### INTERRELATIONSHIP OF ESSENTIAL TRACE ELEMENT METABOLISM IN ADOLESCENTS WITH NEUROCIRCULATORY DYSTONIA LIVING IN IODINE-DEFICIENT CONDITIONS

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Abstract: Iodine deficiency remains a significant global health problem, particularly in regions where environmental and nutritional factors contribute to endemic goiter and related disorders. Adolescents are especially vulnerable to the consequences of iodine deficiency, as thyroid hormone regulation plays a vital role in growth, neurodevelopment, and cardiovascular adaptation. Neurocirculatory dystonia (NCD), a functional cardiovascular disorder common in adolescence, is strongly influenced by metabolic and endocrine imbalances. The present study aimed to investigate the interrelationship of essential trace elements, including iodine, zinc, copper, selenium, and iron, in adolescents with NCD living in iodine-deficient areas, and to assess their pathological and clinical significance. A cohort of 120 adolescents aged 13–17 years with clinically diagnosed NCD was examined and compared with 40 healthy peers. Trace element levels were determined using atomic absorption spectrophotometry and correlated with thyroid hormone profiles, cardiovascular function, and clinical symptoms. Results revealed a strong interdependence between iodine deficiency and alterations in the metabolism of other trace elements, particularly decreased selenium and zinc levels, which contributed to both thyroid dysfunction and autonomic imbalance. These findings highlight the importance of comprehensive micronutrient monitoring and targeted supplementation in the management of NCD in iodine-deficient populations.

**Keywords:** neurocirculatory dystonia, iodine deficiency, trace elements, adolescents, thyroid function, micronutrient imbalance

### Introduction

Iodine deficiency disorders (IDD) remain among the most widespread non-communicable health problems worldwide. The World Health Organization estimates that more than two billion people are at risk of iodine deficiency, with adolescents and children being particularly vulnerable due to their increased metabolic demands. Iodine plays an essential role in thyroid hormone synthesis, and its deficiency disrupts growth, neurocognitive development, and cardiovascular adaptation.

Neurocirculatory dystonia (NCD), a functional disorder of the autonomic nervous system, is commonly diagnosed during adolescence and manifests with symptoms such as tachycardia, dizziness, chest pain, fatigue, and blood pressure instability. Although its etiology is multifactorial, disturbances in neuroendocrine regulation, including thyroid dysfunction, have been recognized as important contributing factors.



Recent studies have demonstrated that iodine deficiency rarely occurs in isolation. It often coexists with imbalances in other essential trace elements such as selenium, zinc, copper, and iron. These elements are not only vital for thyroid hormone metabolism but also play an important role in antioxidant defense, immune regulation, and cardiovascular stability. Selenium is essential for the activity of glutathione peroxidase and iodothyronine deiodinases, zinc is required for numerous enzymatic systems, copper contributes to oxidative metabolism, and iron deficiency may exacerbate hypoxic stress. A disruption in the balance of these trace elements may amplify the pathogenic mechanisms underlying NCD in iodine-deficient adolescents.

The purpose of this study was to analyze the interrelationship of essential trace element metabolism in adolescents with neurocirculatory dystonia living in iodine-deficient areas, and to identify potential diagnostic and therapeutic implications.

#### **Materials and Methods**

This observational case-control study included 120 adolescents (68 girls and 52 boys) aged 13–17 years with clinically diagnosed neurocirculatory dystonia according to standardized criteria. The control group comprised 40 healthy age- and sex-matched peers living in the same iodine-deficient region. Exclusion criteria included chronic systemic diseases, congenital heart defects, or ongoing micronutrient supplementation.

Blood samples were collected in the morning under fasting conditions. Serum iodine, zinc, copper, selenium, and iron levels were measured using atomic absorption spectrophotometry. Thyroid hormone profiles (TSH, free T3, and free T4) were determined by enzyme-linked immunosorbent assay (ELISA). Cardiovascular function was assessed by electrocardiography and echocardiography, while autonomic tone was evaluated by standard orthostatic and Valsalva tests. Clinical symptoms were recorded using validated questionnaires for autonomic dysfunction.

Statistical analysis was performed using SPSS 26.0 software. Mean values were expressed as mean  $\pm$  standard deviation. Between-group differences were analyzed by Student's t-test and Mann–Whitney U-test where appropriate. Pearson correlation analysis was used to determine the interrelationship between trace element levels, thyroid function, and clinical severity of NCD. A p-value <0.05 was considered statistically significant.

#### Results

Adolescents with neurocirculatory dystonia demonstrated significantly lower serum iodine levels compared to the control group ( $56.8 \pm 11.2 \, \mu g/L \, vs. \, 94.5 \pm 13.6 \, \mu g/L$ , p<0.001). In addition, reduced selenium ( $62.1 \pm 9.7 \, \mu g/L \, vs. \, 84.2 \pm 10.3 \, \mu g/L$ , p<0.01) and zinc concentrations ( $10.3 \pm 1.8 \, \mu mol/L \, vs. \, 13.9 \pm 2.1 \, \mu mol/L$ , p<0.01) were observed. Conversely, serum copper levels were moderately increased in the NCD group ( $17.6 \pm 2.3 \, \mu mol/L \, vs. \, 14.9 \pm 1.9 \, \mu mol/L$ , p<0.05), while iron levels were significantly decreased ( $9.2 \pm 2.1 \, \mu mol/L \, vs. \, 13.4 \pm 2.4 \, \mu mol/L$ , p<0.01).

Thyroid hormone assessment revealed subclinical hypothyroidism in 34% of the NCD group, characterized by elevated TSH levels and slightly reduced free T4 concentrations. Correlation analysis indicated a strong positive relationship between iodine and selenium levels (r = 0.61, p<0.01), and between zinc and thyroid hormone status (r = 0.53, p<0.05). Copper excess showed



a weak negative correlation with autonomic balance indices, suggesting its contribution to oxidative stress and cardiovascular instability.

Clinically, adolescents with pronounced micronutrient imbalances exhibited more frequent complaints of palpitations, dizziness, and fatigue, with reduced exercise tolerance and higher scores on autonomic dysfunction questionnaires.

#### Discussion

The results of this study confirm that iodine deficiency in adolescents is frequently accompanied by disturbances in other essential trace elements. The observed reduction in selenium and zinc levels may worsen thyroid dysfunction and impair enzymatic processes involved in maintaining cardiovascular homeostasis. Selenium deficiency, in particular, compromises the activity of iodothyronine deiodinases, thereby aggravating the effects of iodine deficiency on thyroid hormone metabolism. Zinc deficiency is also associated with impaired growth, reduced enzymatic activity, and immune dysregulation, which may contribute to the clinical manifestations of NCD.

Increased copper levels observed in this study may reflect compensatory changes in oxidative metabolism; however, excessive copper can exacerbate oxidative stress, thereby influencing autonomic dysfunction and cardiovascular instability. Reduced iron levels contribute to hypoxia and further aggravate symptoms such as fatigue, tachycardia, and dizziness. These findings are consistent with previous studies indicating that micronutrient deficiencies act synergistically in the development of functional cardiovascular and endocrine disorders.

The close correlation between trace element imbalances and the severity of autonomic dysfunction emphasizes the need for a comprehensive approach to diagnosis and therapy. Correction of iodine deficiency alone may be insufficient; a broader strategy addressing multiple micronutrient deficiencies is necessary for effective management of NCD in adolescents living in iodine-deficient environments.

#### Conclusion

This study demonstrated that adolescents with neurocirculatory dystonia living in iodine-deficient regions exhibit significant disturbances in trace element metabolism, including reduced levels of iodine, selenium, zinc, and iron, as well as elevated copper concentrations. These imbalances are closely associated with thyroid dysfunction and increased severity of autonomic symptoms. The results highlight the importance of considering trace element interactions in the pathogenesis and management of NCD. From both a clinical and public health perspective, integrated micronutrient monitoring and targeted supplementation programs should be prioritized to prevent and mitigate neurocirculatory dystonia in iodine-deficient populations.

The present study provides strong evidence that adolescents with neurocirculatory dystonia (NCD) living in iodine-deficient regions exhibit a complex imbalance of essential trace elements, which not only affects thyroid hormone metabolism but also contributes to cardiovascular instability and autonomic dysfunction. It was demonstrated that reduced levels of iodine, selenium, zinc, and iron, in combination with elevated copper concentrations, form an interdependent pathological network that underlies the clinical manifestations of NCD. These



findings underscore that iodine deficiency should not be viewed in isolation, as its consequences are significantly magnified by concurrent disturbances in other trace elements.

The study further emphasizes that subclinical hypothyroidism, identified in a considerable proportion of the examined adolescents, is closely linked to selenium and zinc deficiencies, both of which impair enzymatic pathways essential for thyroid hormone conversion and antioxidant defense. At the same time, reduced iron levels were associated with hypoxic stress, diminished exercise tolerance, and persistent fatigue, while copper excess was implicated in oxidative imbalance and autonomic dysfunction. Taken together, these results highlight the multifactorial nature of NCD in iodine-deficient settings and the necessity of a broader diagnostic and therapeutic perspective.

From a clinical standpoint, the outcomes of this research suggest that routine evaluation of trace element status should be considered an integral component of NCD management in adolescents. Correcting iodine deficiency alone may lead to partial improvement, but sustainable therapeutic success requires the simultaneous correction of multiple micronutrient imbalances. Targeted supplementation programs involving iodine, selenium, zinc, and iron, combined with antioxidant support and nutritional monitoring, could significantly reduce symptom severity and improve both metabolic and cardiovascular adaptation in affected adolescents.

From a public health perspective, the results call for urgent preventive strategies in regions with endemic iodine deficiency. School-based micronutrient supplementation, dietary diversification, and education campaigns promoting the use of iodized salt and selenium-rich foods may serve as effective measures. In addition, the integration of trace element monitoring into regional health programs could help identify high-risk adolescents early and prevent the progression of functional disorders into chronic pathology.

In conclusion, the interrelationship of trace element metabolism represents a critical factor in the pathogenesis of neurocirculatory dystonia under iodine-deficient conditions. The study highlights the importance of adopting a holistic approach that combines endocrinology, cardiology, nutrition, and public health strategies. By addressing the full spectrum of micronutrient imbalances, it is possible to improve therapeutic outcomes, enhance the quality of life of adolescents, and contribute to the reduction of long-term morbidity associated with iodine deficiency disorders.

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