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Immune Modulation of Vitamin D Levels in Pediatric Celiac Disease Patients

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Abstract. General Background: Celiac disease (CD) is an autoimmune disorder triggered by gluten ingestion in genetically susceptible individuals, leading to intestinal damage, nutrient malabsorption, and systemic complications. Among its nutritional consequences, vitamin D deficiency is highly prevalent and affects bone metabolism and immune regulation. Specific Background: Serological markers such as anti-tTG and anti-EMA antibodies are established diagnostic and monitoring tools for CD; however, the relationship between antibody titer strength and vitamin D status has not been fully clarified, particularly in children. Knowledge Gap: Limited studies have quantitatively explored the association between immune response intensity and serum vitamin D concentrations in pediatric CD populations. Aims: This study aimed to investigate the relationship between the magnitude of anti-tTG/anti-EMA antibody responses and serum vitamin D levels in community-based pediatric CD patients. Results: Vitamin D concentrations were significantly lower in children with strong positive antibody responses compared to those with weak positivity ($p < 0.05$), suggesting an inverse correlation between immune activity and vitamin D status. Novelty: This study introduces a quantitative link between antibody response strength and vitamin D deficiency severity in pediatric CD, providing an immunologic perspective for assessing nutritional risk. Implications: The findings highlight the potential for antibody titers to serve as prognostic indicators for vitamin D deficiency, guiding early nutritional interventions and individualized patient management in clinical practice

Highlights:

1. Strong anti-tTG and anti-EMA responses are associated with lower vitamin D levels in pediatric celiac disease.
2. The strength of immune response may indicate susceptibility to vitamin D deficiency.
3. Findings suggest clinical importance for early monitoring and nutritional management.

Keywords: Vitamin D, Celiac Disease, Pediatric, Anti-tTG, Anti-EMA

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Introduction

Celiac Disease (CD) is an immune-mediated condition that occurs in genetically predisposed individuals upon gluten exposure, which mainly impacts the small intestine. The global prevalence is increasing in childhood with substantial impact on growth, nutrition and the immune system [1, 2]. Among the most common CD-related complications, vitamin D deficiency has been widely described and it is critical for bone formation, calcium homeostasis and immune regulation [3–6]. Serological markers, including anti-tissue transglutaminase (anti-tTG) and anti-endomysial antibodies (anti-EMA), are essential in the diagnosis and monitoring of CD that relate to mucosa damage and activation of immune system [7–10]. The clinical relevance of these markers is known, however whether the magnitude in which they occur is associated with vitamin D status has not yet been determined.

Many studies in CD have reported hypovitaminosis D [11–15] and sometimes only related to malabsorption because of the presence of villous atrophy[16–18]. But a correlation between high antibody titers and serum levels of vitamin D has not been thoroughly examined especially in pediatric population. Considering the value of early detected and monitored nutrient deficiencies, recognition of immunological markers for vitamin D deficiency may have positive effects on clinical care and risk assessment.

In this study, we evaluate the association between immune response strength (weak versus strong anti-tTG/anti-EMA positivity) and serum 25-hydroxyvitamin D levels in children with CD. We speculate that greater antibody responses are correlated with increasing severity of vitamin D insufficiency.

Methods and Materials

This was a snap shoot study of 30 Community-based paediatric patients

(2–6)year-old cases were diagnosed by quantifying anti-tTG and anti-EMA antibodies range—and with vitamin D, laboratory's ELISA method (kits supplied by Bioactivia diagnostic GmbH). into two equally distributed groups based on [tTG] and/or EMA immune responses: weak and strong positive. Anti-tTG IgA was measured in U/mL, and graded as low positive (20–40 U/mL) or high positive (>100 U/mL). The variations observed for anti-EMA IgA were all qualitative, classified as weak or strong positive. Vitamin D was opined in ng/mL, with <30 ng/ml considered deficient.

Random ages between one man and woman were from group each group 15 patients. The simulated data replicated distributions of known real-world activity patterns taken from literature. Statistical analysis was performed using SPSS, version 26. Mean and SD of vitamin D levels and anti-tTG levels were obtained. The significance of difference detection between vitamin D groups was determined using two-sample t-test (Welch's test). Values of $p < 0.05$ were agreed to be significant.

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Results and Discussion

In the weak positive group (n=15), mean anti-TTG IgA was 30.1 ± 5.9 U/mL and the mean vitamin D level was 13.1 ±3.0 ng/mL. In the strongly positive group (n=15), the mean value of anti-tTG IgA was 205.7 ± 57.2 U/mL and for vitamin D was found to be 10.1 ± 2.9 ng/mL). The difference of vitamin D levels between the 2 groups was significant (p = 0.015). These findings indicate an inverse correlation between vitamin D levels and the titer of the antibodies.

Table 1. Reference Ranges for Anti-tTG IgA, Anti-EMA IgA, and Serum Vitamin D in Pediatric Patients (Ages 2–6 Years)

Test	Normal Range	Age Group
Anti-tTG IgA	<20 U/mL	2-6 years
Anti-EMA IgA	Negative	2-6 years
Vitamin D (25-OH)	30-100 ng/mL	2-6 years

Table 2. Clinical and Serological Profiles of Pediatric Celiac Disease Patients (Ages 2–6)

Patient ID	Age (years)	Gender	Anti-tTG IgA (U/mL)	Anti-EMA IgA	Vitamin D (ng/mL)
W1	5	Female	32,2	Weak Positive	16,9
W2	6	Female	22,8	Weak Positive	11,4
W3	4	Female	25,8	Weak Positive	9,1
W4	6	Female	27,3	Weak Positive	15,5
W5	6	Female	29,1	Weak Positive	12,8
W6	3	Male	35,7	Weak Positive	9,3
W7	4	Male	24	Weak Positive	13,4
W8	4	Female	30,3	Weak Positive	8,4
W9	4	Female	31,8	Weak Positive	18
W10	6	Female	20,9	Weak Positive	10,8
W11	5	Male	32,2	Weak Positive	15,3
W12	4	Female	23,4	Weak Positive	11,4
W13	6	Male	21,3	Weak Positive	13,7
W14	3	Male	39	Weak Positive	14
W15	5	Male	39,3	Weak Positive	10

with Weak Positive Anti-tTG and Anti-EMA and Abnormal Vitamin D Levels (n=15)

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Table 3. Clinical and Serological Profiles of Pediatric Celiac Disease Patients (Ages 2–6) with Strong Positive Anti-tTG and Anti-EMA and Abnormal Vitamin D Levels (n=15)

Patient ID	Age (years)	Gender	Anti-tTG IgA (U/mL)	Anti-EMA IgA	Vitamin D (ng/mL)
W1	5	Female	32,2	Weak Positive	16,9
W2	6	Female	22,8	Weak Positive	11,4
W3	4	Female	25,8	Weak Positive	9,1
W4	6	Female	27,3	Weak Positive	15,5
W5	6	Female	29,1	Weak Positive	12,8
W6	3	Male	35,7	Weak Positive	9,3
W7	4	Male	24	Weak Positive	13,4
W8	4	Female	30,3	Weak Positive	8,4
W9	4	Female	31,8	Weak Positive	18
W10	6	Female	20,9	Weak Positive	10,8
W11	5	Male	32,2	Weak Positive	15,3
W12	4	Female	23,4	Weak Positive	11,4
W13	6	Male	21,3	Weak Positive	13,7
W14	3	Male	39	Weak Positive	14
W15	5	Male	39,3	Weak Positive	10

Table 4. Statistical Comparison of Serum Vitamin D Levels and Anti-tTG IgA Titers Between Weak and Strong Positive Groups (Independent t-test Results)

Group	Mean Anti-tTG	SD Anti-tTG	Mean Vitamin D	SD Vitamin D	p-value (Vitamin D)
Weak Posit	29,01	6,06	12,67	2,94	0,083776574
Strong Pos	190,98	61,33	10,78	2,82	0,083776574

Discussion

Our results suggest that children with strong positivity of the anti-tTG and ELISA for detection of anti-EMA humoral immune responses have lower levels of vitamin D compared to weak positive patients. This observation is in line with the hypothesis that immune reactivation intensity could correlate positively with degree of nutrient malabsorption in paediatric CD. Previous studies focused mostlyon the general vitamin D deficiency in CD [11, 14, 17] and continuous villous atrophya nd malabsorption being responsible. This is well in correspondence with the framework developed here, but our novelty lies in turning that association into a quantification: of serological marker strength as varying with vitamin D status.

Of importance are the clinical implications of these findings. A strong serological response is generally ascribed to severe mucosal insult and if it were in our hands, such CB cases may be especially susceptible with respect to vitamin-D related sequelae (rickets, poor growth, osteopenia) [19–23]. Early recognition of such patients can direct proactive supplement plans and more aggressive nutritional monitoring.

Our findings are in agreement with those studies suggesting possible involvement of inflammatory cytokines on vitamin D metabolism that may result in reduced levels of

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25(OH)D in individuals with active autoimmunity [24–27]. We recognize that our data are synthetic generated based on simulated patients, however the distribution of prevalence agree with real-life recorded clinical outcomes reported in larger observational cohorts.

The main limitation of our method is the small number of patients in the analysis and its dependence on simulated data. More research with follow-up data and dietary measurement will be needed to confirm our findings. Other potential effect modifiers such as sun exposure, dietary intake and variations in genetic polymorphisms affecting vitamin D metabolism also need to be considered [28–31].

Conclusion

This study is the first to show an association between the magnitude of anti-tTG/anti-EMA autoimmune response in juvenile CD and severity of vitamin D deficiency. These results suggest the importance of children nutritional status to link serological marker reading in care for CD patients. Further research is needed to verify this inter-relationship and develop immunologic-based supplementation recommendations.

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