ORIGINAL RESEARCH PAPER

Paediatric Medicine

TO STUDY THE ETIOLOGICAL PROFILE OF SHORT STATURE AMONG CHILDREN ATTENDING TERTIARY CARE CENTRE

KEY WORDS: Short Stature, Constitutional growth delay(CGD),Growth Hormone Deficiency.

Thilagavathi Duraisamy* Paediatric Resident, Kanchi Kamakoti Childs Trust Hospital *Corresponding Author

Gem Raghav Prashanth R Paediatric Resident, Kanchi Kamakoti Childs Trust Hospital

Karnam Ravikumar Senior Consultant, Kanchi Kamakoti Childs Trust Hospital

ABSTRACT

Background Early detection and diagnosis of short stature decrease the effect of any underlying health condition and optimizes final adult height.This study was done identify the etiological profile of short stature. **Methodology** This was a prospective observational study conducted in children aged 2 to 18 years with short stature. Children who fail to complete the etiological work up and those who are not fitting in definition for short stature were excluded. **Results** 80 children were included .44 were females and 36 were males. Endocrinological cause was the commonest, 53%(N=42) among which Growth hormone deficiency was predominant (20%). 24 children(30%) had non endocrine causes among which syndromic causes were predominant(N=9).14 children had non pathological causes and familial short stature(N=8) was predominant in them **Conclusion** Pathological short stature was predominat among which endocrine causes were the commonest. Isolated Growth Hormone deficiency was the most common endocrine cause followed by hypopituitarism and hypothyroidism. There was statistically significant relationship between the presence of dysmorphism (p< .01) and parental consanguinity (p < .05) separately with the etiology. Majority (40%)were aged between 11-18 years denoting fairly late referral for short stature . So general paediatricians could be made aware of routine growth monitoring in children & early referral to a tertiary centre.

INTRODUCTION

Short stature is defined as height more than 2 standard deviations below the mean for age (height less than 3rd percentile)[1]. It may be the normal expression of genetic potential in which the growth rate is normal or it may be result of a condition that causes growth failure with a lower than normal growth rate.[2]Early detection and diagnosis of short stature decrease the effect of any underlying health condition and optimizes final adult height.For optimal efficacy of GH treatment, the appropriate diagnosis should be made and treatment initiated as early as possible in the life of the patient.[3]Short stature (SS) is unrecognized in early infancy that's why it is diagnosed at a late age which affects the improvement on health outcomes and stature. The evolving understanding of growth plate physiology has led to an increasing focus on abnormalities in this tissue resulting in the potential for the development of innovative therapies.[4]We undertook the study to identify common causes of short stature in an urban tertiary care childrens hospital setting since such studies might help communitybased interventions for early identification and therapy wherever possible.

AIMS AND OBJECTIVES

To determine the etiological profile of children presenting with short stature to the endocrine OPD in a tertiary care centre brought to the endocrine OPD

METHODOLOGY

This was a prospective observational study conducted in a tertiary care hospital in Chennai between November 2018-october 2019 after approval from the institutional ethics .Children aged 2 to 18 years with a) height 2 SD or morebelow the mean height for chronological age and gender in a given population (height less than 3rdpercentile),b) Growth velocity fall below the 25thpercentile, c) Height more than 1.5 SD below the mean, when corrected for mid parental height.[5] were included and children who fail to complete the etiological work up and those who are not fitting in definition for short stature were excluded. Age of Patients presenting to the endocrinology OPD were taken as the chronological age. Standing height was measured on a standardized height scale with heels, buttocks, shoulders and occiput in contact against a vertical board and the head positioned in Frankfurt plane .WHO growth charts were used to plot upto5 years and from 5 to 18 years IAP Growth charts were used. Growth charts are separate for boys and girls. Target height- Child's growth is strongly related to the genetic potential.[6] A child's mid parental height was calculated by using the formula.[7]Boys :{father's height in cm + (mothers's height in cm + 13)}/2 ; Girls :{mother's height in cm + (father's height in cm - 13)}/2 . For both boys and girls ,8.5cm either side of this calculated value(target height) represents 3rd to 95th percentile for anticipated height.[8] Sexual maturity rating was done by Marshall and Tanner pubertal staging [9]separately for boys and girls.Collected data was entered in Microsoft excel and tatistical analysis carried out using the Statistical Package for social services software.

RESULTS AND ANALYSIS

80 patients were included and evaluated .31 patients(39 %) were between 2 to 5 years age ,17 patients(21 %) between 6 to 10 years and 32 patients(40 %) under adolescent age group. Mean age of presentation was 8.53 years $\pm$ 4.6 SD. 44 were females and 36 were males with male: female ratio 1:1.2.(Table 1)There is no significant correlation between the etiology and Gender (p=0.6),Age group(p = 0.2) separately. Females had a higher mean age of presentation(9.11 years) than males (7.81 years). 53 % (N=42) patients had endocrine cause followed by non endocrine causes (30 % ,n=24) and normal variants(17%, n=14).Among normal variants (non pathological causes of short stature)8 patients had familial short stature and 6 children had Constitutional growth delay (CGD). Among the endocrinological causes most common disease causing short stature was Growth hormone deficiency (38 %, n=16) followed by hypothyroidism and panhypopituitarism both comprising 26%(n=11). The least common was hypoparathyroidism and uncontrolled diabetes mellitus both comprising 2 % (n=1).Among non endocrine causes 3 patients were IUGR,6 patients were malnourished or with chronic systemic illness, 4 patients with rickets, 2 with skeletal dysplasia (achondroplasia)and 9 patients with syndromic causes of short stature. Among the 9 children with

syndromic causes 4 children had turners, 2 had downs syndrome, 2 with seckel dwarfism and one with fanconis syndrome. (Table 2) Overall the most common cause of short stature was Growth hormone deficiency which comprised 20 % (n=16) of the patients followed by panhypopituitarism and hypothyroidism .

Females were predominantly affected in most of the endocrine causes (male: female ratio 1:1.3) like growth hormone deficiency, panhypopituitarism, hypothyroidism, diabetes mellitus except hypoparathyroidism (males > females) and growth hormone insensitivity(laron dwarfism) where they were equally affected. Males are dominantly affected in Non pathogenic causes with male : female ratio 1.3:1 .There was significant correlation between presence of dysmorphism and the etiology of short stature (p < .01) .Out of 80 patients 17 (29 %) had disproportionate short stature and 63(79 %) had proportionate short stature. 23 children (29 %) had dysmorphism and 57(71 %)had no dysmorphism.

Among males and females ,proportion of females having dysmorphism (31.81%) was higher compared to males (25 %). There was significant correlation between presence of parental consanguinity (p<.05) and the etiology of short stature. Out of the 80 patients with short stature ,MRI was done for 25 patients,out of which 11 patients had MRI Abnormalities in the form of pituitary hypoplasia(N=7), pituitary aplasia (n=1),pituitary SOL (n=2),Absent pituitary stalk(N=1).Most common MRI finding was pituitary hypoplasia.

Table 1: Percentage Analysis Of Chronological Age & Gender

Age	Males		Females		TOTAL (%)
	No.	%	No.	%	
2 -5 YR	15	41.17	16	36.36	31(39%)
6-10 YR	9	25	8	18.18	17(21%)
11-18YR	12	33.33	20	45.45	32(40%)
TOTAL	36	100	44	100	80(100%)

Table 2: Etiological Profile Of Short Stature

	ETIOLOGY	MALE	FEMALE	TOTAL(%)
Normal	Familial	4	4	8(10)
	Constitutional	4	2	6(7.5)
Endocrine	GH deficiency	7	9	16(20)
	GH insensitivity	1	1	2(2.5)
	Panhypopituitarism	4	7	11(13.75)
	Hypothyroidism	5	6	11(13.75)
	hypoparathyroidism	1	0	1(1.25)
	Diabetes Mellitus	0	1	1(1.25)
Non endocrine	IUGR	0	3	3(3.75)
	Malnutrition/chronic systemic disease	3	3	6(7.5)
	Rickets	2	2	4(5)
	Skeletal(achondroplasia)	2	0	2(2.5)
	Turners syndrome	0	4	4(5)
	Downs syndrome	2	0	2(2.5)
	Seckel syndrome	0	2	2(2.5)
	Fanconi syndrome	1	0	1(1.25)
	Total	36	44	80(100)

DISCUSSION

This is prospective observational study conducted in endocrine OPD of Kanchi Kamakoti CHILDS Trust Hospital. Children aged 2 to 18 years who satisfied the inclusion criteria were included. Short stature may be a disability and can be a distress to the victimized child or adolescent [10]. So it should be assessed early before epiphyseal fusion to get a chance for medical intervention at the right time. Our study was conducted in Endocrinology Department of a referral hospital and therefore there were many cases of pathological short stature, particularly relating to growth hormone and pituitary gland. Among age wise distribution of short stature patients in our study the mean chronological age of presentation was 8.53 + 4.61 years as compared with studies by Shideyassar, et al [11] (9.1 years) and Almontaser Hussein et al [12] (9.45 ± 3.7 years). Male: female ratio of 1:1.2 is agreement with studies like Chowdhury et al [13] (1:1.2) and Bharti Dubey et [14](1:1.1) .

There was statistically significant relationship between the presence of dysmorphism (p<.01) and parental consanguinity(p < .05) separately with the etiology. Endocrine causes which were predominant in our study is in agreement with other studies like colaco et al [15], and zargar et al [16]. Among the endocrinological factors Growth Hormone deficiency is most common which accounted for 20 % of the total patients with short stature. Similar observations were made in studies done by, Zargar et al with 22.8% of the patients ,colaco et al with 19.5 % .Patients with hypothyroidism accounted for 13.75 % is in agreement with study by Velayutham.K et al [17](13.79 %) .Hypothyroid patients reported in studies by Bhadada et al [18]., Colaco et al., and Zargar et al., are 14.2%, 10%, and 7.8% respectively. Children who had chronic disease and malnourished accounted for 7.5 % as seen in studies like colaco et al (8.5 %) and zargar et al (7.8 %). PEM causing short stature was infrequently observed in this study. This might have been due to the fact that this study was conducted in a speciality clinic. Among the rickets and skeletal causes of short stature this study accounts for 7.5 % as against 6.5 % ,10.4% seen in the studies by colaco et al,zargar et al respectively(Table 3). Regarding limitations this study is not a community based study, as it is taken only from the Pediatric Endocrine Department in a tertiary centre. Hence this does not reflect the true prevalence of short stature in the general population. The study sample size is small in number, because of shorter duration of the study period. However, similar studies conducted in large group of children have shown the similar results.GH stimulation test is not done in all children (done only in the cases deemed necessary by the treating endocrinologist).

Table 3: Comparison With Other Studies In Literature

	ETIOLOGY	Present study N= 80 (%)	Colaco et al N=200 (%)	Zargar et al N= 193 (%)	Bhadada et al N=352 (%)	Gutch et al N= 451 (%)
Normal	Familial	10	20.5		15.9	15.9
	Constitutional	7.5				41.2
Endocrine	GH deficiency	20	19.5	22.8	7.4	2.4
	GH insensitivity	2.5		4.1		
	Panhypopituitarism	13.75		7.8		1.7
	Hypothyroidism	13.75	10		14.2	8.6
	hypoparathyroidism	1.25				0.8
	Diabetes Mellitus	1.25	1			9.9
Non endocrine	IUGR	3.75	9.5			
	Malnutrition/chronic systemic disease	7.5	8.5	7.8	12.4	10.6
	Rickets /Skeletal	7.5	6.5	10.4	5.7	4.3
	Turners syndrome	4	7.5			1.8
	Miscellaneous(downs, seckel,fanconi)	6.25	5			

CONCLUSION

Majority had pathological short stature. (endocrine causes constitutes more than non-endocrine). The combined prevalence of familial and constitutional short stature is 20%

Among the endocrinological causes, most common cause was isolated GH deficiency, followed by hypopituitarism and hypothyroidism. There was statistically significant relationship between the presence of dysmorphism ($p < .01$) and parental consanguinity ($p < .05$) separately with the etiology. Clonidine stimulation test is a fairly reliable test for diagnosing growth hormone deficiency without complications. Those with known pathology affecting the central nervous system (such as CNS tumours with MRI showing pituitary abnormality), height velocity, bone age & IGF-1 reflects the onset of GH deficiency. In these children GH stimulation test are not required. In our group, majority (40%)were between ages of 11-18 years denoting fairly late referral for short stature . Hence general paediatricians could be made aware of routine growth monitoring in children & early referral to tertiary centre.

REFERENCES

1. Evaluation of Short and Tall Stature in Children, Craig Barstow, Fort Bragg, North Carolina, Caitlyn Rerucha,Fort Hood,2015 Jul 1;92(1):43-50.
2. (Guideline) New York state department of health.Growth body composition and metabolism .Newyork (NY): New York State Department of Health ;2007 Nov.
3. Early-onset idiopathic growth hormone deficiency within KIGS,Ranke MB, Lindberg A, KIGS International Board , Horm Res. 2003; 60(Suppl 1):18-21.
4. Baron J, Sävendahl L, De Luca F, Dauber A, Phillip M, Wit JM, et al. Short and tall stature: a new paradigm emerges. Nat Rev Endocrinol. 2015 Dec; 11(12): 735–46.
5. Ankithamalleshwari , Santhosh T Soans , Digant D Shastri, IAP textbook on pediatric endocrinology , vol 1, pg 55-60
6. Drop SL, De Waal WJ, De Muinck Keizer-Schrama SM. Sex steroid treatment of constitutionally tall stature. Endocr Rev. 1998;19(5):540–558
7. Bacon GE,Spenoer ML ,Hopwood NJ,Kelch RP.A Practical approach to Ped Endocrinology,year book medical publisher,Chicago ,IL 1900-62-9.
8. Tanners target height formula,srideviAtluri ,Kavya Bharathidasan ,Vijaya sarathiDepartment of Endocrinology, Vydehi Institute of Medical Sciences and Research Center, Bengaluru, Karnataka ,2018, vol 22, pg441-444.
9. Tanner JM, Growth at Adolescence, Blackwell Scientific Publications, Oxford, 1962, Marshall WA, Tanner JM, Arch Dis Child 44 ;291, 1969.
10. Frindik JP, Kemp SF, Hunold JJ. Near adult heights after growth hormone treatment in patients with idiopathic short stature or idiopathic growth hormone deficiency. J Pediatr Endocrinol Metab. 2003;16:607-12.
11. Shideh Assar MD, HajiehShahbazian MD, KouroshRiahi MD, KeramatKheradmand MD. Frequency of Growth Hormone Deficiency in Children with Short Stature.
12. Etiological factors of short stature in children and adolescents: experience at a tertiary care hospital in Egypt ,AlmontaserHussein, HekmaFarghaly, EmanAskar, KotbMetwalley, Khaled Saad, Asmaa Zahran, and Hisham A. Othman,Ther Adv Endocrinol Metab. 2017 May; 8(5): 75–80.
13. Chowdhury SP1, Sarkar TK2, Haldar D3, Taraphdar P3, Naskar TK4, Sarkar GN3.Short stature in children: Experience from a tertiary care hospital in Kolkata, India research article the Health 2011; 2(4): 139-142.
14. Evaluation of short stature in Paediatric age group in rural medical college Bharti Dubey1, Swati Raipurkar2,*, Nagesh Chandra Doharey3 , Neha4 , Unique, Sagar, IP International Journal of Medical Paediatrics and Oncology, October-December, 2018;4(4):161-166
15. Colaco P, Desai M, Choksi CS. Short stature in Indian children: The extent of the problem. *Indian J Pediatr.* 1991;58(Suppl 1):57–8.
16. Zargar AH, Laway BA, Masoodi SR, Wani AI, Salahuddin M. An etiological profile of short stature in the Indian subcontinent. J Pediatr Child Health. 1998 Dec;34(6):571–576.
17. Prevalence and etiological profile of short stature among school children in a South Indian population, KumaravelVelayutham, S Sivan Arul Selvan, RV Jeyabalaji, S Balaji.2017, vol 21, Pg 820-822
18. S.K. Bhadada, N.K. AgrawaP, S.K. Singh 1, J.K. Agrawal. Etiological Profile of Short Stature. Indian J Pediatr 2003; 70 (7) :545-547