

THE ASSOCIATION BETWEEN METABOLIC SYNDROME AND ELEVATED
ALANINE AMINOTRANSFERASE LEVEL IN SCHOOL-AGED OBESE CHILDREN¹*Fatima Bress, MD, ²Ahmad Chreitah, PhD and ³Mazen Ghalia, PhD^{1,2,3}Department of Pediatrics, Tishreen University, Faculty of Medicine, Lattakia, Syria.

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ABSTRACT

Background: Liver enzymes, particularly alanine aminotransferase, are considered surrogate markers for non-alcoholic fatty liver disease, which is emerging as a component of metabolic syndrome. **Objective:** Determine the association between metabolic syndrome and elevated alanine aminotransferase in school-aged obese children. **Materials and Methods:** An observational analytic cross-sectional study was conducted in 130 obese patients aged 5-17 years (54 males 41.5% and 76 females 58.5%) who were followed up at the pediatric endocrine clinic at Tishreen University Hospital in Latakia between April 2023 and March 2024 and who met the eligibility criteria and had complete data. **Results:** Out of 130 obese children, 60 children (46.2%) were diagnosed with metabolic syndrome, and 41 children (31.5%) had elevated alanine aminotransferase levels. The percentage of elevated alanine aminotransferase levels among individuals with the syndrome was 65.9%. Additionally, a significant positive correlation was observed between elevated alanine aminotransferase levels and blood sugar, triglyceride levels, and waist circumference. **Conclusion:** The study revealed a significant association between metabolic syndrome and elevated alanine aminotransferase levels. Moreover, unexplained increases in alanine aminotransferase levels in obese children may be indicative of nonalcoholic fatty liver disease.

KEYWORDS: Metabolic syndrome, elevated alanine aminotransferase, non-alcoholic fatty liver disease, obese children.

INTRODUCTION

The association between Metabolic Syndrome (MetS) and elevated levels of Alanine Aminotransferase (ALT) in school-aged obese children is a critical area of research, particularly given the rising prevalence of obesity in this demographic. MetS is characterized by the presence of at least three of the following conditions: including increased waist circumference, high blood pressure, elevated fasting glucose, and dyslipidemia, which collectively increase the risk of cardiovascular disease and type 2 diabetes.^[1]

Elevated ALT levels serve as a biomarker for liver injury, and their increase is often indicative of liver inflammation or damage, commonly associated with Non-alcoholic fatty liver disease (NAFLD).^[2] NAFLD is particularly concerning in children, as it can progress to more severe liver conditions, including non-alcoholic steatohepatitis (NASH), fibrosis, and cirrhosis.^[3]

The prevalence rate of NAFLD is dramatically increasing in parallel with the rising prevalence of obesity and metabolic syndrome. It reaches a prevalence of 38% among obese children and approximately 25% globally.^[4,5]

The presence of elevated ALT levels in obese children with Metabolic Syndrome underscores the potential hepatic complications associated with this metabolic condition.^[6,7]

Investigating the relationship between Metabolic Syndrome and elevated ALT levels in school-aged obese children not only sheds light on the pathophysiological mechanisms underlying these conditions but also informs healthcare professionals about the necessity of early detection and intervention strategies to prevent adverse health outcomes.^[8,9,10]

METHODS AND PATIENTS

Study the population

The study concentrated on obese children attending the Pediatric Endocrine Clinic at Tishreen University Hospital in Lattakia, excluding those with preexisting liver disease, hemochromatosis, and genetic syndromes associated with obesity, such as Prader-Willi syndrome. Additionally, participants taking medications that affect metabolic syndrome or ALT levels were not included in the study. Following informed consent from the child's guardian, a comprehensive assessment was conducted. This included measuring the child's waist circumference

waist circumference (WC), weight, height and body mass index (BMI) to determine obesity levels according to CDC guidelines as follows: Overweight with BMI \geq 85th and $<$ 95th, obese with BMI \geq 95th and $<$ 99th and severe obese with BMI \geq 99th.

Blood pressure was recorded in accordance with American Academy of Pediatrics (AAP) standards. A morning venous blood sample was also collected to analyze various biomarkers, including fasting blood sugar, lipid profiles, and ALT levels.

Metabolic Syndrome (MetS) was diagnosed based on pediatric and adolescent criteria adapted from the National Cholesterol Education Program Adult Treatment Panel Third (NCEP-ATP III) definition. Children meeting three or more of the following criteria were diagnosed with MS: FBG \geq 100 mg/dl, TG \geq 110 mg/dl, WC \geq 90th percentile for age and sex, systolic or diastolic blood pressure \geq 90th percentile for age and sex and HDL cholesterol \leq 40 mg/dl.^[11]

Based on these evaluations, participants were classified into two groups: those with metabolic syndrome and those without.

Statistical analysis

The statistical analysis included both descriptive and inferential statistics based on the tests of statistics. Descriptive statistics were used for quantitative variables calculating the mean and standard deviation, and for qualitative variables, frequencies and percentages were calculated. Inferential statistics were conducted using the Chi-square test to study the relationship between qualitative variables. The results were considered statistically significant with a p-value \leq 5%. The IBM SPSS statistics (version 25) program was used to calculate statistical coefficients and analyze results.

RESULTS

A total of 130 children, 76 of whom were females, who constituted 58.5% of the sample, and 54 of whom were males, who constituted 41.5%. The children's ages ranged from 5 to 17 years, with an average age of 10.06 ± 2.7 years. Among the age groups, the 8-12 age range represented the largest percentage of the research sample at 49.2%. Additionally, the study identified 45 children classified as overweight (34.6%), 51 as obese (39.2%), and 34 as severely obese (26.2%).

Table 1: Distribution of study sample according to the occurrence of metabolic syndrome and elevated levels of (ALT).

Metabolic Syndrome	Number	Percentage %
Positive	60	46.2%
Negative	70	53.8%
Total	130	100%
Elevated levels of (ALT)	Number	Percentage %
Present	41	31.5%
Absent	89	68.5%
Total	130	100%

As shown in Table 1, 31.5% of obese children had high ALT values, and 46.2% of these children had metabolic syndrome. The investigation into the relationship between high ALT values and factors such as gender, age, and obesity levels did not reveal any statistically significant associations, except to note that obese children constituted the largest proportion of individuals with elevated ALT values.

Table 2: Distribution of study sample by the relation between elevated ALT values and metabolic syndrome.

Metabolic Syndrome	Elevated levels of (ALT)		P-value
	Present	Absent	
Positive	27 (65.9%)	33 (37.1%)	0.002
Negative	14 (34.1%)	56 (62.9%)	

Based on the results presented in Table 2, elevated ALT levels in obese children are statistically significantly associated with metabolic syndrome, with a p-value of 0.002. There was a strong correlation between elevated ALT levels and a positive diagnosis of metabolic syndrome in 65.9% of cases with elevated ALT levels.

Table 3: Distribution of the study sample according to the occurrence of elevated ALT values and the diagnostic criteria for metabolic syndrome.

the diagnostic criteria for (MetS)	Elevated levels of (ALT)		P-value
	Present	Absent	
↑TG	19 (46.3%)	24 (26.9%)	0.03
↓HDL	16 (39%)	32 (36%)	0.7
↑GLU	18 (43.9%)	18 (20.2%)	0.005
↑WC	27 (65.9%)	40 (44.9%)	0.02
↑BP	11 (26.8%)	16 (17.9%)	0.4

TG: Triglycerides, HDL: High-density lipoprotein, GLU: Glucose, WC: Waist circumference, BP: Blood pressure.

Based on Table 3, a statistically significant relationship was observed between elevated ALT values and blood sugar, triglycerides, and waist circumference except for high blood pressure and low HDL.

DISCUSSION

The association between metabolic syndrome and elevated ALT levels in obese children is critical for elucidating the connections between these conditions and their implications for pediatric health.

The metabolic syndrome is considered a risk factor for cardiovascular diseases, type 2 diabetes, and multi-cause mortality, in addition to other disorders such as fibrinolysis, thrombosis, and inflammation.^[12,13]

Elevated ALT levels may be associated with the development of metabolic syndrome, diabetes, and cardiovascular diseases.^[14]

In this study, metabolic syndrome was diagnosed in 46.2% of the participants according to the NCEP-ATP III criteria, and 31.5% of the total sample exhibited elevated levels of Alanine aminotransferase (ALT). The prevalence of elevated ALT levels was 65.9% among individuals with metabolic syndrome versus 34.1% among those without.

The relationship between elevated ALT levels and blood glucose, triglycerides, and waist circumference was significant, with the strongest correlation observed between elevated ALT levels and high blood glucose levels.

The association between elevated ALT levels and variables such as sex, age, and degrees of obesity was investigated, revealing no statistically significant correlation with any of these factors. However, obese children represented the highest percentage of those with elevated ALT levels.

These findings emphasize the need for comprehensive metabolic syndrome and liver health screenings in pediatric obesity clinics. Additionally, further research is needed to understand the specific mechanisms connecting metabolic syndrome and elevated ALT levels in obese children. This knowledge is essential to developing targeted interventions and improving health outcomes in this vulnerable population.

However, the potential mechanisms explaining the relationship between ALT levels and the occurrence of metabolic syndrome may include the association of elevated ALT with increased liver fat content, which is accompanied by insulin resistance.^[15] Additionally, hyperinsulinemia leads to hepatic steatosis through increased triglyceride synthesis and decreased protein synthesis.^[16] Furthermore, the relationship between ALT and insulin sensitivity has been demonstrated regardless of body mass index^[17], where plasma ALT levels in individuals with well-controlled diabetes have been associated with reduced insulin sensitivity as well as reduced endothelial function.^[18] Aside from hepatic steatosis, insulin resistance also contributes to fibrosis through increased beta-oxidation of fatty acids and oxidative stress.^[19] The liver also becomes susceptible to lipid metabolism disorders, including elevated total cholesterol, triglycerides, and LDL-C levels.^[20]

Zhao et al. Explored biochemical markers related to metabolic syndrome among Beijing adolescents, which highlights the public health significance of metabolic disorders in the youth population.^[21]

Similarly, Park et al. Reported a connection between elevated serum alanine aminotransferase (ALT) levels and metabolic syndrome in Korean adolescents, suggesting that liver function tests may act as biomarkers for assessing metabolic syndrome.^[22]

In a study involving Mexican children, Elizondo-Montemayor et al. Identified a significant association between ALT levels and metabolic syndrome, further reinforcing the correlation observed across various ethnic groups.^[23]

More recently, research by Bergmann et al. and Valle-Martos et al. has continued to emphasize the role of liver enzymes, including both fasting and postprandial levels, in predicting metabolic syndrome and related conditions such as prediabetes and obesity in prepubertal children.^[24]

The study had several limitations, including a small sample size and a cross-sectional design that made it difficult to establish causal relationships with accuracy. Although liver biopsy remains the gold standard for diagnosing NAFLD, the study used ALT as a surrogate for the disease. However, research suggests that ALT is a more sensitive indicator of NAFLD compared to aspartate aminotransferase (AST).^[25] Furthermore, the NASPGHAN has recommended the use of ALT to diagnose NAFLD in overweight and obese children beginning at the age of 9 years, with a sensitivity of 88% and a specificity of 26%.^[26]

CONCLUSION

According to these findings, metabolic syndrome is significantly associated with elevated ALT levels, emphasizing the importance of early detection and intervention in vulnerable populations. Therefore, we recommend routine screening for both metabolic syndrome and ALT levels in obese children across various age groups. Additionally, more longitudinal or interventional studies should be conducted to gain a deeper understanding of the causal relationship between these two conditions.

Declarations

Ethical approval and consent to participate:

Ethical approval for this study was obtained from the Scientific Research Ethics Committee at Tishreen University in April 2023 following the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of Data and Materials

All the data generated or analyzed during this study are included in this published article. The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests: None.

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Author Contribution

Fatima Bress collected the data, checked the quality of the data collection, analyzed and interpreted the data, designed and coordinated the study, undertook and checked the quality assessment, produced the first draft of the manuscript, wrote and edited the manuscript and approved the final manuscript before submission.

The project was supervised by Ahmad Chreitah and Mazen Ghalia. The authors conducted the quality assessment, evaluated the collected data, analyzed and interpreted the data, checked the quality assessment, edited the manuscript and approved the final manuscript.

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