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Original Article

Is Hypothyroidism a Hidden Culprit of Short Stature in Inflammatory Bowel Disease and Celiac Disease?

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Abstract:

Background: Inflammatory bowel disease (IBD) and celiac disease are characterized by chronic intestinal inflammation, and extra-intestinal manifestations.

Aim of the work: To assess if hypothyroidism is a contributing factor in short stature in children with IBD and celiac disease**.**

Subjects and Methods: This cross-sectional study included 150 children divided into three groups (50 in each group). Group A included those with confirmed IBD and group B with confirmed celiac disease. Group C included healthy children as a control group. All children underwent detailed anthropometric measurements, and ELISA test for TSH, free T4, and free T3 levels.

Results: The IBD group mean ± SD (median, range) age was 7.68 ± 3.27 (7.34, 1.69 – 14.46) years, 19 (38%) were females and 31(62%) were males. The celiac disease group mean ± SD (median, range) age was 9.42 ± 3.79 (7.55, 1.52 – 15.36) years, 25 (50%) were females and 25 (50%) were males, compared to the control group mean ± SD (median, range) age of 9.88 ± 3.25 (9.58, 3.49 – 16.53) years, 29 (58%) were females and 21 (42%) were males (p= 0.04, p= 0.095 respectively). The mean ± SD (median, range) of disease duration of IBD was 4.06 ± 2.1 (2.85, 1.6-9.2) years, while the mean ± SD (median, range) of disease duration of celiac disease was 4.39 ± 2.4 (4-, 1.55-12.5) years (p=0.5). The mean ± SD (median, range) weight Z score of IBD group was -0.42 ± 1.53 (-0.65, -4.24 – 2.42), and height Z score was -1.08 ± 1.6 (0.98, -3.64 –1.47), while the mean ± SD (median, range) weight Z score of celiac disease group was -0.72 ± 1.44 (-0.85, -3.68 – 2.24), and height Z score was -1.57± 1.29 (-1.4, -4.58 – -0.76) compared to the mean ± SD (median, range) weight Z score of the control group of -0.28 ± 0.89 (-0.29 , -1.6 – 1.87) , and height Z score was -0.53 ± 1.02 (-0.54-, -1.77–1.32) (p =0.008, p=0.000 respectively). Short stature (height Z score< -2 SD), was present in 17 (34%) of patients in celiac group, 13 (26%) of patients in IBD group and none of the control group (p=0.001). All had normal T3, T4 and TSH levels.

Conclusion: Short stature is common among children with IBD and celiac disease. Hypothyroidism is not a main cause of short stature in IBD and celiac disease, other contributing factors to short stature in IBD and celiac disease should be searched for.

Keywords: short stature; ulcerative colitis; celiac disease; Crohn's disease; hypothyroidism

Abbreviations: 5-ASA: 5- amino-salicylic acid; BMI: body mass index; ELISA: enzyme-linked immunosorbent assay; FT3: free triiodothyronine; FT4: free thyroxine; GFD: gluten free diet; IBD: inflammatory bowel disease; TSH: thyroid-stimulating hormone; UC: ulcerative colitis

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Introduction

Inflammatory bowel disease (IBD) is a chronic, non-specific inflammatory condition of the digestive tract that includes Crohn's disease and ulcerative colitis (UC) (*1*). The precise etiology of IBD remains uncertain. IBD pathogenesis is linked to intestinal dysbiosis, genetic susceptibility, environmental factors, and dysregulated immune responses (*2*). Although IBD primarily affects the gastrointestinal tract, extra-intestinal manifestations in other organs are common. Short stature is a complication in children and adolescents with inflammatory bowel disease (IBD), particularly Crohn's disease. This can be caused by chronic Inflammation, malnutrition and malabsorption, delayed puberty which occur in about 10%of IBD patients, corticosteroid use and vitamin D deficiency (*3*). Celiac disease is a systemic autoimmune disorder that develops in genetically predisposed individuals following the consumption of gluten (*4*). The only treatment is adherence to a lifelong gluten-free diet (*5*). Short stature is one of the main symptoms of celiac disease and can be the only symptom, often without

gastrointestinal complaints. Short stature in celiac disease can be attributed to malabsorption of essential nutrients especially iron, zinc, calcium, and fat-soluble vitamins, impaired growth hormone secretion or resistance, elevations of cytokines like TNF-α and IL-6, which can interfere with growth hormone signaling and bone formation (*6*). Autoimmune hypothyroidism is known to complicate celiac disease and can be a hidden cause for short stature (*7*). Hence, we aimed to study if hypothyroidism is a contributing factor in short stature in patients with IBD and celiac disease.

Subjects and Methods

This cross-sectional descriptive study was conducted at the Pediatric Gastroenterology Outpatient Clinic, Children Hospital, Cairo University Hospitals, Cairo, Egypt, from October 2022 to December 2023, over 15 months. The Scientific Research Ethical Committee of the Pediatric Department, and Ethical Committee of Faculty of Medicine, Cairo University approved the study (approval number MS-584-2021). Before enrolment, informed consent was obtained from all parents or their legal guardians. The research design adhered to the latest revision of the Helsinki Declaration for studies involving human subjects (*8*).

Participants

A total of 150 children and adolescents, of both sexes, were included in the study and divided into three groups. Group (A): comprised 50 children with confirmed IBD based on clinical, laboratory, and endoscopic criteria (*9–11*). Group (B): comprised 50 children with confirmed celiac disease based on clinical, laboratory, and endoscopic criteria (*12*). Group (C): comprised 50 apparently healthy children (a control group). Children with any chronic gastrointestinal, extraintestinal disease, congenital anomalies, system failure or endocrine diseases such as congenital hypothyroidism, patients on growth hormone treatment and patients on steroid therapy were excluded. The IBD diagnosis was confirmed according to the European Society for Paediatric Gastroenterology, Hepatology and Nutrition "Porto" criteria (*9*). Crohn's disease diagnosis was confirmed by lab results, imaging, and gross appearance of the mucosa during the initial upper GI endoscopy, and histopathological analysis of biopsies taken during the initial endoscopy, classified using the Marsh classification. Laboratory investigations included initial total IgA (mg/dL), initial anti-tissue transglutaminase) antibodies (anti-TTG IgA) (IU/mL), endomysial antibodies, and serum albumin levels. The diagnosis of Crohn's disease was made according to the European Society for Paediatric Gastroenterology, Hepatology and Nutrition celiac scoring, which considers four items: symptoms, antibodies, human leukocyte antigen (HLA), and biopsy findings, each contributing once. Four points were required to make the diagnosis (*13*).

Methods

The severity of IBD was determined using the Pediatric Modification of the Montreal classification for IBD (the Paris classification) (*10*). The study participants were classified according to their age into the following categories: infantile onset (I)-IBD (0 to < 2 years), very early onset (VEO)-IBD (2 to < 6 years), early onset (E)-IBD (6 to < 10 years), and pediatric onset (P)-IBD (10 to < 17 years). Additionally, they were sub-classified based on localization into Crohn's disease, ulcerative colitis (UC) and IBD-unclassified (IBD-U). Extra-intestinal manifestations were assessed. Regarding the assessment of UC disease activity, a score < 10 was defined as remission, 10–34 as mild disease, 35–64 as moderate disease, and > 65 as severe disease activity (*14*). The Crohn's disease activity index was categorized as < 10 for remission, 10–27.5 for mild disease, 30–37.5 for moderate disease, and > 40 for severe disease. Additionally, the degree of compliance with a gluten-free diet at the time of study enrollment was assessed among celiac patients. The weight was measured using a calibrated electronic digital scale. Height/Length: Length for young children (under 3 years) was measured using an infantometer, while older children were measured barefoot using a vertical stadiometer. The equipment was checked for accuracy before each use. The standard deviation of height was calculated according to WHO growth curves using the Anthrocal program (*15*). According to WHO child growth standards, patients' height/length Z-score for age and sex between -2 and 2 was considered normal, below -2 was stunted, and below -3 was severely stunted. Body mass index (BMI): BMI was calculated as follows: weight in kg / (height in meters) (*14*). All the 3 groups underwent measurement of serum free T4, and free T3 using ELISA kit (manufactured by Monocent, Inc., USA) and TSH levels using ELISA kit (manufactured by Calbiotec, USA, Catalog No: TS227T.

Statistical Analysis

Sample size calculation was done using the OpenEpi sample size calculator with an alpha error of 0.05 and a study power of 0.95, an anticipated prevalence of 8%, a design effect of 1, and a total number of 864 patients during the study period, it was determined that 101 patients would be required to reject the null hypothesis (*16*).

Data were statistically described in terms of mean ± standard deviation (± SD), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student t test for independent samples. For comparing categorical data, Chi-square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5. P values less than 0.05 was considered statistically significant. All statistical calculations were done using computer program IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) release 22 for Microsoft Windows.

Results

The IBD group mean ± SD (median, range) age was 7.68 ± 3.27 (7.34, 1.69 – 14.46) years, 19 (38%) were females and 31(62%) were males. The celiac disease group mean ± SD (median, range) age was 9.42 ± 3.79 (7.55, 1.52 – 15.36) years, 25 (50%) were females and 25 (50%) were males, compared to the control group mean ± SD (median, range) age of 9.88 ± 3.25 (9.58, 3.49 – 16.53) years, 29 (58%) were females and 21 (42%) were males (p value = 0. 04), p value 0.095 respectively). The mean ± SD (median, range) of disease duration of IBD was 4.06 ± 2.1 (2.85, 1.6-9.2) years, while the mean ± SD (median, range) of disease duration of celiac disease was 4.39 ± 2.4 (4-, 1.55-12.5) years (p=0.5). The mean ± SD (median, range) weight Z score of IBD group was -0.42 ± 1.53 (-0.65, -4.24 – 2.42), and height Z score was -1.08 ± 1.6 (0.98, -3.64 – 1.47), while the mean ± SD (median, range) weight Z score of celiac disease group was -0.72 ± 1.44 (-0.85, -3.68 – 2.24) , and height Z score was -1.57± 1.29 (-1.4, -4.58 – -0.76) compared to the mean ± SD (median, range) weight Z score of the control group of -0.28 ± 0.89 (-0.29 , -1.6 – 1.87) , and height Z score was -0.53 ± 1.02 (-0.54, -1.77–1.32) (p =0.008, and p=0.000 respectively). Short stature (height Z score< -2 SD), was present in 17 (34%) of patients in celiac group, 13 (26%) of patients in IBD group and none of the control group (p=0.001). All had normal T3, T4 and TSH levels.

Among the IBD group, 19 (38%) were females, and 31(62%) were males, with a mean ± SD age 7.68 ±3.27 years (median: 7.34, IQR: (4.93 – 9.51), range: 1.69 - 14.46 years). Among those in the celiac disease group, 25 (50%) were females, and 25 (50%) were males, with a mean ± SD age 9.42 ±3.79 years (median: 7.55-, IQR: (6.12 – 11.89), range: 1.52 - 15.36 years), compared to the control group, 29 (58%) were females, and 21 (42%) were males, with a mean ± SD age 9.88 ± 3.25 years (median: 9.58, IQR:- 6.44 – 12.1, range: 3.49 – 16.53 years), the three groups were age and sex matched with no statistically significant difference between them (p=0. 07) and (p= 0.095) respectively. (Table 1) The lowest weight Z score -0.85(-3.68 – 2.24), and height Z score -1.4(-4.58 – -0.76) was in celiac disease group (p=0.0080 and p=0.000 respectively). Short stature (height Z score< -2 SD), was present in 17 (34%) of patients in celiac group, 13(26%) of patients in IBD group and none of the control group (p=0.001).

The IBD group comprised 50 patients, with Crohn's disease 19 (38 %) with ulcerative colitis 22 (44%) and IBD unclassified (IBD-U) 9 (18%). Among the Crohn's disease 19 patients, 15 (78.9%) patients had a non-structuring, non-penetrating (B1) disease course, 2 had stricturing behavior (B2), and 2 had both stricturing and penetrating disease course. Two (10.5%) patients had L1 (lesion in the terminal ileum ± limited cecal disease), three had L2 (colonic involvement), six had L3 (ileocolonic involvement), one had L2 and L4a (upper disease proximal to the ligament of Treitz), three had both L3 and L4a disease, two had L3 and upper disease distal to the ligament of Treitz and proximal to the distal 1/3 of the ileum (L4b), and two had L3, L4a, and L4b disease locations. Additionally, 16 Crohn's disease patients had normal growth (G0), while the remaining 3 had growth delay (G1). This classification was defined according to the pediatric modification of the Montreal classification for inflammatory bowel disease (Paris classification). All IBD patients received 5- amino-salicylic acid (5-ASA) on dose 75 mg per kg per day, 41 (82.0%) patients received immunomodulators (azathioprine) on a dose 2 mg per kg per day, 29 (58.0%) received corticosteroids 2 mg per kg per day divided into 3 doses after meals for two weeks then gradual withdrawal along 8 weeks, and 11 (22.0%) received biological therapy; 9 (18%) received infliximab infusion and 2 (4%) patients received adalimumab subcutaneously. The dose of infliximab used was 5 mg/kg intravenously at weeks 0, 2, and 6 during the induction phase and 5 mg/kg every 8 weeks during the maintenance phase. For those

with Crohn's disease, adalimumab dose was according to weight: 17–<40 kg: 80 mg (Day 1), 40 mg (Day 15), then 20 mg every other week and for those ≥40 kg: 160 mg (Day 1), 80 mg (Day 15), then 40 mg every other week. Though therapeutic drug monitoring was recommended to ensure adequate drug levels for remission but it was not available in our center. The patients were followed up closely, and CBC was done twice monthly.

The Celiac disease group: the age of patients at the time of diagnosis ranged from 1 to 12 years, with a median (IQR) of 4.42 (2.41-8) years. At the time of the study, the duration since diagnosis ranged from 1.55 to 12.5 years, with a median (IQR) of 4 (2.3-5.3) years. Family history of celiac disease and thyroid diseases was positive in 3 (6%) and 9 (18%) patients, respectively. The main clinical presentation of celiac patients in our study was failure to thrive with abdominal distention 40 (80%), followed by attacks of diarrhea 7 (14%) and 3 (6%) suffered from constipation. Thirty-six (72%) had extraintestinal manifestations. The most frequent extra-intestinal manifestation was refractory iron deficiency anemia in 15 patients, followed by hypocalcemia, rickets, and delayed bone age in 10 patients. Insulin-dependent diabetes mellitus (IDDM) complicated 8 (16%) cases, generalized edema in six patients, autoimmune hepatitis and liver biochemical abnormalities in 5(10%) patients, peripheral neuropathy 2(4%) patients, and teeth and gingival lesions 2 (4%) patients. Myopathy, dermatitis herpetiformis, and arthritis were each observed in 1(2%) case. Upper endoscopy biopsy at initial presentation revealed gastrointestinal involvement as follows: 27 (54%) patients had mosaic patterns, 10 patients (20%) showed scalloping, 7 patients (14%) had reduced fold height, 5 patients (10%) had a mixed nodularity and mosaic pattern, and 1 patient (2%) showed nodularity. According to the Marsh classification system, the histopathologic analysis of biopsied samples obtained during the initial endoscopy revealed the following distribution: 25 patients (50.0%) had Marsh type 3b, 14 (28.0%) patients had Marsh type 3c, 9 patients (18.0%) had Marsh type 3a, and 2 patients (4.0%) had Marsh type 2. Before introducing a gluten free diet (GFD), all patients had normal total IgA, and none had IgA deficiency. Of them 27 (54.0%) patients had elevated anti-TTG IgA levels (ranging from 20 to 200 IU/mL), while 15 patients (30.0%) had anti-TTG IgA levels above 200 IU/mL. Six (12.0%) patients had hypoalbuminemia, and anti-endomysial antibodies was positive in 4 (8.0%) patients. Regarding adherence to a GFD, 37 (74.0%) patients were strictly adherent, 6 (12.0%) were partially adherent, and 7 (14.0%) were not adherent. (Table 2).

Table 1. Characteristics of the studied groups

	Children with IBD		Children with Celiac disease		Control group		P-value
	Number	%	Number	%	Number	%	
Sex							
Male	31	62%	25	50%	21	42%	0.070
Female	19	38%	25	50%	29	58%	
	Mean ±SD	Median (IQR)	Mean ±SD	Median (IQR)	Mean ±SD	Median (IQR)	
Age (years)	7.68 ±3.27	7.34 (4.93 – 9.51)	9.42 ±3.79	7.55 (6.12 – 11.89)	9.88 ± 3.25	9.58 (6.44 – 12.1)	0.090
Age at diagnosis	4.96± 2.75	3.84 (2.36-7.5)	5.27±3.1	4(2.3-5.3)	–	–	0.590
Disease Duration	4.06 ± 2.1	2.85 (2-5.3)	4.39 ± 2.4	4(2.3-5.3)	–	–	0.500
Weight Z score	-0.42 ± 1.53	-0.65(-1.28 - 0.17)	-0.72 ± 1.44	-0.85(-1.29 – 0.12)	-0.28 ± 0.89	-0.29(-0.74-0.39)	0.008
Height Z score	-1.08 ± 1.6	-0.98(-2.07 – -0.19)	-1.57± 1.29	-1.4(-2.4 – -0.78)	-0.53 ± 1.02	-0.54(-1.21 – 0.09)	0.000
BMI Z score	0.17±1.44	-0.17(-0.82 – 0.76)	0.18±1.39	0.13(-0.66 – 0.96)	0.06±1.24	-0.08(-0.85 – 0.88)	0.680
	Number	%					
Severity of disease							
Mild-Moderate	31	62	22	44			0.07
Severe	19	38	28	56			
Compliance to Management							
Yes	44	88	37	74			0.06
No	6	12	13	26			
Disease Control in response to Management							
Yes	31	62	22	44			0.160
No	19	38	28	56			

All participants in the three groups had normal T3, T4 and TSH levels (p=0.14). Those with celiac disease had the lowest Z score of weight and height of corresponding age in comparison to IBD and control group (p=0.008 and p=0.00 respectively). (Figure 1).

Despite the significant associations between short stature and sex, using logistic regression analysis sex was not predictive of short stature (p=0.1240, 95% confidence interval 0.5768-1.0735), diagnosis either IBD or celiac disease also was not predictive of short stature (p=0.0585,

95% confidence interval 0.5414-1.0188), both diagnosis and sex were not predictive of short stature (p=0.2662, 95% confidence interval 0.5823-1.0951 and 0.5554-2.7824). The presence of extraintestinal manifestation in both groups was not predictive of short stature (p=0.7907, 95% confidence interval 0.8468-1.6696), also compliance was not predictive of short stature (p=0.7907, 95% confidence interval 0.7307-1.5097), combining both compliance and extraintestinal manifestations did not differ as predictive of short stature (p=0.3282, 95% confidence interval0.7044-1.4831 and 0.7858-5.8088), compliance and different diagnoses either IBD or celiac disease were not predictive of short stature (p=0.09641, 95% confidence interval 0.7268-1.5236 and 0.3908 – 2.6922) in our studied cohort. There was a positive correlation between the height and age of onset of disease (p =0.001). Yet, the duration of the disease was not a predictive of short stature (p=0.8261, confidence interval (0.6178- 1.4689). Severity of the disease was not predictive of short stature (p=0.1241, 95% confidence interval 0.9313-1.7354). The control of disease was not predictive of short stature as well (p=0.5706, 95% confidence interval 0.6774-1.2398).

Table 2. Factors associated with short stature among our studied cohorts

	Group with Short Stature (Number= 30)		**Group with Normal Stature (Number= 70)**		**P value**
	Number	**%**	**Number**	**%**	
Sex					
Males	10	33.30	46	65.70	0.001
females	20	66.70	24	34.30	
IBD	13	26	37	74	0.003
Celiac disease	17	34	33	66	0.020
Extra-intestinal Manifestations	24	80	35	50	0.000
Management					
Compliance to gluten-free diet for Celiac					
Strict	15	88.20	22	31.40	0.100
Partial adherence	1	5.90	5	7.10	
No adherence	1	5.90	6	8.60	
IBD medication					
-5 Amino salicylic acid (5-ASA) only	1	7.70	6	16.25	0.460
5-ASA + Azathioprine	7	53.80	6	16.25	0.004
5-ASA + corticosteroids	0	0	2	5.40	0.500
5-ASA+ Azathioprine+ Corticosteroids	2	15.40	15	40.50	0.140
5-ASA+ Azathioprine+ Biologics*	0	0	1	2.70	0.950
5-ASA+ Azathioprine+ Corticosteroids+ Biologics	3	23.10	7	18.90	0.170
Activity Index in IBD (*11*)					
Remission	1	7.70	19	51.40	0.003
Mild disease	4	30.80	7	18.90	0.050
Moderate disease	5	38.40	8	21.60	0.130
Severe disease	3	23.10	3	8.10	0.060
	Mean ± SD		**Mean ± SD**		
Age at disease onset	6 ± 1.77		4.78 ± 2.8		0.018
Disease Duration	3.69 ± 1.77		4.2 ± 2.2		0.200

5-ASA: 5 Amino salicylic acid; Biologics: adalimumab or infliximab

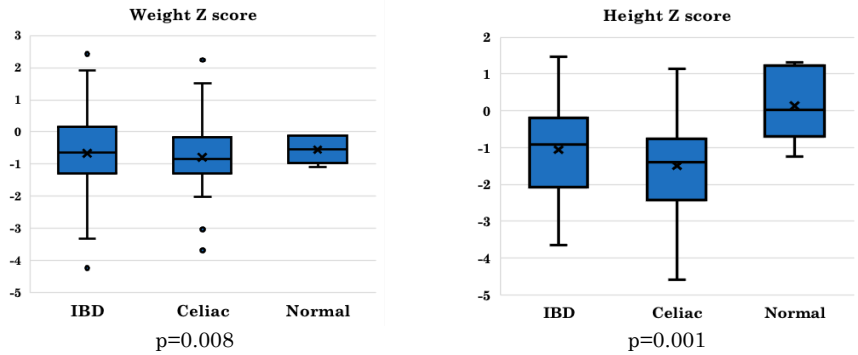

Figure 1. Boxplot comparison between IBD, celiac and control groups weight and height Z-scores

Discussion

Short stature, was present in 17 (34%) of patients in celiac group, 13(26%) of patients in IBD group and none of the control group (p=0.001), that was not attributed to hypothyroidism (*17*). Despite the immune nature of both disease and the reported association, hypothyroidism was not a contributing factor to the short stature among our studied cohort (p= 0.14).

Short stature in celiac disease can be caused by many factors: one of them poor dietary adherence to GFD. Gluten free diet is difficult to be achieved as many patients do not know the possible cross-contamination with gluten with many foods and other items such as: play dough, stamp, envelope glues, vitamins and herbal products. The high price and the unpalatable taste of GFD are important factors that interfere with the adherence to GFD (*18*). In our studied cohort, most of patients --- (74%) reported they were adherent to GFD, compliance was not the responsible factor of short stature (p= 0.7907). This might be attributed to the subjective nature of reporting compliance, and lack of true assessment of compliance, or a refractory nature of celiac disease, and both factors need further studying beyond the scope of our current study.

The duration of disease in both IBD and celiac disease can significantly impact linear growth and final adult height, especially when onset occurs during childhood or adolescence (18, 19). The duration of disease in our patient was not predictor of short stature (p=0.783) We did not compare the height Z scores at initial presentation before institution of management and at recruitment in our current study. Hence, what we are sure of is that the recruited children were shorter than the control group, but we do not know if there is a significant catch up compared to their initial Z scores, that needs further growth velocity assessment and if they will eventually reach their mid-parental adult height centiles by puberty as our study was not prospective but a cross-sectional one. Follow up would address the long-term effect of duration of disease on their final adult heights. The presence of extraintestinal manifestations in celiac disease and IBD: such as anemia, delayed puberty, or endocrine dysfunction can aggravate short stature, especially when diagnosis is delayed (*19*), but in our patients extraintestinal manifestation in both groups was not predictive of short stature (p= 0.7907) and this may be attributed to the good compliance in our patients, dietary supplementation and the early diagnosis. Celiac disease tends to have a higher prevalence of short stature as a presenting symptom than IBD (*6*). Our cohort with celiac disease was shorter than those with IBD and healthy control group. The inflammatory bowel disease irrespective of the diagnosis either IBD or celiac disease in our patient was not predictive of short stature (p=0.0585), this difference may be elicited with bigger sample size. It may be attributed to younger age at diagnosis and early prompt management. The latter assumption is supported by the fact that there was a positive correlation between the height Z score and age of onset of disease (p =0.001). Hence, it seems that the short stature is a complication of the IBD and celiac disease that is potentially reversible.

Not only was hypothyroidism not a culprit for short stature in our studied cohort, but all other factors as diagnosis (p=0.0585), sex (p=0.1240), the presence of extraintestinal manifestations (p=0.7907), and compliance to management (p=0.7907) were also not responsible for the short stature in our studied cohort. There are many important factors that were beyond the scope of our study that maybe responsible for short stature in both IBD and celiac disease and need to be addressed by future research. The metabolomics, microbiome and micronutrients deficiencies (iron, vitamin D, vitamin B12, zinc, folate, magnesium, and vitamin A) are major contributors to growth impairment in both celiac disease and IBD, that are inherent to the nature of the IBD and celiac disease, as villous atrophy in the small, reduced the intake, malabsorption, and medication side effects (e.g., corticosteroids) all contribute (*20*).

In both IBD and celiac disease, several endocrinopathies have been documented, either due to autoimmune associations, chronic inflammation, or treatment side effects. They include autoimmune thyroiditis, type 1 diabetes mellitus, hypogonadism, growth hormone deficiency, and growth hormone axis suppression (*21*). In our study hypothyroidism was screened in all patients using thyroid profile, with no difference between normal control and both diseased group (p= 0.14), further investigations for thyroid diseases should be done: thyroid antibodies and thyroid ultrasonography for better screening but the high cost was one of the limitations in our study. Other associated endocrinopathies were not studied among our studied cohort, hence we the contribution of early or subclinical endocrinopathies to their short stature. Potential limitations of this study include the relatively small sample size, particularly in subgroup analyses, and reliance on cross-sectional data, which precludes assessment of growth trajectories over time. Additionally, factors such as pubertal status, socioeconomic variables, and detailed nutritional assessments were not addressed and may influence growth outcomes. Other unmeasured confounders could influence growth outcomes and should be explored in future studies.

Conclusion

Short stature is common among children with IBD and celiac disease. Hypothyroidism is not a main cause of short stature in IBD and celiac disease, and we need to search for other contributing factors. The logistic regression analysis demonstrates that sex, diagnosis (IBD or celiac disease), presence of extraintestinal manifestations, and compliance are not significant predictors of short stature in this cohort of patients. Hence, our work provides evidence the short stature is a complication of the IBD and celiac disease that is potentially reversible. Early recognition, comprehensive management, and ongoing monitoring are essential to optimize growth and health outcomes in these vulnerable pediatric populations

Author Contributions

All authors shared equally in the study. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in connection with the reported study.

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