

CLINICAL SIGNIFICANCE OF NITRIC OXIDE AND L-ARGININE DISTURBANCES IN CHILDREN WITH ACUTE VIRAL HEPATITIS C

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Introduction

Acute viral hepatitis C in children remains a clinically important problem because of its heterogeneous course, metabolic consequences, and potential for severe liver dysfunction. In recent years, nitric oxide (NO) has attracted growing attention in hepatology due to its broad role in intracellular homeostasis and bioregulatory processes. Nitric oxide is synthesized from L-arginine by nitric oxide synthase and participates in protein synthesis, carbohydrate metabolism, detoxification, and cytochrome P-450-dependent reactions in hepatocytes. The stable oxidation products of NO, nitrite and nitrate, are considered indirect markers of nitric oxide production in tissues. Disturbances in the NO–L-arginine system may reflect the degree of hepatocellular damage and may be associated with disease severity. This study aimed to evaluate the impact of disturbances in the regulatory role of nitric oxide and L-arginine on the clinical course of acute viral hepatitis C in children.

Materials and Methods

A total of 85 children aged 3 to 14 years were examined. The main group included 65 children with acute viral hepatitis C, while the control group consisted of 20 apparently healthy children comparable in age and sex. All patients underwent comprehensive dynamic evaluation including clinical examination, biochemical blood testing, serum bilirubin assessment (total and fractions), alanine aminotransferase, aspartate aminotransferase, thymol test, total serum protein, hemogram, and serological investigations. Etiological diagnosis was performed using enzyme-linked immunosorbent assay for hepatitis markers including anti-HCV. Serum L-arginine levels were measured, and the amino acid composition of

serum was determined by high-performance liquid chromatography on a DuPont chromatograph using a Nucleosil 5C18 column. Serum nitrite was assessed as an indirect indicator of nitric oxide production. Ultrasound examination of the abdominal organs was performed in the acute phase and during follow-up using Toshiba-Sal-35 and SIM-5000 devices. Statistical analysis included descriptive assessment and correlation analysis between NO-related markers, amino acids, and biochemical indicators of liver injury.

Results

The mean serum nitrite level in the control group was 0.9089 ± 0.0012 $\mu\text{mol/L}$. In children with mild acute viral hepatitis C, this value increased to 1.289 ± 0.06 $\mu\text{mol/L}$; in moderate disease, to 1.820 ± 0.09 $\mu\text{mol/L}$; and in severe disease, to 2.623 ± 0.13 $\mu\text{mol/L}$. Thus, serum NO_2 levels showed a progressive rise with increasing disease severity.

A similar pattern was observed for L-arginine. In healthy children, the mean serum L-arginine level was 567.46 ± 2.44 nmol/L . In mild disease it increased to 801.7 ± 20.0 nmol/L , in moderate disease to 1053.1 ± 26.01 nmol/L , and in severe disease to 1601.2 ± 40.0 nmol/L .

Correlation analysis demonstrated clinically relevant associations between NO metabolism and biochemical parameters of liver injury. In mild disease, positive correlations were found between NO and tyrosine ($r=+0.495$), histidine ($r=+0.432$), arginine ($r=+0.379$), valine ($r=+0.370$), leucine ($r=+0.370$), proline ($r=+0.202$), methionine ($r=+0.129$), alanine ($r=+0.069$), aspartate ($r=+0.074$), and cysteine ($r=+0.046$). In moderate and severe forms, positive correlations were also observed with histidine, aspartate, cysteine, valine, tryptophan, proline, methionine, and glycine. In severe disease, the strongest correlations were identified between NO and isoleucine ($r=+0.461$), glycine ($r=+0.431$), valine ($r=+0.309$), arginine ($r=+0.297$), and methionine.

Overall, the study showed that the level of final nitric oxide products in the serum of children with acute viral hepatitis C was 40.7% higher than in healthy children. The increase in NO metabolites and L-arginine became more pronounced with clinical progression from mild to severe disease.

Discussion

The results indicate that the NO–L-arginine metabolic pathway is closely related to the clinical course of acute viral hepatitis C in children. The gradual increase in serum nitrite from mild to severe disease suggests that nitric oxide production intensifies in parallel with inflammatory activity and hepatocellular injury. Since hepatocytes themselves can produce nitric oxide, elevated NO levels may represent both a compensatory response and a marker of pathological activation of inflammatory and monooxygenase systems.

The rise in L-arginine with increasing disease severity supports the concept that amino acid metabolism is deeply involved in hepatic dysfunction. Because L-arginine is the main substrate for NO synthesis, its increasing concentration may reflect altered utilization and metabolic imbalance during the acute phase of the disease. The identified correlations between NO and amino acids, as well as between NO and conventional biochemical liver markers, suggest that disturbances in nitric oxide metabolism are integrated into the pathogenesis of acute viral hepatitis C.

From a clinical perspective, the observed laboratory trends indicate that serum nitrite and L-arginine may be useful as additional biomarkers for estimating severity and prognosis. Their progressive increase in more severe forms of hepatitis supports their potential role in risk stratification of pediatric patients.

Conclusion

Disturbances in nitric oxide and L-arginine metabolism play a significant role in the clinical course of acute viral hepatitis C in children. Serum NO₂ and L-arginine levels increased progressively from mild to severe disease. Correlation analysis revealed meaningful associations between nitric oxide metabolites, amino acid profile, and standard biochemical markers of liver injury. These findings suggest that elevated NO and L-arginine levels may serve as informative indicators of disease severity and potentially unfavorable prognosis in pediatric acute viral hepatitis C.

Table 1. Serum nitric oxide and L-arginine levels by disease severity

Group	Serum NO ₂ (μmol/L)	Serum L-arginine (nmol/L)
Control	0.9089 ± 0.0012	567.46 ± 2.44
Mild	1.289 ± 0.06	801.7 ± 20.0
Moderate	1.820 ± 0.09	1053.1 ± 26.01
Severe	2.623 ± 0.13	1601.2 ± 40.0

Figure 1. Serum NO₂ levels by disease severity

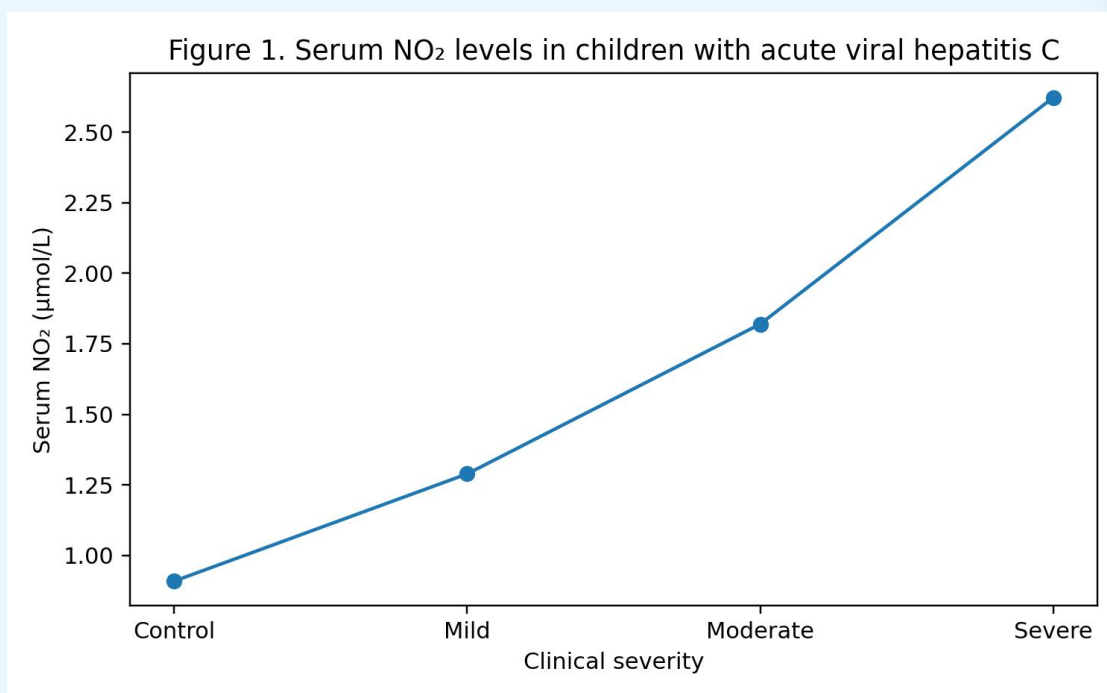
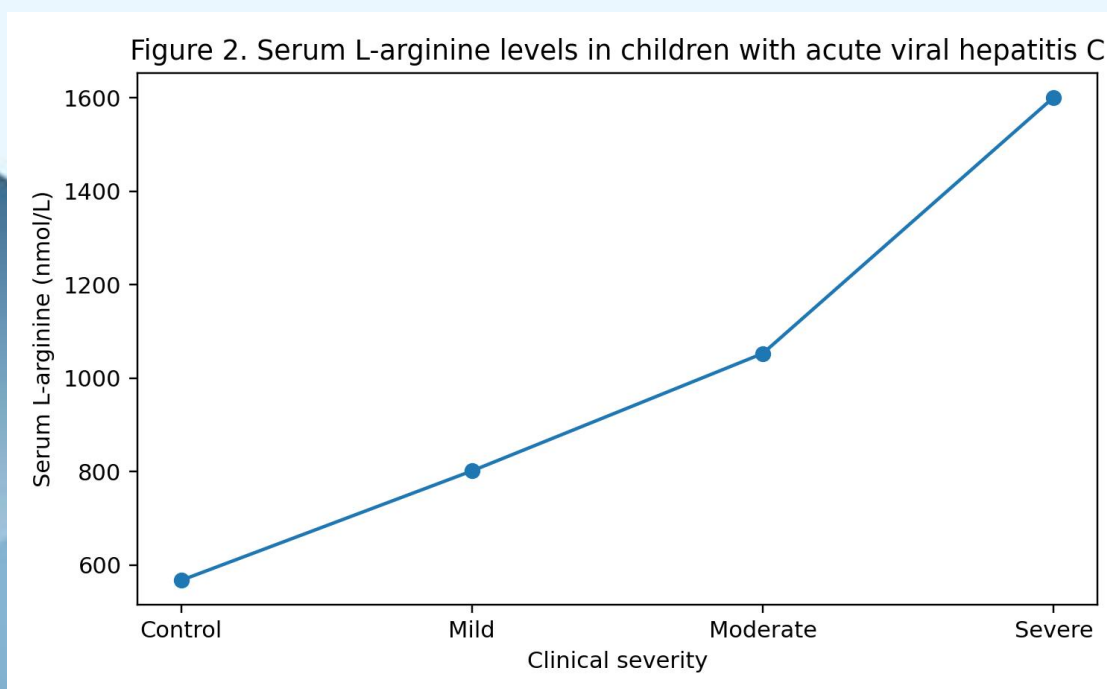


Figure 2. Serum L-arginine levels by disease severity



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