

# Growth hormone treatment outcomes in Indian children with celiac disease and Growth hormone deficiency.

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## Introduction

Celiac Disease (CD) is as an immune-mediated enteropathy characterized by a inflammatory reaction to gluten. Up to 4% of children seeking medical care due to short stature might have CD and many of them do not have any gastrointestinal symptoms [1]. These children may usually present with reduction of insulin-like growth factor 1 (IGF1), IGF2 and insulin-like growth factor binding protein 3 (IGFBP-3), increase of IGFBP-2 and IGFBP-1 levels, and a blunted GH response to pharmacological stimuli. Children with CD start showing improvement in height velocity and weight when initiated on gluten free diet. However few children with CD do not show any catch-up despite good adherence to gluten free diet. It is in this sub-population that the possibility of growth hormone deficiency (GHD) should be evaluated even as the association of CD and GHD is very rare.

## Study Design

### Subjects:

A retrospective study was conducted from 2010 to 2017 in Indraprastha Apollo Hospital. Data was collected from patient records of children being treated with recombinant growth hormone (rGH) in 2 groups as follows: children with CD having growth hormone deficiency (CD group) children with GHD only (isolated GHD group)

### Inclusion criteria:

17 pre-pubertal children with Celiac Disease (CD) with growth hormone deficiency and 17 age and sex matched GHD children without coeliac disease or any other co-morbidities were included in the study.

### Screening and Diagnosis of Celiac disease:

All children with Celiac disease (CD) were screened for CD by anti-ttg IgA antibodies and positive cases were confirmed with endoscopic examination of the upper gastrointestinal tract with at least four biopsies of the distal duodenal mucosa. Only those confirmed patients who did not show catch up growth and continued to have short stature after 12 months of gluten free diet and demonstrated a reversion to seronegativity for anti-ttg antibodies were included in the study.

### Methods:

#### Diagnosis of GHD

In all of the patients, the diagnosis of GHD was established when GH response to 2 pharmacological stimuli was <10 ng/mL in the presence of short stature.

#### Parameters assessed

Auxological data of height, weight, BMI, bone age, chronological age was recorded at the time of initiation of growth hormone and at the end of therapy.

#### Growth hormone therapy

All patients received treatment with recombinant synthetic human GH for at least 12 months, GH was administered by daily subcutaneous injections at the dose 35µg/kg/day.

## Statistical analysis

Height, weight, BMI, predicted adult height was all expressed as standard deviation scores.

Independent *t*-test and paired *t*-test were used to compare the various pre-treatment and post-treatment data

### References:

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**Conflict of Interest:** The authors have no real or perceived conflicts of interest in any matters, including financial issues, relating to this work.

## Results

**Table: 1.** SDS of pre and post treatment data of GHD and Celiac disease

	Group	N	Zscore	Std Deviation	t-value	p-value
Height pretreatment (cm)	GHD	15	-1.9800	.85342	1.233	.227
	Coeliac	16	-2.3438	.78870		
Weight Pretreatment (kg)	GHD	15	-.7093	1.10083	2.436	.021
	Coeliac	16	-1.6700	1.09386		
BMI Pretreatment	GHD	15	.3393	1.04762	2.481	.019
	Coeliac	16	-.6406	1.14490		
Height Post-treatment	GHD	15	-1.2067	1.00731	1.255	.220
	Coeliac	16	-1.6044	.74632		
Weight Post-treatment	GHD	15	-.2707	.89965	-.794	.434
	Coeliac	16	.0100	1.05546		
BMI Post-treatment	GHD	15	.4020	.72727	-1.469	.153
	Coeliac	16	.9125	1.14612		
PAH Pretreatment	GHD	15	-1.1453	.83340	.843	.406
	Coeliac	16	-1.4269	1.01147		
PAH2 Post-treatment	GHD	15	-.1593	1.07734	-3.729	.001
	Coeliac	16	-0.5625	0.81394		

## Conclusion

- This is the first study from India analyzing the association of CD with GHD with a comparison of growth outcomes in these children.
- Even though the final height outcomes were better in GHD than CD, there was an improvement in the auxological parameters within each group after treatment with rGH.
- Hence a timely diagnosis along with rGH therapy could be an effective option in this rare association of GHD with CD for rewarding results. This study also warrants the need for future studies with larger sample size and long term follow up.