MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2024.11.71.76

Pathological and Syndromic Short Stature in Children: Clinical and Etiological Profile

[1]Zhahid Hassan Baigh, [2]Dara Sudhakar, [3]Iqra Fayaz and [4]Irfan Ali

[1-4]*Department of Medicine, GMC, Srinagar, India*

OPEN ACCESS

Key Words
Short stature, syndromic short stature, growth and development pathological short stature, paediatric health

Corresponding Author
Zhahid Hassan Baigh,
Department of Medicine, GMC, Srinagar, India

Author Designation
[1]Assistant Professor
[2,3]Post Graduate
[4]Associate Professor

Received: 20 August 2024
Accepted: 10 October 2024
Published: 12 October 2024

Citation: Zhahid Hassan Baigh, Dara Sudhakar, Iqra Fayaz and Irfan Ali, 2024. Pathological and Syndromic Short Stature in Children: Clinical and Etiological Profile. Res. J. Med. Sci., 18: 71-76, doi: 10.36478/makrjms.2024.11.71.76

ABSTRACT
Short stature is one of the most common concerns in pediatric health, with causes that range from physiological to pathological, each accounting for roughly half of the cases. This study aims to explore the clinical profiles of children presenting with pathological short stature, with a particular focus on identifying its diverse causes, including syndromic conditions. By investigating the full spectrum of underlying factors, the study seeks to enhance understanding and management of pathological short stature in pediatric populations. Retrospective study was conducted in outpatient clinic of endocrinology unit in dept of medicine at SMHS Hospital, Karan Nagar, Srinagar J and K, where the data of children who met the inclusion criteria were collected from the case records of 1.5 years period from Feb 2022 to August 2023. Data collected was tabulated and analyzed using appropriate statistical methods. In the present study, the overall incidence of short stature was found to be 9.7%. Among the cases, proportionate short stature accounted for 91%, while disproportionate short stature comprised 9%. Etiologically, pathological short stature (68%) was more prevalent than physiological short stature (32%). Within the pathological category, genetic causes were the most common, contributing to 41.2% of cases, followed by endocrine disorders (17.6%), central nervous system involvement (11.8%), respiratory system issues (11.8%), renal conditions (11.8%) and haematological disorders (5.9%). Among the 33% of cases categorized as physiological short stature, nutritional deficiency was the most common accounting for 37.5% of cases followed by familial history of short stature (25%) and delayed puberty (25%). Genetic abnormalities and endocrine disorders are the most common causes of pathological short stature. Given that many of these conditions can be effectively treated when identified early, a thorough evaluation is essential for timely diagnosis and intervention.

INTRODUCTION

As living conditions in underdeveloped nations have gradually improved, more parents are becoming concerned about their children's development. Growth abnormalities were not adequately assessed or recognized in this region of the world in the past due to a lack of knowledge and the unavailability of investigative facilities. These illnesses are being studied more frequently now that people are increasingly aware of the potential for treatable problems and the accessibility of diagnostic tools.

Short stature is a common paediatric endocrine concern. A child's growth-reflected in their height and weight-should be measured annually, as normal growth is a vital indicator of overall health in childhood. A child who is growing at a normal rate is unlikely to have any significant underlying physical or mental health issues. Growth can be influenced by a range of factors, including genetic, perinatal, postnatal, and environmental factors, all of which play a critical role in determining a child's developmental trajectory[1].

Short stature can arise from a variety of pathological causes, involving a broad spectrum of medical conditions that affect growth and development. While some individuals may be genetically predisposed to shorter stature, others may experience growth impairments due to underlying health issues that require medical intervention. Below are some common pathological causes of short stature:

Growth Hormone Deficiency (GHD): Growth Hormone Deficiency is a condition in which the pituitary gland does not produce enough growth hormone, a key regulator of growth, cell reproduction and regeneration. While GHD can occur at any age, it is most diagnosed in children. **Thyroid Disorders:** Thyroid imbalances, such as hypothyroidism or hyperthyroidism, can disrupt the hormones essential for growth. Thyroid hormones play a crucial role in skeletal growth, both directly and by enabling the action of growth hormone. Disruptions in this balance can result in short stature. **Genetic Disorders:** Several genetic conditions can affect growth. For instance, Turner syndrome, a disorder affecting females, results in short stature and other developmental issues. Similarly, conditions like Noonan syndrome and Russell-Silver syndrome (RSS) can cause multiple developmental problems, including short stature. **Bone Disorders:** Conditions that affect bone development, such as skeletal dysplasias or genetic disorders like achondroplasia, can lead to short stature due to abnormalities in bone formation and growth. **Chronic Illnesses:** Chronic illnesses, such as inflammatory bowel disease, celiac disease and chronic kidney disease, can impede growth and development in children, often resulting in short stature. **Constitutional Growth Delay:** Some individuals may experience a delayed growth spurt during adolescence, leading to a later onset of puberty and delayed bone maturation. While these individuals generally catch up over time, their stature may be shorter during childhood and adolescence. **Malnutrition:** Insufficient nutrition, particularly during key growth phases, can significantly impede normal development and is a major contributor to short stature. Intrauterine **Growth Restriction (IUGR):** When fetal growth is restricted in the womb, it often leads to low birth weight, which can consequently result in shorter stature during childhood. **Syndromic Short Stature:** Syndromic short stature refers to a condition where reduced height is just one characteristic of a broader syndrome-a cluster of signs and symptoms that define a specific medical condition. Such syndromes can be genetic or chromosomal and may also include developmental delays, facial abnormalities, organ malformations and other clinical manifestations. Examples include conditions like Down syndrome and Prader-Willi syndrome, where short stature is just one part of a more complex clinical presentation[2-4]. In addition, several genetic syndromes are associated with short stature, each presenting with distinct clinical features: **Turner Syndrome** is a genetic disorder that affects females and is characterized by the partial or complete absence of one X chromosome (monosomy X). Affected individuals commonly present with short stature, along with features such as a webbed neck, broad chest and ovarian insufficiency, which can result in infertility and delayed sexual development. **Noonan Syndrome** is another genetic condition that impacts various body systems. Individuals with Noonan Syndrome often exhibit short stature, along with distinctive facial features, congenital heart defects, and developmental delays. The syndrome may also lead to skeletal and hematological abnormalities. **Prader-Willi Syndrome** is characterized by a spectrum of physical, cognitive and behavioral features. Early infancy is marked by hypotonic and feeding difficulties, while older individuals frequently develop hyperphagia, leading to obesity. Short stature is a prominent feature, often requiring growth hormone therapy as part of the management strategy. **Sotos Syndrome** is primarily associated with excessive growth during early childhood. Despite initial overgrowth, individuals with Sotos Syndrome may experience a deceleration in growth during adolescence, often resulting in shorter adult stature than initially anticipated. Intellectual disability and distinctive facial characteristics are also common. **Russell-Silver Syndrome (RSS)** is a rare

congenital growth disorder characterized by intrauterine growth retardation, low birth weight and postnatal growth failure. Children with RSS typically present with short stature, a triangular face, a relatively large head and body asymmetry. Other features may include clinodactyly (curved pinky fingers) and feeding difficulties. The exact etiology of RSS remains unclear, though a combination of genetic and epigenetic factors is thought to be involved. Management includes growth hormone therapy, nutritional interventions and physical therapy to address the specific symptoms associated with the syndrome[5].

Diagnosing the specific cause of short stature requires a thorough medical evaluation, including physical examination, growth charts analysis and often laboratory tests. Treatment approaches vary depending on the underlying cause and may include hormonal therapy, nutritional interventions, or addressing the specific medical condition contributing to the short stature. Early detection and intervention are crucial for optimizing outcomes and ensuring that individuals with short stature receive appropriate support and care. Hence this study aimed to understand the clinical characteristics and causes of short stature in children. Given that 68% of short stature cases are due to pathological causes, early identification of these underlying conditions is crucial for timely intervention and management. By recognizing the specific causes, appropriate treatment can be initiated and parents can be better informed about the condition.

MATERIALS AND METHODS

A retrospective study was conducted in the Department of General medicine, SMHS Hospital, Karan Nagar, Srinagar where the data of children who met the inclusion criteria were collected from the case records of 1.5 years period from February 2022 to August 2023.

Inclusion Criteria: All children diagnosed as short stature i.e. height below 3rd centile or less than two standard deviations (SDs) below the median height for that age and sex according to the population standard. IAP growth charts were used and due to some pathological disorder being diagnosed using various investigations like, complete hemogram with erythrocyte sedimentation rate, bone age, urinalysis, stool examination, renal function test, calcium, phosphate, alkaline phosphatase, venous gas, fasting sugar, liver function tests, hormone assays like Insulin like growth factor assay/growth hormone stimulation tests, thyroid function test, karyotyping, mutation analysis (wherever possible) and neuroimaging as per the presentation and cause.

RESULTS AND DISCUSSIONS

A total of 257 patients were admitted between February 2022 and August 2023. Among these, 25 patients presented with short stature, accounting for an incidence of 9.7%. This data reflects the prevalence of short stature in the cohort of admissions during this period (Table 1).

Table 1: Incidence of Short Stature in Admitted Patients

Total no. of admissions (Feb 2022- Aug 2023)	257
Total no. of patients of short stature	25
Incidence (%)	9.7%

The total number of patients with short stature was 25 as mentioned earlier, with a male-to-female ratio of 1.08:1. Most cases (52%) were observed in the age group of 1-5 years, indicating that early childhood is a critical period for the manifestation of growth issues. This data suggests that short stature predominantly affects children in early childhood and there is a relatively balanced gender distribution with a slight male predominance (Table 2).

Table 2: Age and Sex

Age	Male	Female	Number	Percentage
2 m-1 y	1	1	2	8%
1 y-5 y	7	6	13	52%
5 y-9 y	3	3	6	24%
9 y-12 y	2	2	4	16%
Total	13	12	25	-
Percentage	52%	48%	-	100%

Among the 25 patients with short stature, 68% (17 cases) were found to have a pathological cause, while the remaining 32% (8 cases) were classified as physiological. This distribution highlights that most short stature cases in the cohort were due to underlying pathological conditions (Table 3).

Table 3: Etiological Profile

Etiology	Number	Percentage
Pathological	17	68%
Physiological	8	32%

Among the 17 patients diagnosed with pathological short stature, the distribution by body system is as follows: Genetic disorders were the most common cause, accounting for 7 cases (41.2%), including Down syndrome (2 cases), Turner syndrome (1 case), Russell-Silver syndrome (1 case), skeletal dysplasia (1 case), Ellis van Creveld syndrome (1 case) and Rabson Mendenhall syndrome (1 case). Endocrine disorders contributed to 3 cases (17.6%), with 1 case of growth hormone deficiency and 2 cases of hypothyroidism. Renal conditions were responsible for 2 cases (11.8%), including nephrotic syndrome (1 case) and chronic kidney disease (1 case). Respiratory conditions

Table 4: Systemic Involvement

	Body system	Number (N=16)	Percentage
a) Genetic	Downs-2 Turner-1	7	
	Russell silver syndrome-1 Skeletal dysplasia - 1		
	Ellis van Creveld syndrome -1 Rabson		
	Mendenhall syndrome-1		741.2%
b) Endocrine	GH deficiency-1 Hypothyroidism- 2	3	17.6%
c) Renal	Nephrotic syndrome-1. Chronic kidney		
	disease-1	2	11.8%
d) Respiratory	Asthma-1 Tuberculosis-1	2	11.8%
e) CNS	C. Palsy - 1 TbME-1	2	11.8%
f) Hematological	Thalassemia-1	1	5.9%

accounted for 2 cases (11.8%), including asthma (1 case) and tuberculosis (1 case). Central Nervous System (CNS) disorders were identified in 2 cases (11.8%), involving cerebral palsy (1 case) and tubercular meningitis (TbME, 1 case). Hematological disorders were seen in 1 case (5.9%) of thalassemia. (Table 4).

Out of the 8 cases of physiological short stature, the causes were distributed as follows: Nutritional deficiency was the most common, accounting for 3 cases (37.5%). Delayed puberty was observed in 2 cases (25%). Family history of short stature was noted in 2 cases (25%). Chronic illness was responsible for 1 case (12.5%). These findings highlight that nutritional factors and developmental delays play a significant role in physiological short stature, while genetic predisposition and chronic illnesses also contribute to a lesser extent (Table 5).

Table 5: Distribution of Etiological Factors in Physiological Short Stature

Condition	Total Number = 8	Percentage
Delayed puberty	2	25%
Nutritional deficiency	3	37.5%
Family history	2	25 %
Chronic illness	1	12.5%

As per our study, delayed development is found among 3 (12.5%) patients that includes patients of hypothyroidism, genetic syndrome and some chronic systemic illness e.g. cerebral palsy.

Table 6: Developmental History

Normal	21 (87.5%)
Delayed	3 (12.5%)

The incidence of disproportionate short stature was found to be 2 (9%).

Table 7: Short Stature Type

Proportionate	22 (91%)
Disproportionate	2 (9%)

Some specific and rare syndromic short stature cases that came across our study period: The present study aimed to evaluate the clinical and etiological profile of children with short stature admitted to the Department of Medicine at SMHS Hospital, Karan Nagar, over a 1.5-year period. The study identified an incidence of 9% of short stature, with a predominance of pathological causes (66%) over physiological causes (33%).

Fig.1A-C: Positive findings for RSS: Wide Shark Like Teeth, Dental Caries. 1a and 1b: Triangle Shaped Face, Underweight, Severe Short Stature, Relative Macrocephaly

Fig. 2: Chest: Cage Deformity, Skeletal Dysplasia, Underweight, Short Stature

Fig. 3: A Case of Skeletal Dysplasia-Spondyloepiphyseal Dysplasia with Short Stature and Normal Bone Age

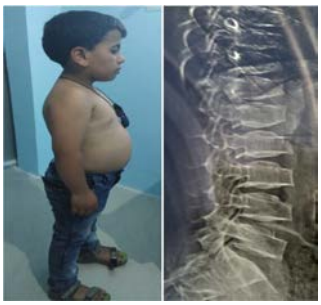

Fig. 4: A Case of Skeletal Dysplasia-Spondyloepiphyseal Dysplasia with Short Stature and Normal Bone Age

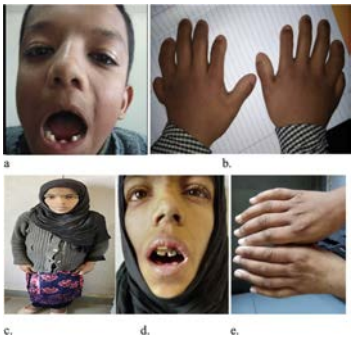

Fig.5A-E: Cases of Syndromic Short Stature: a, b-Ellis Van Creveld Syndrome (Enamel Hypoplasia and Ectodermal Dysplasia). c, d, e-Rabson Mendenhall Syndrome (Insulin Resistance Syndrome with Ectodermal Hypoplasia, Enamel Hypoplasia)

The findings are consistent with prior studies, which underscore the importance of early detection and intervention in managing growth abnormalities in children.

The 9% incidence of short stature in this study aligns with similar prevalence rates observed in hospital-based studies across different regions. For example, a study conducted by Rajput *et al.* reported a 10.49% incidence of short stature among paediatric and adolescent admissions[6]. This prevalence suggests that short stature remains a significant concern in paediatric healthcare, particularly in low-resource settings. In our study, genetic disorders emerged as the leading cause of pathological short stature, accounting for 41.2% of the cases. This finding is consistent with a study by Phadke[7], which highlighted a significant prevalence of genetic conditions, including syndromic disorders such as Turner syndrome and skeletal displace, as prominent contributors to short stature[7]. Endocrine disorders, including growth hormone deficiency (GHD) and hypothyroidism, accounted for 17.6% of the cases in our study. This is in line with findings by Song K *et al.*, who reported GHD as the most prevalent cause comprising 38.9% of cases[8]. The variation in the prevalence of GHD between different studies highlights the heterogeneity in etiological profiles across populations. Such discrepancies may stem from variations in diagnostic criteria, genetic predispositions and demographic factors, as well as differences in healthcare access and screening protocols across regions. Our study also identified respiratory (11.8%) and renal (11.8%) system involvement as contributors to short stature, which are consistent with several studies who have observed that chronic systemic illnesses such as asthma and chronic kidney disease often impede normal growth due to long-term effects on metabolism and nutrient absorption[9,10]. In our study, nutritional deficiency was the leading cause of physiological short stature, accounting for 37.5% of cases. This finding is consistent with the study by Garg P, which reported that protein-energy malnutrition and chronic diseases were the most common causes of short stature in Indian children, comprising 53.5% of cases[11]. These results emphasize the role that malnutrition and chronic health conditions play in growth delays, particularly in resource-limited settings where nutritional deficiencies are prevalent and also highlight the need for comprehensive management strategies that address underlying malnutrition and chronic illnesses to improve growth outcomes. Nutritional interventions and appropriate counselling are essential in managing these cases, emphasizing the need for public health initiatives to address childhood malnutrition. These findings emphasize the critical role that malnutrition and chronic health conditions play in growth delays, particularly in resource-limited settings where nutritional deficiencies are widespread. They also underscore the need for comprehensive management strategies that not only address underlying malnutrition and chronic illnesses but also focus on improving overall growth outcomes. Nutritional interventions, coupled with appropriate counselling, are essential in managing such cases. This highlights the importance of public health initiatives aimed at reducing childhood malnutrition through education, early intervention and sustained support programs.

The male-to-female ratio of 1.08:1 observed in our study, with a predominance of cases in the 1-5 years age group reflects similar demographic trends noted in other studies[12]. But our results also contrasts with findings from a study done in Bangladesh, where the male-to-female ratio was 0.92:1 and the most common age group affected was 6-11 years[13]. The later study noted a slightly higher prevalence of short stature in girls, which may be attributed to gender-specific growth patterns and underlying genetic factors. These differences in age distribution and gender prevalence could reflect variations in socio-demographic factors and health practices between the two regions. Early childhood, particularly the 1-5 years age group, is a critical period for growth and any deviation from normal growth trajectories during this time warrants thorough investigation to prevent long-term health consequences.

The findings of this study reinforce the importance of early identification and intervention in children with short stature, particularly when pathological causes are suspected. Genetic testing, endocrine evaluations and comprehensive assessment of systemic conditions are essential components of managing short stature. Given the high incidence of treatable causes, including growth hormone deficiency and hypothyroidism, early

diagnosis and therapeutic interventions can result in significant improvements in growth outcomes.

CONCLUSION

Short stature is a complex and multi factorial condition influenced by a range of genetic, environmental and medical factors. While some individuals may have a natural genetic predisposition to shorter height, others may be affected by nutritional deficiencies, hormonal imbalances, or underlying medical conditions. It is vital to approach short stature with empathy and understanding, recognizing that height does not determine an individual's worth, abilities, or potential. Early detection and intervention for any underlying medical causes of short stature are critical for ensuring optimal growth and development. Continued research into the genetic and environmental contributors to height, along with advancements in medical interventions, will deepen our understanding of short stature and may lead to improved treatment options. A holistic and compassionate approach is necessary to address the varied factors contributing to short stature, ensuring comprehensive support for individuals affected by this condition.

REFERENCES

1. Kamboj, M., 2005. Short stature and growth hormone. The Indian J. Pediatr.s, 72: 1-10.0.
2. Feldt-Rasmussen, U. and M. Klose 2022. Adult Growth Hormone Deficiency-Clinical Management. Endotext. 0 1-10.0.
3. Ranke, M.B., C.P. Schwarze, K. Mohnike, K.E. von Mühlendahl, E. Keller, H. Willgerodt and W. Kiess, 1998. Catch-Up Growth after Childhood-Onset Substitution in Primary Hypothyroidism: Is It a Guide towards Optimal Growth Hormone Treatment in Idiopathic Growth Hormone Deficiency? Hormone Res. Paediatrics, 50: 1-10.0.
4. Butler, M.G., B.S. Miller, A. Romano, J. Ross and M.J. Abuzzahab *et al.,* 2022. Genetic conditions of short stature: A review of three classic examples. Front. Endocrinol., Vol. 13 .10.3389/ fendo.2022.1011960 1-10.0.
5. Siklar, Z. and M. Berberoglu, 2014. Syndromic Disorders with Short Stature. J. Clin. Res. Pediatr. Endocrinol., 6: 1-10.0.
6. Rajput, R., M. Rani, M. Rajput and R. Garg, 2021. Etiological Profile of Short Stature in Children and Adolescents. Indian J. Endocrinol. Metab., 25: 1-10.0.
7. Kaur, A. and S.R. Phadke 2012. Analysis of short stature cases referred for genetic evaluation. Indian J Pediatr. 79: 1-10.0.
8. Song, K.C., S.L. Jin, A.R. Kwon, H.W. Chae, J.M. Ahn, D.H. Kim and H.S. Kim, 2015. Etiologies and characteristics of children with chief complaint of short stature. Ann. Pediatr. Endocrinol. and Metab., Vol. 20 .10.6065/apem.2015.20.1.34 1-10.0.
9. Bhadada, S.K., A. Bhansali, P. RaviKumar, R. Kochhar, C.K. Nain, P. Dutta and S. Lal, 2011. Changing Scenario in Aetiological Profile of Short Stature in India-Growing Importance of Celiac Disease: A Study from Tertiary Care Centre. The Indian J. Pediatr.s, 78: 1-10.0.
10. Becherucci, F., R.M. Roperto, M. Materassi and P. Romagnani, 2016. Chronic kidney disease in children. Clin. Kidney J., Vol. 9 .10.1093/ckj/sfw047 1-10.0.
11. Garg, P., 2009. Short stature in Indian children: Experience from a community level hospital. Sri Lanka J. Child Health, Vol. 34 .10.4038/ sljch.v34i3.399 1-10.0.
12. Yadav, A.K. and S.T. Karki, 2024. Short Stature in Children Visiting Endocrine Out Patient Department of Kanti Children's Hospital, Nepal. J. Coll. Med. Sci.-Nepal, Vol. 17 .10.3126/ jcmsn.v17i1.36053 1-10.0.
13. Karim, M.R., K.J. Shamaly, B.B. Tithi, R. Akter, I. Jahan and S. Begum, 2020. Etiology of short stature in children attending pediatric endocrinology clinic of a tertiary care hospital in Bangladesh. Int. J. Contemp. Pediatr.s, 7: 1-10.0.