and Discussion

3.1. The effect of different metal elements on the risk of hypertension

Univariate logistic regression analysis was used to investigate the relationship between plasma metallic element measurements in 2009 and hypertension outcomes in 2008, 2011, 2014, and 2018. The analysis found a significant association between copper (Cu) and selenium (Se) levels in 2009 and hypertension outcomes in 2011. The estimated coefficient for copper ($p=0.0076$) was 0.779, indicating that copper levels were inversely associated with the risk of hypertension. This suggests that higher copper levels are associated with a reduced likelihood of developing high blood pressure. At the same time, the effect of copper on hypertension risk was statistically significant and may be clinically relevant. The estimated coefficient for selenium ($p=0.0332$) was 0.997, indicating a very weak negative association between selenium levels and hypertension risk. While the effect was small and almost negligible, the relationship was statistically significant. So the actual effect of selenium on hypertension risk is likely to be very small and may not be of substantial clinical importance.

Stepwise logistic regression analysis revealed important insights into the combined effects of copper (Cu) and selenium (Se) on hypertension risk. When considered alone, copper was significantly negatively associated with high blood pressure risk, suggesting that higher copper levels were associated with a lower likelihood of developing high blood pressure. Selenium, while also showing a negative association, had a much weaker effect on high blood pressure risk. When both elements were included in the final model, copper remained a strong protective factor against hypertension, with odds ratios significantly lower than 1, indicating a substantial reduction in risk. Although the effect of selenium was small, it still showed a statistically significant association, although its reduction in the risk of hypertension was almost negligible. The absence of interaction terms in the model suggests that the effects of copper and selenium are additive rather than interacting. This means that their combined effect on reducing the risk of high blood pressure is cumulative, with copper playing a dominant role and selenium, although less effective, helping to reduce the overall risk.

The findings suggest that higher plasma copper levels are consistently associated with a reduced risk of hypertension, while the relationship between selenium levels and hypertension, although statistically significant, appears to have a negligible effect size. These findings are consistent with previous studies [9], and different clinical and experimental studies have confirmed the same point that copper plays an important role in the cardiovascular system [10-19].

3.2. Regional Variations in Plasma Metal Concentrations and Hypertension Risk

This study examined the relationships between plasma copper (Cu) and selenium (Se) concentrations and hypertension risk across five Chinese provinces (Henan, Hubei, Hunan, Guangdong, and Guangxi), stratified by residential type (urban, town, and rural). The analysis revealed significant regional differences in how these trace elements relate to hypertension risk.

3.3. Copper Concentrations and Hypertension Risk

Provincial changes:

In Hubei and Guangxi, higher copper levels were significantly associated with a lower risk of hypertension, especially in rural areas. This suggests a potential protective effect of copper against high blood pressure in these areas. Data from Guangdong showed that the relationship between copper levels and hypertension risk varied by residence region, suggesting that the effect of copper may be influenced by local environmental or lifestyle factors. In Henan and Hunan, there was no significant association between copper concentration and the risk of hypertension by residence type.

Influence of urban and rural residence

Among older adults living in city areas, higher copper concentrations were associated with a lower prevalence of hypertension among city residents in most provinces, especially Hubei and Guangxi. However, the relationship between copper levels and hypertension risk among town residents showed significant differences, especially in Guangdong, where there was no clear trend. In rural areas,

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especially Hubei and Guangxi, a strong negative association was observed between copper concentrations and the risk of hypertension.

The negative correlation between copper levels and hypertension risk, particularly in rural areas of Hubei and Guangxi, suggests that specific environmental or dietary factors unique to these regions may influence copper's protective role against hypertension [20-22]. However, the lack of significant correlation in Henan and Hunan provinces indicates potential regional differences in the interaction of copper with other hypertension risk factors, requiring further investigation into local dietary patterns, environmental exposures, and genetic susceptibility.

3.4. Selenium Concentrations and Hypertension Risk

Provincial changes:

In Guangdong, selenium levels were significantly negatively associated with the risk of hypertension, especially in rural areas, suggesting a protective effect. In Hubei, the effect of selenium on hypertension risk varied by residential area, with no consistent trend. Other provinces showed less significant or inconsistent associations between selenium and high blood pressure risk.

Influence of urban and rural residence

The relationship between selenium levels and hypertension in city residents varied by province. In Henan and Hunan, high selenium concentrations were associated with an increased risk of hypertension, while in Guangdong, high selenium levels were associated with a lower prevalence of hypertension. However, the relationship between selenium and hypertension in town residents is more complex, and the high selenium level in some provinces (such as Hubei and Guangxi) has a slight positive correlation with the risk of hypertension. In rural areas, especially Guangdong, higher selenium concentrations are strongly associated with a reduced risk of hypertension.

Notably, the protective effect of selenium is more pronounced in Guangdong, especially in rural areas, possibly reflecting regional differences in dietary selenium intake or environmental selenium exposure [23]. The regional differences in the relationship between trace elements and hypertension underscore the importance of considering environmental, geographic, and socioeconomic factors when assessing hypertension risk [24, 25] The results suggest that public health strategies for preventing hypertension should be tailored to the specific needs of different populations, taking into account local environmental exposures and dietary habits.

3.5. Interaction of plasma metal elements with other health factors

After analyzing the relationship between diabetes, cardiovascular disease, and stroke and cardiovascular disease, and the relationship between metal elements and hypertension, we found that cardiovascular disease was significantly associated with this relationship ($p=0.0072$). At the same time, after studying multiple interaction terms, it can be found that the interaction term between selenium and cardiovascular disease was significant (p value 0.0002), indicating that the interaction between selenium concentration and cardiovascular disease has a significant impact on hypertension risk. Specifically, the interaction was estimated to be -0.00421, suggesting that an increase in selenium concentration may affect cardiovascular disease through some mechanism, thereby reducing the risk of hypertension.

In a follow-up study, we focused on the effects of copper and selenium concentrations and cardiovascular disease on the risk of hypertension.

The relationship between selenium concentration and hypertension risk among different levels of cardiovascular disease did not show a significant trend of decreasing or increasing risk as selenium levels changed. The effect of selenium on hypertension risk remained relatively stable in the cardiovascular disease state. For the cardiovascular disease = 8 group, the risk of hypertension increased slightly as selenium concentrations increased. In other populations, changing selenium levels had little effect on the risk of hypertension, and selenium concentrations had little effect on the risk of hypertension in these populations.

The interaction between copper concentration and cardiovascular disease on hypertension risk showed greater variability between groups than selenium. With the increase in copper concentration, the

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risk of hypertension in different populations changed significantly. For the cardiovascular disease = 8 group, the risk of hypertension was significantly reduced as copper concentrations increased, suggesting that high copper levels may be associated with a reduced risk of hypertension in this group. In the other groups, the effect of different copper levels on the risk of hypertension was less pronounced, especially when the copper concentration was between 0 and 4, and for these populations, the effect of copper concentration changes on the risk of hypertension was small.

These data suggest that the effects of selenium and copper on hypertension risk may be attenuated by the presence of cardiovascular disease, with different patterns emerging for different disease states. For example, increasing copper concentrations appeared to reduce the risk of hypertension in individuals with cardiovascular disease status, while the effect of selenium on hypertension risk remained relatively consistent and low across all individuals.

4. Conclusion

This study investigated the relationship between plasma concentrations of trace elements, particularly copper and selenium, and the risk of hypertension among elderly populations in China. The findings suggest that higher plasma copper levels are significantly associated with a reduced risk of hypertension, especially in rural areas of Hubei and Guangxi provinces. Although the association between selenium and hypertension was statistically significant, its effect size was negligible, indicating that copper plays a more crucial role in reducing hypertension risk.

However, the study's cross-sectional design limits the ability to establish causality, and the reliance on single time-point measurements may not fully capture the long-term exposure to these trace elements. Future research should focus on longitudinal studies to confirm these associations, explore the underlying mechanisms, and consider the interaction of trace elements with other dietary and environmental factors across diverse populations. These findings highlight the need for region-specific public health strategies to manage hypertension among the elderly.

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DOI: 10.54254/2753-8818/70/2024.18203

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