THE ROLE OF IMBALANCE IN ESSENTIAL TRACE ELEMENTS (CA, MG, ZN, CU) IN THE SEVERITY OF CONNECTIVE TISSUE DYSPLASIA PHENOTYPE IN CHILDREN

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Introduction: Connective tissue dysplasia (CTD) represents a heterogeneous group of polygenic disorders characterized by defects in the extracellular matrix (ECM) structure and function. In children, CTD manifests not only through musculoskeletal abnormalities—such as joint hypermobility, scoliosis, and chest deformities—but also through visceral involvement, including mitral valve prolapse and autonomic dysfunction. The clinical heterogeneity of CTD suggests that beyond the genetic predisposition, significant modifying roles are played by exogenous metabolic and nutritional factors.

The structural integrity of connective tissue depends fundamentally on the proper synthesis and maturation of collagen and elastin fibers. This process is enzyme-dependent and requires specific micronutrients as essential cofactors. Copper (Cu) is a critical component of lysyl oxidase, the enzyme responsible for cross-linking collagen and elastin peptides; a deficiency in copper can lead to poor tensile strength of tissues, mimicking genetic connective tissue disorders. Zinc (Zn) , as a cofactor for matrix metalloproteinases (MMPs) and various transcription factors, is indispensable for tissue remodeling and repair. Furthermore, the balance between Calcium (Ca) and Magnesium (Mg) is crucial for neuromuscular excitability and bone mineralization. Magnesium deficiency, in particular, has been implicated in asthenic syndrome and muscle hypotonia—two hallmark features of pediatric CTD.

Despite the acknowledged importance of these elements, routine clinical assessment of children with CTD rarely extends beyond phenotypic description to include a detailed analysis of their micronutrient status. Existing literature often focuses on singular elements (e.g., magnesium supplementation) but lacks a comprehensive evaluation of the synergistic or antagonistic interactions between these ions, particularly in the pediatric population where nutritional demands are high due to growth.

Therefore, the **aim of this study** is to conduct a comprehensive analysis of the serum levels of Calcium, Magnesium, Zinc, and Copper in children diagnosed with connective tissue dysplasia and to establish a correlation between the degree of micronutrient imbalance and the severity of clinical phenotypic manifestations. We hypothesize that a combined deficiency in magnesium and copper is a significant modifier that exacerbates the clinical course of CTD.

Methods: The study will involve a cohort of 100 children (aged 6–17) diagnosed with CTD. Phenotypic severity will be scored using a standardized scale (e.g., Milov's or

Beighton criteria). Serum concentrations of Calcium (Ca), Magnesium (Mg), Zinc (Zn), and Copper (Cu) will be measured using atomic absorption spectrometry. Statistical analysis (multivariate regression) will be used to assess the correlation between trace element levels and the phenotypic expression score.

Expected Results: We expect to find a statistically significant negative correlation between serum Mg and Cu levels and the severity of CTD. It is anticipated that children with the most severe phenotypes will exhibit the lowest levels of these elements, while imbalances in the Zn/Cu ratio may correlate with specific skeletal abnormalities.

Conclusion: Identifying specific micronutrient deficiencies could allow for targeted metabolic correction. Serum levels of Mg and Cu may serve as potential biomarkers for the clinical progression of CTD, justifying the inclusion of these elements in pathogenetic therapy.