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Etiology of Short Stature in Children Presenting At a Tertiary Care Hospital

Arusa Farooq[1*], Qamar Uz Zaman[1], Hina Nasir[2], Nida Mukhtar[1] and Hira Siddique[1]

[1]Department of Pediatrics, Shalamar Hospital, Lahore, Pakistan
[2]Department of Pediatric Medicine, Mayo Hospital, Lahore, Pakistan

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***Corresponding Author:**
Arusa Farooq
Department of Pediatrics, Shalamar Hospital, Lahore, Pakistan
arusafarooq92@yahoo.com

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ABSTRACT

Short stature is frequently a rationale for consultation with pediatric endocrinology departments. It may arise from a multitude of origins, encompassing both physiological variations and pathological conditions. **Objective:** To ascertain the prevalence of various etiologies of short stature in pediatric patients attending a tertiary care medical facility. **Methods:** This cross-sectional study was carried out within the Pediatric Department of Shalamar Hospital, Lahore from August 2024 to February 2025. Subjects comprised 180 children exhibiting short stature as per operational definition, height falling beneath the 3rd percentile or two standard deviations below the mean corresponding to age and gender, included via non-probability consecutive sampling. Comprehensive history taking, physical assessments, anthropometric evaluations, and pertinent diagnostic tests were conducted. Data were analyzed using SPSS version 25.0 and various etiologies of short stature were presented as percentages and frequencies. Data were stratified by age, gender, residence, and socioeconomic status. **Results:** Familial Short Stature (FSS) constituted the predominant diagnosis among the pediatric population, impacting 20.6% of the subjects, followed closely by Constitutional Delay of Growth and Maturation (CDGM) and Primary Malnutrition, each accounting for 16.1%. Growth Hormone Deficiency (GHD) was identified in 15.6% of cases, while Hypothyroidism was present in 11.1%. Less prevalent etiologies included Celiac Disease (8.3%), Type 1 Diabetes Mellitus (T1DM)(7.8%), and Turner Syndrome, which affected 4.4% of the cohort. **Conclusions:** The main causes of short stature in children are familial and constitutional growth delay, along with endocrine disorders like hypothyroidism and growth hormone deficiency. Timely intervention is essential for optimal growth potential.

INTRODUCTION

Short stature, characterized as a measurement falling beneath the 3rd percentile or exceeding 2 standard deviations below the normative mean for age and sex, is modulated by an array of genetic, environmental, nutritional, and endocrinological determinants that affect growth on a global scale [1, 2]. Short stature negatively affect the health related quality of life [3]. Globally, around 144.0 million children under five suffer from short stature [4]. In Pakistan, UNICEF reports that 38% of children under 5 are stunted [5]. Common causes include idiopathic short stature such as familial short stature and constitutional growth and maturation delay [6, 7]. A comprehensive review explored the causes, diagnostic approach, and clinical evaluation of short stature in children [8]. Constitutional growth and maturation delay: growth velocity is normal, bone age corresponds with height age but is less than chronological age, and there is a delayed onset of puberty with a family history. Familial short stature: no delay in bone age, normal growth velocity, and a final height that is short yet remains within the target height range [9]. Additional etiologies: chronic illnesses, endocrine abnormalities, skeletal dysplasias, and genetic or chromosomal anomalies [10-13]. In a study, the prevalent etiologies of reduced stature encompassed Familial Short Stature (FSS) at 21.3%, hypothyroidism at 17.2%, Growth Hormone Deficiency (GHD) at 10.7%, Type 1 Diabetes Mellitus (T1DM) at 9.5%, Constitutional Delay of Growth and Maturation (CDGM) at 6.5%, primary malnutrition at 4.7%,

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celiac disease at 3.6%, and Turner syndrome at 3% [10]. In an alternative study, the distribution of different etiologies of short stature was elucidated: 11.8% exhibited a deficiency in growth hormone, 42% were classified as having familial short stature, 15.8% demonstrated constitutional growth delay, and 6.6% were diagnosed with celiac disease [14, 15]. Data on short stature etiology in Pakistan is scarce. Being a resource-limited developing country, over a third of children under 5 are stunted. Short stature commonly prompts emotional and social stress in children, motivating my study on identifying and preventing its causes by age group.

The aim was to decrease disease burden and improve quality of life by addressing avoidable factors leading to short stature promptly.

METHODS

The study was conducted at the Department of Pediatrics, Shalamar Hospital Lahore, over a period of 6 months from August 2024 to February 2025. A cross-sectional study design was employed with non-probability consecutive sampling technique. A sample size of 180 children was calculated using 3% prevalence of Turner syndrome as reported in a study using formula for single proportion with 95% confidence interval and 2.5% margin of error [10]. The investigation encompassed children aged 3 to 12 years of both gender presenting with short stature, operationally defined as height or length falling below the 3rd percentile on the CDC growth charts or below 2 standard deviations on the WHO charts, adjusted for age and sex. Children exhibiting contractures, scoliosis, kyphosis, or abnormalities of the lower limbs were systematically excluded from participation in the study. The research protocol received ethical clearance from the Hospital Ethical Committee of Shalamar Medical and Dental College, Lahore (IRB no 0794) and written informed consent was procured from the parents or guardians of the pediatric subjects prior to enrollment. Comprehensive demographic and clinical data were gathered for each participant. Standing height was assessed without footwear or headgear utilizing a stadiometer and subsequently plotted on the relevant CDC or WHO growth charts. Target height was computed employing the mid-parental height formula: [(father's height in cm) + (mother's height in cm) + 13] divided by 2 for male subjects, and [(father's height in cm)– 13 + (mother's height in cm)] divided by 2 for female subjects. The upper to lower segment ratio (US/LS) was calculated by deducting sitting height from standing height. Weight was measured accurately using an electronic scale. Parents were requested to provide historical medical records. Laboratory investigations encompassed a complete blood count, Erythrocyte Sedimentation Rate (ESR), urinalysis, hepatic and renal function tests, bone metabolism parameters, Anti-tTG IgA and IgG, free T4, and Thyroid-Stimulating Hormone (TSH). Elevated levels of Anti-tTG prompted further evaluation via duodenal biopsy. Additionally, hand and wrist radiographs were analyzed for signs of rickets and to estimate bone age, utilizing the Greulich and Pyle Atlas as a reference tool. Short stature causes categorized as follows: Familial Short Stature (FSS) – bone age equals or exceeds chronological age, both above height age; Hypothyroidism – Free T4 < 0.93ng/dL, TSH > 6.4 uIU/ml; Growth Hormone Deficiency (GHD) - levels < 10ng/ml on insulin stress test; Type 1 diabetes mellitus (T1DM) – HbA1c ≥ 6.5%; Constitutional delay of growth and maturation(CDGM)– bone age equals or below height age, both under chronological age; Primary malnutrition – weight < 60% of expected per NCHS standards, history of reduced caloric intake; Celiac disease – duodenal mucosal changes in biopsy, transglutaminase antibodies raised (IgA > 7U/ml, IgG > 17U/ml); Turner syndrome - short neck, low set ears, shield-like chest, and 44A+OX genotype. Growth hormone deficiency was assessed with insulin tolerance test in those children with strong clinical suspicion and all baseline investigations were normal. The blood glucose level was checked at baseline via glucometer and rapid acting insulin given at a dose of 0.1IU/kg intravenously. Blood samples for blood glucose and serum growth hormone were drawn at 0, 30, 60, 90 and 120 minutes and values below 10ng/ml were considered growth hormone deficient. Data collected were analyzed using SPSS version 25.0 to present mean ± standard deviation for quantitative variables like age, height, and weight. Qualitative data such as gender, socio-economic status, residence, and causes of short stature were shown as frequencies and percentages. Stratification based on gender, age, residence, and socio-economic status was done to address effect modifiers. Chi-square tests were used to assess associations between categorical variables. Where expected cell counts were below 5, Fisher's Exact Test was applied instead. In cases where subgroup sizes were too small to meet test assumptions and could not be meaningfully grouped, results were interpreted with caution, a significance threshold of $p \leq 0.05$ was applied post-stratification.

RESULTS

The study comprised 94 males (52.2%) and 86 females (47.8%). Regarding age distribution, 112 children (62.2%) were between 7-12 years, while 68 children (37.8%) were between 3-6 years, with a mean age of 7.47±2.54 years. Most participants (73.9%) resided in rural areas, with only 26.1% from urban settings. The socioeconomic status distribution showed that 43.3% belonged to low socioeconomic status, 38.9% to middle, and 17.8% to high socioeconomic status. Among the causes of short stature, Familial Short Stature (FSS) was the most prevalent, affecting 37 children (20.6%), followed by Constitutional Delay of Growth and Maturation (CDGM) and Primary Malnutrition, each accounting for 29 cases (16.1%). Growth Hormone Deficiency (GHD) was identified in 28 children

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(15.6%), while Hypothyroidism was diagnosed in 20 children (11.1%). Less common causes included Celiac Disease (8.3%), Type 1 Diabetes Mellitus (T1DM) (7.8%), and Turner Syndrome, which was the least common cause, affecting only 8 children (4.4%).

Table 1: Frequency Distribution of Different Variables (n=180)

Variables	Categories	Frequency (%)/ Mean ± SD
Gender	Male	94 (52.2)
	Female	86 (47.8)
Age Groups	3-6 Years	68 (37.8)
	7-12 Years	112 (62.2)
	Mean Age (Years)	7.47 ± 2.54
Residence	Rural	133 (73.9)
	Urban	47 (26.1)
Socio-Economic Status	Low	78 (43.3)
	Middle	70 (38.9)
	High	32 (17.8)
Causes of Short Stature	Familial Short Stature (FSS)	37 (20.6)
	Growth Hormone Deficiency (GHD)	28 (15.6)
	Constitutional delay of growth and maturation (CDGM)	29 (16.1)
	Primary Malnutrition	29 (16.1)
	Hypothyroidism	20 (11.1)
	Type 1 Diabetes Mellitus (T1DM)	14 (7.8)
	Celiac Disease (CD)	15 (8.3)
	Turner Syndrome	8 (4.4)

Tables 2-5 presented the stratification of various causes of short stature with respect to gender, age groups, residence, and socio-economic status among the 180 children included in the study. Table 2 compares short stature causes between males and females, noting no significant differences except for T1DM and Turner syndrome. Type 1 Diabetes Mellitus (T1DM) was more common in males (11.7% vs. 3.5%), while Turner syndrome only occurred in females.

Table 2: Stratification of causes of short stature with respect to gender

Causes of Short Stature	Categories	Gender		p-Value
		Male Frequency (%)	Female Frequency (%)	
Familial Short Stature (FSS)	Yes	19 (20.2)	18 (20.9)	0.905[a]
	No	75 (79.8)	68 (79.1)	
Growth Hormone Deficiency (GHD)	Yes	15 (16.0)	13 (15.1)	0.876[a]
	No	79 (84.0)	73 (84.9)	
Constitutional delay of growth and maturation (CDGM)	Yes	14 (14.9)	15 (17.4)	0.642[a]
	No	80 (85.1)	71 (82.6)	
Primary Malnutrition	Yes	15 (16.0)	14 (16.3)	0.953[a]
	No	79 (84.0)	72 (83.7)	
Hypothyroidism	Yes	12 (12.8)	8 (9.3)	0.460[a]
	No	82 (87.2)	78 (90.7)	
Type 1 Diabetes Mellitus (T1DM)	Yes	11 (11.7)	3 (3.5)	0.051[b]
	No	83 (88.3)	83 (96.5)	
Celiac Disease (CD)	Yes	8 (8.5)	7 (8.1)	0.928[b]
	No	86 (91.5)	79 (91.9)	
Turner Syndrome	Yes	0 (0.0)	8 (9.3)	0.002[b]
	No	94 (100.0)	78 (90.7)	

([a]Chi-Sqaure Test,[b]Fisher Exact Test)

Table 3 showed that older kids had more growth hormone deficiency, while younger ones had more celiac disease.

Table 3: Stratification of Causes of Short Stature with Respect to Age Groups

Causes of Short Stature	Categories	Age Groups Frequency (%)		p-Value
		3-6 Years	7-12 Years	
Familial Short Stature (FSS)	Yes	13 (19.1)	24 (21.4)	0.710[a]
	No	55 (80.9)	88 (78.6)	
Growth Hormone Deficiency (GHD)	Yes	4 (5.9)	24 (21.4)	0.005[b]
	No	64 (94.1)	88 (78.6)	
Constitutional delay of growth and maturation (CDGM)	Yes	15 (22.1)	14 (12.5)	0.091[a]
	No	53 (77.9)	98 (87.5)	
Primary Malnutrition	Yes	12 (17.6)	17 (15.2)	0.662[a]
	No	56 (82.4)	95 (84.8)	

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Hypothyroidism	Yes	8 (11.8)	12 (10.7)	0.828[a]
	No	60 (88.2)	100 (89.3)	
Type 1 Diabetes Mellitus (T1DM)	Yes	3 (4.4)	11 (9.8)	0.256[b]
	No	65 (95.6)	101 (90.2)	
Celiac Disease (CD)	Yes	12 (17.6)	3 (2.7)	0.001[b]
	No	56 (82.4)	109 (97.3)	
Turner Syndrome	Yes	1 (1.5)	7 (6.3)	0.262[b]
	No	67 (98.5)	105 (93.8)	

([a]Chi-Sqaure Test, [b]Fisher Exact Test)

Table 4 indicated hypothyroidism was more prevalent in urban areas. Turner syndrome cases were in rural regions.

Table 4: Stratification of Causes of Short Stature with Respect to Residence

Causes of Short Stature	Categories	Residence		p-Value
		Rural Frequency (%)	Urban Frequency (%)	
Familial Short Stature (FSS)	Yes	28 (21.1)	9 (19.1)	0.781[a]
	No	105 (78.9)	38 (80.9)	
Growth Hormone Deficiency (GHD)	Yes	20 (15.0)	8 (17.0)	0.747[a]
	No	113 (85.0)	39 (83.0)	
Constitutional Delay of Growth and Maturation (CDGM)	Yes	25 (18.8)	4 (8.5)	0.112[b]
	No	108 (81.2)	43 (91.5)	
Primary Malnutrition	Yes	20 (15.0)	9 (19.1)	0.510[a]
	No	113 (85.0)	38 (80.9)	
Hypothyroidism	Yes	11 (8.3)	9 (19.1)	0.041[b]
	No	122 (91.7)	38 (80.9)	
Type 1 Diabetes Mellitus (T1DM)	Yes	11 (8.3)	3 (6.4)	1.000[b]
	No	122 (91.7)	44 (93.6)	
Celiac Disease (CD)	Yes	10 (7.5)	5 (10.6)	0.506[b]
	No	123 (92.5)	42 (89.4)	
Turner Syndrome	Yes	8 (6.0)	0 (0.0)	0.114[b]
	No	125 (94.0)	47 (100.0)	

([a]Chi-Square Test, [b]Fisher Exact Test)

Table 5 revealed a socio-economic link with hypothyroidism more common in high-status groups. The absence of celiac disease and Turner syndrome in high-status groups was noteworthy. These findings support previous research on short stature causes across demographics, such as the male predominance in type 1 diabetes and the higher hypothyroidism prevalence in urban and high-status children, possibly due to better healthcare access.

Table 5: Stratification of Causes of Short Stature with Respect to Socio-Economic Status

Causes of Short Stature	Categories	Socio-Economic Status			p-Value
		Low Frequency (%)	Middle Frequency (%)	High Frequency (%)	
Familial Short Stature (FSS)	Yes	14 (17.9)	16 (22.9)	7 (21.9)	0.746[a]
	No	64 (82.1)	54 (77.1)	25 (78.1)	
Growth Hormone Deficiency (GHD)	Yes	10 (12.8)	12 (17.1)	6 (18.8)	0.661[a]
	No	68 (87.2)	58 (82.9)	26 (81.3)	
Constitutional Delay of Growth and Maturation (CDGM)	Yes	15 (19.2)	8 (11.4)	6 (18.8)	0.394[a]
	No	63 (80.8)	62 (88.6)	26 (81.3)	
Primary Malnutrition	Yes	15 (19.2)	11 (15.7)	3 (9.4)	0.440[a]
	No	63 (80.8)	59 (84.3)	29 (90.6)	
Hypothyroidism	Yes	7 (9.0)	5 (7.1)	8 (25.0)	0.021[b]
	No	71 (91.0)	65 (92.9)	24 (75.0)	
Type 1 Diabetes Mellitus (T1DM)	Yes	4 (5.1)	8 (11.4)	2 (6.3)	0.338[b]
	No	74 (94.9)	62 (88.6)	30 (93.8)	
Celiac Disease (CD)	Yes	9 (11.5)	6 (8.6)	0 (0.0)	0.138[b]
	No	69 (88.5)	64 (91.4)	32 (100.0)	
Turner Syndrome	Yes	4 (5.1)	4 (5.7)	0 (0.0)	0.399[b]

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	No	74 (94.9)	66 (94.3)	32 (100.0)	

([a]Chi-Square Test, [b] Fisher Exact Test)

DISCUSSION

The present study identified Familial Short Stature (FSS) as the most prevalent cause of short stature (20.6%), followed by Constitutional Delay of Growth and Maturation (CDGM) and primary malnutrition (16.1% each), Growth Hormone Deficiency (GHD) (15.6%), hypothyroidism (11.1%), celiac disease (8.3%), Type 1 Diabetes Mellitus (T1DM) (7.8%), and Turner syndrome (4.4%). These findings are consistent with several previous studies that have reported normal variants of growth as the predominant causes of short stature in children. Sultan *et al.*, conducted a study in 214 children with short stature and found that constitutional growth delay (17.3%), familial short stature (15%), malnutrition (9.8%), celiac disease (6.5%), and growth hormone deficiency (6.1%) were the five most common etiological factors [13]. Similarly, a study by Hussein *et al.*, reported that 63.6% of children with short stature had normal variants, with 42% having familial short stature, 15.8% having constitutional growth delay, and 5.5% having a combination of both [16]. A study analyzed the causes and clinical characteristics of short stature in children at a tertiary care reported most common causes were growth hormone deficiency and normal variant short stature [17]. In a recent study from Bangladesh, Karim MR *et al.*, identified familial short stature as the most common cause (51%), followed by constitutional growth delay (14%) and hypothyroidism (12%) and in another recent study conducted by Islam *et al.*, common causes were normal growth variant (59.26%) and endocrinal causes comprised (31%) [18, 19]. Another study from Bangladesh by Jasim S *et al.*, also reported familial short stature as the most common cause (20.57%), followed by hypothyroidism (13.14%) and familial short stature co-existing with nutritional problems (8.6%) [20]. However, some studies have reported different patterns. According to this study, three main etiological groups were identified normal variant of growth delay (55%), endocrinological diseases (28%) and non-endocrinological (17%) [21]. Similarly, Penugonda N *et al.*, reported that growth hormone deficiency (28%) and normal variant short stature (26%) were the predominant causes of short stature [17]. The prevalence of endocrine disorders in this study (34.5% combined for GHD, hypothyroidism, and IDDM) is higher than reported by some studies but lower than others [14, 15, 17, 21]. This variation might be attributed to differences in study settings, referral patterns, and diagnostic criteria. The findings of growth hormone deficiency in 15.6% of cases is higher than reported by Sultan *et al.*, (6.1%) but lower than reported by Penugonda N *et al.*, (28%) [13, 17]. The prevalence of hypothyroidism (11.1%) in this study reported by Islam MR and Mosharaf M (12%), and Jasim S *et al.*, (13.14%), but lower than reported by Lashari *et al.*, (15%) [19-21]. The prevalence of celiac disease (8.3%) is higher than reported in most studies, which might reflect increased awareness and improved diagnostic facilities [18, 19, 21]. The study's limitations include its cross-sectional design hindering assessment of temporal relationships and long-term outcomes. It was conducted at a single tertiary care center, potentially causing referral bias and limiting generalizability. A small sample size of 180 children may have limited statistical power, especially for uncommon causes. Diagnostic criteria for certain conditions, like growth hormone deficiency, relied on single stimulation tests rather than multiple, affecting accuracy. Socioeconomic classification was based solely on monthly income. The study did not consider seasonal growth variations or psychosocial factors. Despite these limitations, it offers valuable insights into short stature etiology in children at a regional tertiary care hospital.

CONCLUSIONS

In conclusion common causes of short stature are familial and constitutional growth delay, along with endocrine disorders like hypothyroidism and growth hormone deficiency. It stresses the need for thorough evaluation, early diagnosis, and tailored interventions to enhance growth outcomes and quality of life. Future studies should explore natural history and treatment outcomes of short stature causes with larger samples and longer follow-up.

Authors Contribution

Conceptualization: AF
Methodology: AF, QUZ, HN, NM, HS
Formal analysis: AF, HN, HS
Writing, review and editing: AF, QUZ, HN, NM, HS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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