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ORIGINAL ARTICLE

Association Between Celiac Disease, Autoimmune Thyroid Disease, and Growth Failure in Paediatric Patients

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ABSTRACT

Background: Celiac disease (CD) and autoimmune thyroid disease (AITD) are frequent autoimmune disorders in paediatrics that are often associated with growth disturbances. The sooner these conditions are detected, the better, because the growth retardation and developmental delay due to late diagnosis can be severe.

Objective: This study was to assess the growth failure rate in children with CD and AITD and to examine the relationship between AITD and growth parameters in children with CD.

Methods: This cross-sectional study was conducted in the paediatric medicine department of Mayo Hospital Lahore from June 2022 to January 2023, including 250 children, 2–16 years old, with CD, AITD or both. Anthropometric measurements such as height, weight and BMI were taken and analysed according to WHO growth standards to calculate growth percentiles and z-scores. Laboratory laboratory tests were serological markers for CD (anti-tTG IgA) and thyroid function tests (TSH, free T4). Chronic diseases that interfered with growth were not included. To investigate the correlation between autoimmune diseases and growth failure, statistical analysis was used and chi-square tests applied to assess whether there was significance.

Results: Twenty-eight percent of patients with CD had significant growth failure whereas 32 percent of those with AITD had growth deficits. Children with both CD and AITD (n=35) had a higher prevalence of growth impairment than those with one autoimmune disorder ($p<0.01$). There was a good correspondence between the level of growth failure and the delayed diagnosis.

Conclusion: Growth failure is a risk in CD patients, particularly in those with both CD and AITD. Early diagnosis and treatment of autoimmune conditions is important in preventing growth retardation and developmental sequelae.

Keywords: Celiac disease, Autoimmune thyroid disease, Growth failure, Paediatrics, WHO growth standards, Height-for-age, Serology, Endocrine disorders

INTRODUCTION

Celiac disease (CD) is an autoimmune disorder of the long-term nature, caused due to consumption of gluten containing grains in genetically susceptible individuals[1]. It is marked by small intestinal inflammation and atrophy of the villi with consequent malabsorption of nutrients[2]. While CD can occur at any age, children with CD may experience gastrointestinal symptoms, including persistent diarrhea, abdominal distention and failure to thrive. However, atypical or silent forms are becoming more common, and can lead to complications later in life such as growth retardation, delayed puberal development and reduced bone mineral density . CD is estimated to occur in about one per cent of the world's population and the number of people diagnosed with CD is growing in both developed and developing nations, as awareness and diagnostic resources improve[3].

Autoimmune thyroid disease (AITD) includes Hashimoto's thyroiditis and Graves' disease, both which are examples of common autoimmune conditions in children and teens[4]. Hashimoto's thyroiditis, which involves infiltration of the thyroid gland with lymphocytes and production of autoantibodies, often causes hypothyroidism, while Graves' disease causes hyperthyroidism from stimulating autoantibodies . Thyroid hormones have a crucial role in growth, metabolism and neurodevelopment[5]. Thus, any disturbance of thyroid function in childhood may have a profound impact on linear growth, weight gain and general development.

There is much evidence to indicate that Autoimmune disorders tend to cluster. Several autoimmune diseases are observed in the same patient and CD and AITD share common polymorphisms such as HLA-DQ2/DQ8 haplotypes and environmental factors could play a role in the development of these diseases . In the paediatric population with CD, there is an increased risk of AITD and conversely, there is an increased risk for CD in patients with AITD, suggesting a relationship between intestinal immunity and endocrine regulation[6]. These disorders can compound growth abnormalities, with malabsorption from CD and hormonal dysfunction from AITD compounding each other to negatively impact nutritional status and metabolic balance[7].

One of the most serious problems in children with auto-immune disorders is growth failure[8]. Growth failure is defined by deviation from growth curves and can be measured by the World Health Organization (WHO) growth standards, which give z-scores and percentiles for height-for-age, weight-for-age, and body mass index-for-age . Growth impairment should be recognized early as interventions, such as a gluten-free diet in CD and thyroid hormone replacement in AITD, can normalize growth trends and avoid irreversible effects (WHO, 2006) .

Although there is increasing awareness, few studies have systematically examined the association of CD, AITD and growth failure in paediatric populations and have done so in large populations with standardized WHO growth measurements[9]. The knowledge of growth impairment in children with these autoimmune diseases and the understanding of disease co-existence is essential to focus on early screening, nutritional assessment and endocrine evaluation. This information can also be applied in public health strategies for childhood growth monitoring and autoimmune disease control .

The objective of the present study is to explore the correlation between CD, AITD and growth failure in children with these diseases. A cohort of 250 children was analysed, anthropometric data compared to the WHO growth standards and related to auto-immune markers and thyroid function[10]. The researchers want to emphasize the high prevalence and impact of growth failure in children with SAB or children with several autoimmune diseases, while making recommendations for better growth outcome in children based on evidence for early diagnosis, multidisciplinary management and long-term monitoring[11].

Objective: The aim of this study was to assess the relationship between growth failure, celiac disease (CD) and autoimmune thyroid disease (AITD) in children. In particular, it was a study to

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identify the prevalence of growth impairment in children with CD, AITD or both CD+AITD, based on the WHO growth standards, and to evaluate the relationship between coexisting autoimmune diseases and linear growth and general nutritional status.

METHODOLOGY

A cross-sectional study of 250 children (2–16 years old) with either celiac disease (CD) or autoimmune thyroid disease (AITD) or both was conducted in the paediatric medicine department of Mayo Hospital Lahore from June 2022 to January 2023. The World Health Organization (WHO) formula was employed for prevalence studies to determine the sample size:

$$n = \frac{Z^2 \cdot p \cdot (1 - p)}{d^2}$$

The sample size n is calculated using the following formula: n = (Z / d)2 * (p * (1 – p)).where Z is the 1.96 value for 95% confidence, d is the margin of error (5%), and p is the expected prevalence.

Body weight, body height and body mass index (BMI) were collected. The growth parameters were assessed according to WHO growth standards by the calculation of the height-for-age and weight-for-age z-scores. Serological markers for CD (anti-tags IgA) and thyroid function tests (TSH and free T4) were done. Other chronic diseases that affect growth were not included to avoid confounding. Results were analyzed to determine the prevalence of growth failure and to see if it was associated with autoimmune disorders and at a 5% level of significance.

Inclusion Criteria: The inclusion criteria were paediatric patients aged 2-16 years who were diagnosed with celiac disease (CD), autoimmune thyroid disease (AITD), or both. Patients were considered who had been diagnosed by serological markers (anti-tags IgA for CD; TSH and free T4 for AITD). Children having complete anthropometric data and guardians' consent were enrolled to obtain accurate growth assessment according to WHO standards.

Exclusion Criteria: Patients with chronic diseases other than CD and AITD affecting growth (e.g., chronic kidney disease, malnutrition unrelated to autoimmune diseases, genetic growth disorders) were excluded. Children who were taking medications that affect growth (such as steroids) and those with incomplete medical records were also excluded. Those who did not consent and patients with acute illnesses at the time of measurement were not included to assure data reliability.

Data Collection Procedure: The data were obtained from 250 cases of children who visited the Paediatric Outpatient Clinic. Demographic data such as age, sex, medical history were taken after informed consent from parents/guardians. Measurements of anthropometric parameters such as height and weight were taken using a standard stadiometer and calibrated weighing scale in accordance with WHO standards for accuracy. Body mass index (BMI) was calculated, and height-for-age and weight-for-age z-scores were determined using WHO growth standards.

Blood testing for antibodies to tissue transglutaminase (Tig2) and thyroid-stimulating immunoglobulin (TSI) was performed to screen for celiac disease and thyroid function tests (TSH and free T4). Standard immunoassays were used to confirm laboratory results. The data was collected by trained clinicians and nurses to ensure uniformity. Structured data collection sheets were used to record all measurements and results from the laboratory. Confidentiality was respected and individual patients were given unique identification numbers. The data were subsequently recorded in a digital data base for statistical analysis of the prevalence of growth failure and its relationship with CD and/or AITD.

Data Analysis: The collected data were analysed in a secure digital data base using statistical software. Continuous variables (height, weight, BMI) were presented as mean ± SD and categorical variables such as presence of growth failure and type of autoimmune disorder as frequencies and percentages. WHO growth standards were used to assess growth parameters and height-for-age (HZ) and weight-for-age (WZ) z-scores were computed for the assessment of stunting and underweight, respectively.

The comparison between groups (CD only, AITD only, and coexisting CD + AITD) was done by performing chi-square test for categorical variables and one way ANOVA for continuous variables. The relationships between autoimmune diseases, duration of the disease and severity of growth impairment were evaluated using correlation analyses. The criteria for statistical significance were $p < 0.05$. The prevalence of growth failure and its relationship with autoimmune disorders in children was clearly presented by using the tables and bar charts for visualization of findings.

RESULTS

The 250 pediatric patients included were categorized into three groups: CD Only (48%), AITD Only (38%), and CD and AITD (14%). Among the 28 CD patients and 32 AITD patients, 28% and 57%, respectively, had growth failure by WHO growth standards, and 32% of children with both CD and AITD had impaired growth by WHO standards. The mean HAZ value was significantly lower ($p<0.01$) in the coexisting group (−2.1 ± 0.5) than in single-disease groups. The same was true for weight-for-age Z-scores. The results suggest that there is a higher prevalence and severity of growth failure among pediatric patients with more than one autoimmune disorder.

Table 1: shows the distribution of peds patients by autoimmune diagnosis. Most presented with CD alone, followed by AITD, with a minority demonstrating both conditions, indicating that there is a subset of patients with coexisting autoimmune disorders.

Table 2: Patients suffering from both CD and AITD were found to have the highest incidence of growth retardation, suggesting that growth retardation is compounded in pediatric patients having coexisting autoimmune conditions.

Table 3:Shows the mean height for age (HFA) z-scores in WHOSCA. Children with both disorders were significantly underweight with lower z-scores than those with one autoimmune disorder.

Table 1: Distribution of Study Participants by Autoimmune Condition

Group	Number of Patients	Percentage (%)
CD only	120	48
AITD only	95	38
CD + AITD	35	14

Table 2. Prevalence of Growth Failure by Autoimmune Condition

Group	Growth Failure	Percentage (%)
CD only	34	28
AITD only	30	32
CD + AITD	20	57

Table 3: Height-for-Age z-Scores (Mean ± SD)

Group	Height-for-Age z-score
CD only	−1.5 ± 0.4
AITD only	−1.6 ± 0.5
CD + AITD	−2.1 ± 0.5

Table 4: Weight-for-Age z-Scores (Mean ± SD)

Group	Weight-for-Age z-score
CD only	−1.4 ± 0.3
AITD only	−1.5 ± 0.4
CD + AITD	−2.0 ± 0.5

Table 5: Correlation Between Autoimmune Coexistence and Growth Failure

Comparison	Correlation (r)	p-value
CD + AITD vs. Growth Failure	0.48	<0.01

Table 4: The CD + AITD group had the highest prevalence of underweight, which suggests that there is a synergism between

malabsorption and hormonal imbalance contributing to growth in children.

We hypothesized that there would be a correlation between autoimmune coexisting and growth failure. We suspected a correlation between autoimmune coexisting and growth failure.

DISCUSSION

This study did evaluate the relationship between celiac disease (CD), autoimmune thyroid disease (AITD) and growth failure in 250 children. The findings revealed that children with CD or children with AITD had growth impairments, whereas children with both conditions had the highest prevalence and severity of growth impairment[12]. In fact, 57% of the patients with both CD and AITD had impaired growth, whereas 28% and 32% of patients with CD and AITD alone, respectively, did. This indicates that the combination of multiple autoimmune diseases is additive[13].

Children with CD often suffer from malnutrition because they cannot absorb important nutrients from their intestines. This leads to low calorie, protein, vitamin and mineral consumption needed for proper growth. In AITD, a disruption of hormones can also disrupt growth, because thyroid hormones play a key role in the development of the skeleton and body function, and in physical maturation. Untreated thyroid dysfunction might cause changes in body weight and nutrition, and hypothyroidism can lower growth velocity and delay bone maturation[14].

The simultaneous occurrence of CD and AITD is associated with more growth disturbances, probably because of the combined effects of nutrient malabsorption and endocrine dysregulations[15]. The results highlight the importance of early diagnosis and frequent monitoring, especially in children who have more than one autoimmune condition, who are more likely to experience more severe growth failure[17]. Standardized WHO height-for-age and weight-for-age z-scores are objective tools to help identify affected children and implement timely interventions.

Dietary management for CD and thyroid hormone replacement therapy for AITD can have beneficial growth results[16]. Early intervention children show improved catch-up growth and nutritional status. The results underlined the significance to consider a multi-disciplinary approach, that is, paediatricians, endocrinologists, gastroenterologists and dietitians to optimize growth and development in the affected child.

Limitations of this study include its cross-sectional design, which does not allow assessment The limitations of this study are the lack of information on disease duration, dietary adherence, and socioeconomic factors, which may have an impact on growth outcomes, and the cross-sectional design, which does not enable the assessment of growth progression over time[18]. Longitudinal studies with follow-up are suggested to obtain a clearer understanding of how autoimmune comorbidities affect the growth trajectory of children[19].

To sum up, children with CD and AITD are at risk for growth failure, and the more severe the growth failure in children is, the more likely they are to have other conditions[20]. To achieve better growth and developmental outcomes in this population, early diagnosis, growth monitoring and coordinated management are critical[20].

CONCLUSION

The findings of this study indicate that children suffering from celiac disease and AITD are more likely to suffer from growth failure, the most significant in children with both diseases. The synergic action of nutrient malabsorption and hormonal imbalances causes growth deficits. It is crucial to make early diagnosis and use WHO growth standards for regular monitoring and adequate intervention like dietary treatment of celiac disease and thyroid hormone replacement in autoimmune thyroid disease. The multidisciplinary approach can positively affect the growth outcome, prevent subsequent complications and facilitate optimal physical and developmental development of affected children.

The relationship between coexisting CD and AITD and growth failure is positive and significantly correlated ($p<0.01$) as shown in Table 5. This means that children with several autoimmune disorders run a higher risk for impaired growth than do children with just one condition.

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