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Research Article

SEROPREVALENCE OF COELIAC DISEASE IN SHORT STATURED CHILDREN IN SOUTH INDIA: A HOSPITAL-BASED STUDY

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ABSTRACT

Objective: The objective of this study was to assess the seroprevalence of coeliac disease among children with short stature in a tertiary care setting in South India.

Methods: A prospective observational study was conducted at JSS Hospital, Mysuru, from November 2018 to August 2020. Children aged 2–18 years with height <−2 standard deviation for age and sex were enrolled after informed consent. Detailed clinical evaluation, anthropometric measurements, and mid-parental height were recorded. Serum tissue transglutaminase immunoglobulin A (tTG-IgA) levels were estimated using enzyme-linked immunosorbent assay. Children with positive results (>20 U/mL) were referred for further gastroenterological evaluation. Additional tests such as hemoglobin, thyroid stimulating hormone, and bone age X-rays were done as clinically indicated.

Results: Out of 5450 children screened, 107 with short stature were included in the study. Of these, 92 (86%) had short stature and 15 (14%) had severe short stature. The most common etiology was familial short stature (43.9%), followed by idiopathic (19.6%), nutritional (15.9%), and constitutional delay in growth and puberty (11.2%). Only one child (0.9%) tested seropositive for coeliac disease. A weak but statistically significant correlation was observed between height and tTG-IgA levels (p=0.022).

Conclusion: The seroprevalence of coeliac disease in children with short stature in South India was found to be low (0.9%) compared to Northern Indian data. However, given the treatable nature of coeliac disease, screening remains crucial in the evaluation of short stature. Larger, multicentric studies with confirmatory biopsy and IgA deficiency assessment are warranted to better delineate the true prevalence in Southern India.

Keywords: Short stature, Coeliac disease, Tissue transglutaminase immunoglobulin A, South India, Seroprevalence.

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INTRODUCTION

Coeliac disease is an immune-regulated enteropathy occurring in genetically susceptible individuals following the consumption of gluten-containing proteins found in wheat, rye, and barley. It manifests with a variable combination of gluten-dependent clinical symptoms, HLA-DQ2 or HLA-DQ8 haplotypes, coeliac disease-specific antibodies, and enteropathy. These specific antibodies include autoantibodies against tissue transglutaminase (tTG-IgA), endomysial antibodies, and antibodies against deamidated forms of gliadin peptides. Gluten, a rubbery mass left after washing wheat dough to remove starch and soluble constituents, is rich in prolamines. Studies indicate that all gluten types can be toxic for coeliac disease patients, and recent *in vitro* research has shown that glutenin peptides induce T-cell activation and proliferation in the coeliac bowel [1].

Coeliac disease was first reported in India in 1966 among children and adults [2,3]. Due to a lack of awareness and limited availability of duodenal biopsies, diagnosing coeliac disease in India has been challenging. However, with the emergence of pediatric gastroenterology as a subspecialty and modifications in ESPGHAN criteria, diagnosis has improved. Epidemiological studies suggest that coeliac disease is more prevalent in the wheat-consuming states of Punjab, Uttar Pradesh, Haryana, Rajasthan, Delhi, Bihar, and Madhya Pradesh, largely due to genetic susceptibility and dietary habits. Studies from Delhi and Uttar Pradesh confirm an association with DR3-DQ2 haplotypes, similar to the Western population [4,5]. The *DR3* gene frequency in North India (15%) is comparable to that in Southern India, where it is 11.6% among Piramalai Kallars and 14.34% among Yadavas. The DQ2 allele frequency varies between 31.9% in North India and 12.7% (Piramalai Kallars) and 9% (Yadavas) in Southern India [6,7].

Coeliac disease is more commonly reported in children than adults in India. An increase in case reporting over the past decade suggests heightened awareness within the medical community. Between 1966 and 2000, only 130 cases were documented, whereas 517 cases were reported between 2001 and 2005. The average delay in coeliac disease diagnosis in India ranges from 3.5 to 6 years [8-10], often due to overlapping symptoms with recurrent gastrointestinal infections, diarrhea, anemia, and malnutrition. Many children receive multiple antibiotic courses before reaching tertiary care centers. An epidemiological study by Sood *et al*. in Ludhiana, Punjab – a region within the coeliac disease belt – reported a disease frequency of 1 in 310 children, with a prevalence of 0.3%, comparable to the global prevalence of 0.4% [11,12]. Reports from the Middle East and West Asia also show varied prevalence rates [13-20]. The regional differences may stem from dietary habits (rice vs. wheat consumption) or genetic predisposition. While coeliac disease was historically considered more prevalent in Western countries, increasing data from Northern India over the past decade highlight its rising recognition. However, data on coeliac disease in Southern India remain scarce.

Hence, this study was undertaken to estimate the seroprevalence of coeliac disease in children with short stature presenting to a tertiary care center in South India, where the wheat consumption is lower and the genetic predisposition is presumed to be less prevalent.

METHODS

This hospital-based prospective observational study was conducted at JSS Hospital, Mysuru, between November 2018 and August 2020. Children aged 2–18 years who presented to the pediatric outpatient or inpatient department and had height <−2 standard deviation (SD) from the mean for their age and sex as per World Health Organization growth charts were eligible for inclusion. Written informed consent/ Assent was obtained from the parents or guardians before enrolment into the study.

A detailed clinical history, demographic data, and physical examination findings were recorded using a predesigned pro forma. Anthropometric measurements of both the child and parents were taken, including height, weight, and midparental height. The target height was calculated using standard formulas [21]:

- For boys: (Father's height+Mother's height+13)/2
- For girls: (Father's height+Mother's height−13)/2

Height was measured using a stadiometer with the child in a standing position, ensuring correct posture (Frankfurt plane) with bare feet together and body parts (occiput, back, and buttocks) in contact with the vertical board.

Venous blood (5 mL) was collected under aseptic conditions and the serum was separated and stored at −20°C until testing. The tTG-IgA antibody levels were estimated using an enzyme-linked immunosorbent assay kit: Quanta Lite (INOVA diagnostics), which uses recombinant human tTG-IgA as the antigen. According to the manufacturer's guidelines, tTG-IgA values above 20 U/mL were considered positive.

The sensitivity and specificity of the kit used were 90–100% and 94–100%, respectively. Additional investigations including hemoglobin estimation, serum TSH levels, and bone age X-rays were performed as required based on clinical judgment. Children who were found to be seropositive for tTG-IgA were referred to the pediatric gastroenterology department for further management.

Sample size was calculated based on an expected prevalence of 8.3% of coeliac disease among Indian children, with a 5% margin of error, 95% confidence interval, and 80% power, resulting in a sample size of 138. However, due to the COVID-19 pandemic and reduced patient flow, the final number of cases included was 107. A total of 5450 children aged 2–18 years were screened for short stature, of whom 310 had height <−2SD from the mean. After exclusions, 107 children formed the study population.

Statistical analysis was carried out using the Statistical Package for the Social Sciences software version 21.0. Categorical variables were summarized using frequencies and percentages. Continuous variables were described using mean, median, SD, and interquartile ranges.

RESULTS

The study included 107 children with short stature, with an almost equal gender distribution – 54 females (50.5%) and 53 males (49.5%). The 10–13 year age group formed the largest subset of the study population, contributing to nearly one-third of the participants. Specifically, children aged 10–11 years (11.2%), 11–12 years (10.3%), and 12–13 years (9.3%) made up a significant portion. The youngest and oldest age groups (2–4 years and 14–17 years) had relatively fewer participants. This indicates that the most common age group presenting with short stature was older school-age children and early adolescents, possibly due to heightened awareness of growth issues at this stage or school health screening programs (Table 1).

The most common presenting complaint among the study participants was short stature itself (40.2%), which reflects that growth concerns were a primary reason for seeking medical evaluation. Other frequent symptoms included fever (14%), cough and cold (7.5%), and vomiting/headache (6.5% each), suggesting the coexistence of general pediatric illnesses. Notably, 6 children (5.6%) presented with failure to gain weight, which, along with short stature, could point toward chronic nutritional or systemic conditions. A small percentage reported gastrointestinal symptoms such as loose stools (3.7%) and abdominal pain (1.9%), which are relevant in the context of differential diagnosis for coeliac disease (Table 2).

Out of the 107 children evaluated in the study, 92 children (86%) were classified as having short stature (height <−2 SD from the mean for age and sex), while 15 children (14%) were identified with severe short stature (height <−3 SD). This indicates that the majority of children presented with mild-to-moderate growth delay, while a smaller proportion had more profound growth retardation. The presence of 14% severe cases highlights the need for thorough evaluation to identify underlying pathological or endocrine causes, as these children may benefit from early intervention and specialized (Fig. 1).

The most common cause of short stature in this study was familial short stature (43.9%), where the majority of cases (44 out of 47) were classified as short stature, with only three cases in the severe category, indicating that this condition generally results in milder growth impairment. Idiopathic short stature (19.6%) was the second most frequent etiology, with a higher proportion (26.7%) classified under severe short stature, suggesting a greater impact on growth compared to familial short stature. Nutritional short stature (15.9%) was primarily seen in the short stature category, with only one case in

Table 1: Age and gender distribution of study participants

Age group	Female		Male		Total	
	F	%	F	%	F	%
2–3	1	1.9	2	3.8	3	2.8
3–4	1	1.9	2	3.8	3	2.8
4–5	3	5.6	1	1.9	4	3.7
5–6	4	7.4	6	11.3	10	9.3
6–7	2	3.7	4	7.5	6	5.6
7–8	1	1.9	5	9.4	6	5.6
8–9	6	11.1	2	3.8	8	7.5
9–10	6	11.1	4	7.5	10	9.3
10–11	6	11.1	6	11.3	12	11.2
11–12	8	14.8	3	5.7	11	10.3
12–13	6	11.1	4	7.5	10	9.3
13–14	4	7.4	5	9.4	9	8.4
14–15	2	3.7	3	5.7	5	4.7
15–16	2	3.7	4	7.5	6	5.6
16–17	2	3.7	2	3.8	4	3.7
Total	54	100.0	53	100.0	107	100.0

F: Frequency, %: Percentage. Age is grouped in completed years. Percentages are calculated within each gender and total column separately

Table 2: Distribution of study population with respect to presentation of symptom to the OPD

Symptoms	F	%
Short stature	43	40.2
Fever	15	14
Cough and cold	8	7.5
Vomiting	7	6.5
Headache	7	6.5
Not gaining weight	6	5.6
Giddiness	5	4.7
Loose stools	4	3.7
Abdominal pain	2	1.9
Breathlessness	2	1.9
Others	8	7.5

OPD: Outpatient department. F: Frequency, %: Percentage of total participants (n=107). Only the primary presenting symptom was recorded for each participant

the severe category, emphasizing the role of diet and malnutrition in height retardation. Constitutional delay in growth and puberty (CDGP) (11.2%) had a notable association with severe short stature (26.7%), indicating that delayed puberty can significantly affect growth velocity. Hypothyroidism (7.5%) was also a notable contributor, with 25% of cases presenting with severe short stature, highlighting the importance of thyroid function in normal growth. Chronic kidney disease (0.9%) was a rare cause, but all cases were categorized under severe short stature, suggesting that systemic illnesses contribute more significantly to growth impairment. Coeliac disease (0.9%) was detected in one child, categorized under short stature but not severe short stature. Overall, severe short stature was predominantly associated with idiopathic short stature (26.7%) and constitutional delay in growth (26.7%), indicating that these conditions may contribute more to profound growth deficits compared to other causes (Table 3).

DISCUSSION

Short stature remains a significant concern worldwide, especially in developing countries where awareness among parents and healthcare providers is often limited. The prevalence of short stature in this hospital-based study was 5.6%, aligning with findings from Mumbai (5.6%) and South India (2.8%) but lower than community-based reports from North India (13.8%) [22-25]. The differences in prevalence can be attributed to study settings, inclusion criteria, and regional nutritional disparities.

In terms of gender distribution, our study showed an almost equal representation of males and females (50.5% and 49.5%, respectively). However, other studies, such as those conducted by Bhadada *et al* and Saengkaew *et al*, reported a male predominance [26,27]. These differences could be due to regional variations, cultural factors, and differential healthcare-seeking behavior.

Most short-statured children in our study were aged 9–13 years. This differs from studies in North India, which reported a higher prevalence among younger children [28]. The discrepancy may be due to variations in referral patterns, dietary habits, and genetic predisposition.

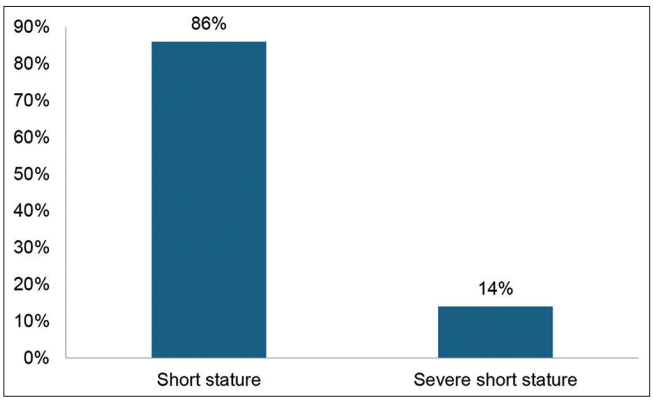

Fig. 1: Classification of short stature

Table 3: Etiology (diagnosis) of all short statured children based on severity of short stature

Diagnosis	Short stature		Severe short stature		Total	
	F	%	F	%	F	%
Familial	44	47.80	3	20.00	47	43.90
Idiopathic	17	18.50	4	26.70	21	19.60
Nutritional	16	17.40	1	6.70	17	15.90
Constitutional delay	8	8.70	4	26.70	12	11.20
Hypothyroidism	6	6.50	2	13.30	8	7.50
CKD	0	0.00	1	6.70	1	0.90
Coeliac disease	1	1.10	0	0.00	1	0.90
Total	92	100	15	100.00	107	100

CKD: Chronic kidney disease

The seroprevalence of coeliac disease in this study was 0.9%, significantly lower than reports from North India (10.9–20.5%) but comparable to findings from Italy (0.63%) and Finland (1.5%) [29-36]. The low prevalence in South India could be attributed to lower wheat consumption and genetic factors. Previous studies indicate that coeliac disease prevalence is higher in North India, where wheat is a staple, compared to South India, where rice is more commonly consumed [37]. Furthermore, coeliac disease awareness and screening practices in South India remain limited compared to Northern regions.

Physiological causes, including familial short stature and CDGP, accounted for 55.1% of cases. These findings are consistent with those from studies conducted in Saudi Arabia (51.8%) and Iran (53%) [38,39]. The diagnosis of familial short stature and CDGP was based on clinical assessment and parental growth patterns, reaffirming the significance of hereditary influences on growth.

Hypothyroidism was identified in 7.5% of the study population, comparable to prevalence rates reported from Iran (8%) and India (14%) [26,40]. The wide variation in prevalence rates across studies may be influenced by regional iodine sufficiency and genetic factors.

CONCLUSION

This hospital-based study highlights that short stature remains a common presentation among children attending pediatric services, with familial and idiopathic causes being the most frequent etiologies. The seroprevalence of coeliac disease among short statured children in this South Indian cohort was found to be 0.9%, significantly lower than that reported in Northern India. This supports the hypothesis that dietary patterns and genetic predisposition play a crucial role in the regional variation of coeliac disease prevalence. Despite the low prevalence, screening for coeliac disease remains important – particularly in children with unexplained short stature or associated autoimmune conditions. Given that coeliac disease is a treatable cause of growth failure, early diagnosis through serological screening followed by confirmatory tests can lead to timely dietary intervention and improved growth outcomes.

AUTHORS' CONTRIBUTIONS

Vasanth Perumal: Design of study, data collection, and data curation. Uma Gayathri Bagavathi Perumal: Conceptualization and methodology. Syed Mohammed Hassan Ali: Conceptualization, methodology, validation, investigation, and supervision. Manjunath Vaddambal: Methodology, supervision, and manuscript.

CONFLICTS OF INTEREST

Nil.

AUTHOR'S FUNDING

Self.

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