



Article

# Evaluation of Circulating Chitotriosidase Activity in Children with Obesity

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**Abstract:** Childhood obesity progresses to metabolic disturbances via low-grade inflammation. Identifying novel molecules that reflect the activity of the immune responses is critical in understanding its underlying pathogenesis. Our exploratory study aimed to evaluate the change of chitotriosidase (CHIT1) plasma activity according to Body Mass Index (BMI)-for-age z score in pediatric patients. The study evaluated 68 children consisting of 47.1% girls with a mean age of  $12.47 \pm 3.71$  years and 52.9% boys with a mean age of  $11.93 \pm 3.18$  years. The effect of the most frequent CHIT1 gene variants, the 24 base pair duplication (*dup24*) and *G102S* polymorphism, upon the association between circulating CHIT1 activity and the obesity level, was also investigated. A significantly higher logCHIT1 plasma activity was found in children with extreme obesity than in children with overweight ( $p = 0.048$  for the uncorrected CHIT1 and  $0.026$  for the corrected CHIT1). The BMI-for-age z score significantly ( $p = 0.031$ ) predicts increased CHIT1 activity in children with overweight, obesity, and extreme obesity after controlling for the two gene variants, age, gender, and time since weight gain. *Dup24* and *G102S* polymorphism were also significant independent predictors ( $p$ -values  $< 0.002$ ) for the change of CHIT1 plasma activity. Circulating CHIT1 might be an accurate indicator of inflammation in children with obesity. Its role and the effect of the *dup24* and *G102S* variants on the CHIT1 activity should be validated in a larger cohort.

**Keywords:** inflammation; Body Mass Index (BMI); human chitotriosidase (CHIT1); 24 bp duplication (*dup24*); *G102S* polymorphism; macrophage activation; obesity-driven inflammation

## 1. Introduction

Chronic low-grade inflammation is a process that links obesity with metabolic disturbances via macrophage polarization and activation of the acquired immune cells [1,2]. A high level of obesity results in a 17-fold increase in the cardiovascular risk in children and leads to obesity-driven complications such as metabolic syndrome and type 2 diabetes mellitus [3,4]. In clinical practice, it is a challenge to find indicators and biomarkers for the

# Chronic Inflammatory Markers in Overweight and Obese Children: A Cross-sectional Analytical Study

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## Abstract

**Introduction:** Childhood obesity is associated with chronic low-grade systemic inflammation, which results in obesity-related comorbidities. This study compared the inflammatory markers between obese and normal children and assessed obesity-related comorbidities. **Methods:** In this cross-sectional analytical study, 40 obese children between 5-18 years of age were recruited as cases, and an equal number of age and gender-matched normal children as the control. The inflammatory markers-high sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), interleukin-10 (IL-10), and adiponectin were compared between the groups. Hypothyroidism, dyslipidemia, insulin resistance, hypertension, and nonalcoholic fatty liver disease (NAFLD) were screened among obese children. **Results:** We observed a male-female ratio of 1.5:1 in each group. The median hs-CRP between obese and normal children were 2.53 mg/L (0.94,6.85) and 0.77 mg/L (0.19,7.19), and the median IL-6 levels were 3.56 pg/ml (2.17,5.48) and 3.76 pg/ml (1.08,7.91) respectively. The median IL-10 levels between obese and control groups were 2.06 pg/ml (0.35,6.3) and 1.82 pg/ml (0.41,6.5), and the median adiponectin levels between the groups were 8.6 mcg/ml (6.65,16.04) and 9.79 mcg/ml (8.45,11.91) respectively. We didn't observe significant differences in the markers between the groups. Dyslipidemia, insulin resistance, and metabolic syndrome were seen in 80%, 52.5%, and 45% of obese children, respectively. Other comorbidities-NAFLD, hypertension, and hypothyroidism, were observed in 27.5%, 25%, and 7.5% of obese children, respectively. IL-6 had a significant positive correlation with total cholesterol ( $r = 0.40$ ), LDL levels ( $r = 0.50$ ), and HDL ( $r = 0.32$ ). **Conclusion:** There was no difference in inflammatory markers between obese and normal children. Dyslipidemia and insulin resistance were the most common comorbidities.

**Keywords:** Children, co-morbidity, inflammatory markers, obesity

## INTRODUCTION

Childhood obesity has become an epidemic in the twenty-first century. The prevalence has increased from 5.4% to 7.8% among children aged 3–15 during the COVID-19 pandemic due to social restrictions, decreased physical activity, reduced access to healthy foods, increased stress, screen time and consumption of processed foods and sugary drinks.<sup>[1]</sup> Obesity is associated with low-grade systemic inflammation, which activates the immune system and alters the secretion of inflammatory markers. The development of adipose tissue hypertrophy in obese individuals results in intracellular oxidative stress and hypoxia, triggering the release of proinflammatory cytokines like high sensitivity C-reactive protein (hs-CRP), tumour necrosis factor (TNF) and interleukin-6 (IL-6) and decreased production of anti-inflammatory markers like interleukin-13 (IL-13),

interleukin-10 (IL-10), interleukin-4 (IL-4) and adiponectin, thus resulting in metabolic syndrome.<sup>[2,3]</sup> Also, CRP and IL-6 levels were significantly related to the degree of obesity and tend to increase with the number of components of metabolic syndrome.<sup>[4]</sup> Studies have reported the beneficial effect of anti-interleukin-1 therapy on reducing the HbA1c in type 2 diabetes.<sup>[5]</sup> Thus, identifying these inflammatory markers in children would help us to use targeted therapy against these

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## Review

# Pediatric Obesity: Complications and Current Day Management

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**Abstract:** Obesity affects approximately 1 in 5 youth globally and increases the risk of complications during adolescence and young adulthood, including type 2 diabetes, dyslipidemia, hypertension, non-alcoholic fatty liver disease, obstructive sleep apnea, and polycystic ovary syndrome. Children and adolescents with obesity frequently experience weight stigma and have an impaired quality of life, which may exacerbate weight gain. Pediatric obesity is typically defined using sex-, age-, and population-specific body mass index percentiles. Once identified, pediatric obesity should always be managed with lifestyle modification. However, adolescents with obesity may also benefit from anti-obesity medications (AOM), several of which have been approved for use in adolescents by the US Food and Drug Administration, including liraglutide, phentermine/topiramate, and semaglutide. For children with specific, rare monogenic obesity disorders, setmelanotide is available and may lead to significant weight loss. Metabolic and bariatric surgery may be used for the management of severe obesity in youth; though highly effective, it is limited to specialized centers and has had relatively low pediatric uptake. In this narrative review using pediatric-focused data from original research, reviews, clinical practice guidelines, governmental agencies, and pharmaceutical companies, we review obesity-related metabolic complications in youth and management strategies, including AOM and bariatric surgery.

**Keywords:** obesity; pediatric; type 2 diabetes mellitus; dyslipidemia; hypertension; obstructive sleep apnea; PCOS; anti-obesity medications; bariatric surgery



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## 1. Introduction

Obesity is a growing threat to children's health globally, affecting approximately 20% of children and adolescents in the United States [1] and worldwide [2]. This change has been due largely to the increasing access to, and affordability of, ultra-processed and energy-dense foods, as well as reduced physical activity [3]. Striking inequities in obesity prevalence by race/ethnicity, and socioeconomic status exist [4,5] (though the role of income is reversed in low- versus middle- or high-income countries [6]), contributing to widening disparities in the incidence of obesity-related conditions such as youth-onset type 2 diabetes (T2D) [7,8]. The emergence of such obesity-related complications in childhood underscores the critical importance of pediatric obesity prevention and treatment, as well as assessing for complications including T2D, dyslipidemia, hypertension, non-alcoholic fatty liver disease, obstructive sleep apnea, and polycystic ovary syndrome [9]. Lifestyle management through behavioral modification has a central role in reducing the risk of obesity-associated comorbidities, though the intensity and duration of programs that drive success can also be infeasible for clinicians to implement and for youth and families to attend. In recent years, the United States (US) Food and Drug Administration (FDA) has approved several AOMs for adolescents with obesity. In 2023, the American Academy of Pediatrics (AAP) released clinical practice guidelines (CPG) endorsing the use of such therapies without

Review

# Obesity and Adipose Tissue Dysfunction: From Pediatrics to Adults

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**Abstract:** Obesity is a growing health problem that affects both children and adults. The increasing prevalence of childhood obesity is associated with comorbidities such as cardiovascular disease, type 2 diabetes and metabolic syndrome due to chronic low-grade inflammation present at early stages of the disease. In pediatric patients suffering from obesity, the role of epigenetics, the gut microbiome and intrauterine environment have emerged as causative factors. Interestingly, pediatric obesity is strongly associated with low birth weight. Accelerated weight gain oftentimes occurs in these individuals during the post-natal period, which can lead to increased risk of adiposity and metabolic disease. The pathophysiology of obesity is complex and involves biological and physiological factors compounded by societal factors such as family and community. On a cellular level, adipocytes contained within adipose tissue become dysregulated and further contribute to development of comorbidities similar to those present in adults with obesity. This review provides an overview of the current understanding of adipose tissue immune, inflammatory and metabolic adaptation of the adipose tissue in obesity. Early cellular changes as well as the role of immune cells and inflammation on the progression of disease in pivotal pediatric clinical trials, adult studies and mouse models are emphasized. Understanding the initial molecular and cellular changes that occur during obesity can facilitate new and improved treatments aimed at early intervention and subsequent prevention of adulthood comorbidities.

**Keywords:** obesity; pediatric obesity; adipose immunity; immune system; pediatric obesity and inflammatory dysregulation



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## 1. Introduction

Obesity is a global health epidemic that affects both children and adults. Obese children are more likely to become obese adults [1] and it is estimated that almost half of the world's adult population will be overweight or obese by 2030 [2]. The onset of obesity is occurring at younger ages in the last decade than previous generations [3]. Approximately 18.5% of youth in the United States meet the criteria for obesity (body mass index [BMI]  $\geq$  95th percentile for age and sex), while 8.5% of those 12 to 19 years of age are categorized as severely obese (BMI  $\geq$  120% of the 95th percentile), representing approximately 4.5 million children [4]. Most studies investigating obesity involve adults; however, it is essential for studies to focus on childhood/adolescent obesity to prevent its associated complications such as cardiovascular disease, type 2 diabetes mellitus, metabolic syndrome, and non-alcoholic fatty liver disease. Pediatric obesity has both near and long-term impacts as the physiological changes altered by obesity occur at crucial developmental