Open Access

Original Article

Growth Characteristics in Children with Congenital Adrenal Hyperplasia Visiting Tertiary Care Hospital, Karachi

Abdul Qayyum, Versha Rani Rai, Roshia Memon, Shazia Mahar, Taj Muhammad Laghari, Mohsina Noor Ibrahim

National Institute of Child Health, Karachi Pakistan

ABSTRACT

Objective: To determine the growth characteristics in children with congenital adrenal hyperplasia visiting tertiary care hospital Karachi.

Study Design: Cross-Sectional study.

Place and Duration of Study: Paediatrics Department, National Institute of Child Health, Karachi Pakistan, from Nov 2018 to May 2019.

Methodology: All patients who visited the OPD were included in the study. Growth characteristics like underweight, normal BMI, overweight, obese and short stature were recorded. This information, along with the age of diagnosis, family history of CAH, parental consanguinity, family history of CAH or any abortion or prenatal death, were noted.

Results: The mean age of the patients was 7.40±2.34 years. Out of 69 congenital adrenal hyperplasia patients, 41(59.4%) were males, and 28(40.6%) were females. The short suture was noted in 53(76.8%) patients. 19(27.5%) were underweight, 6(8.7%) were normal weight, 10(14.5%) were overweight, and 34(49.3%) patients w ere obese.

Conclusion: A significant effect of congenital adrenal hyperplasia was documented in the children.

Keywords: BMI, Congenital adrenal hyperplasia, Height, Weight.

How to Cite This Article: *Qayyum A, Rai VR, Memon R, Mahar S, Laghari TM, Ibrahim MN. Growth Characteristics in Children with Congenital Adrenal Hyperplasia Visiting Tertiary Care Hospital, Karachi. Pak Armed Forces Med J 2023; 73(1): 96-98. DOI: https://doi.org/10.51253/pafmj.v73i1.7767*

INTRODUCTION

Congenital adrenal hyperplasia (CAH) is an autosomal recessive illness due to a common deficiency of 21-hydroxylase (21-OH) enzyme action that normally reduces the secretion of cortisol & aldosterone while simultaneously production of androgen increasing.[1,2] Growth is a major concern in treating congenital adrenal hyperplasia (CAH), as newborns often fail to attain their target height. Higher dosages of hydrocortisone may be required to achieve acceptable androgen suppression, resulting in hypercortisolism.[3-5]

According to current literature, the periods when height outcome is also most sensitive to glucocorticoid intake include infancy and puberty.[6,7] The assessment of a specific five biochemical investigation along growth velocity and skeletal maturation is used to monitor treatment throughout these important periods.[8] Skeletal maturation is among the most precise predictors of somatic growth's long-term prognosis.[9] Research shows that children with CAH are more likely to become obese.[10]

The rationale of the study is that the data on this topic is not available locally, and scarce literature is available internationally. Therefore, it is important to identify the growth characteristics in these children so that strategies can be made. Therefore, the present study is designed to generate local data on the growth parameters in patients with CAH. The outcome of this study will help to devise policies to screen such children at the time of presentation.

Correspondence: Dr Versha Rani Rai, National Institute of Child Health (NICh) Karachi-Pakistan

Received: 06 Dec 2021; revision received: 31 Jan 2022; accepted: 01 Feb 2022

METHODOLOGY

The cross-sectional study was conducted from November 2018 to May 2019 at Paediatrics Department, National Institute of Child Health, Karachi Pakistan. The sample size was calculated using the WHO sample size calculator, taking a confidence level of 95%, the reported prevalence of obesity in CAH children as 17.6%.[11] The non-probability consecutive sampling was used.

Inclusion Criteria: Patients of either gender, aged 5 to 15 years, presenting in the Paediatric Department with congenital adrenal hyperplasia (CAH) for treatment were included in the study.

Exclusion Criteria: Children with neural tube defects, confirmed by taking history and medical record Down's and Horners syndrome confirmed by taking history and medical records, were excluded from the study.

A brief history regarding the age, duration of diagnosis, history of CAH, parental consanguinity,

family history of CAH or any abortion or prenatal death was taken. Growth characteristics like underweight, normal BMI, overweight, obese and short stature were recorded in the operational definition. In addition, this information, along with the age of diagnosis, family history of CAH, parental consanguinity, family history of CAH or any abortion or prenatal death, were noted in proforma.

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 21. Quantitative variables were presented as mean and SD. In addition, qualitative variables were presented in terms of frequencies and percentages. The comparison was made to see the effect of the outcome on age, gender, duration of diagnosis, family history of CAH, parental consanguinity, family history of CAH or any abortion or prenatal death. A chi-square test was applied, and the *p*-value of ≤0.05 was considered significant.

RESULTS

In this study, 69 patients of congenital adrenal hyperplasia were included. The mean age was 7.40± 2.34 years. There were 41(59.4%) males and 28(40.6%) were females. The mean duration of diagnosis was 2.36±1.03 months. Out of 69, positive family history was documented in 44(67.7%). Parental consanguinity was present in 17(24.6%) patients, history of abortion was found in 36(52.2%); prenatal death was found in 34(49.3%) and frequency of short stature was noted in 53(76.8%). 19(27.5%) patients were documented as underweight, 6(8.7%) were normal weight, 10(14.5%) were overweight, and 34(49.3%) patients were noted as obese (Table-I).

Table-I: Characteristics of Study Population (n=69)

Characteristics	n(%)	
Duration of Diagnosis Mean±SD		2.36±1.03 Months
Body Mass Index	Underweight	19(27.5%)
	Normal	6(8.7%)
	Overweight	10(14.5%)
Family History of CAH	25(36.2%)	
Parental Consanguinity	17(24.6%)	
History of Abortion	36(52.2%)	
Prenatal Death	34(49.3%)	
Short Stature	53(76.8%)	

Family history and history of abortion significantly associated with short stature (*p*=0.057 and 0.001) (Table-II).

DISCUSSION

The growth parameters of children with congenital adrenal hyperplasia were described in this study. Adrenal hyperplasia children may suffer from obesity. Whereas the exact cause of obesity in those patients is unknown, several factors are at play. It is commonly speculated that obesity is linked to glucocorticoid dosage.[11]

In a recent study, frequency of growth characteristics in CAH showed underweight in 19.1%, normal weight in 57.4%, overweight in 5.9%, obese in 17.6%, whereas short stature in 25.6% of CAH children.[12]

According to a study published in the biomedical journal (BMJ), high hydrocortisone dosages in early childhood, particularly infancy, cause growth retardation and may be connected to a loss of required lengths. Furthermore, if CAH is not treated, the disease will speed up the epiphyseal fusion rate, limiting the patient's height potential.[13,14] In this study, the majority of the patients were of short height. Family short height could be a factor in those patients since their target height falls under the 3rd percentile, while the average mid-parental height among short-statured children was 159.7cm. According to literature, classical CAH patients usually achieve a sub-optimal height compared to their required target height.[15] Retrospective studies have shown that the final height of very well patients is unrelated to the level of hormonal control, implying that hypercortisolism may aggravate the previously mentioned low stature. Furthermore, final height SDS and SDS heights were not associated significantly with age at diagnosis, sex, mid-parental height (*p*=0.425), hydrocortisone dose, or disease control.[16,17]

Table-II: Association of Growth Characteristics with Study Variables (n=69)

Growth Characteristics		Short Stature		*p*-value
		Yes (n=53)	No (n=16)	
Age Groups	5-8 Years	41(75.9%)	13(24.1%)	0.740
	>8 years	12(80.0%)	3(20.0%)	
Duration (Months)	1-3	40(74.1%)	14(25.9%)	0.307
	> 3	13(86.7%)	2(13.3%)	
Family History	Yes	16(64.0%)	9(36.0%)	0.057
	No	37(84.1%)	7(15.9%)	
Parental Consanguinity	Yes	13(76.5%)	4(23.5%)	0.960
	No	40(76.9%)	12(23.1%)	
History of Abortion	Yes	34(94.4%)	2(5.6%)	0.001
	No	19(57.6%)	14(42.4%)	
Prenatal Death	Yes	29(85.3%)	5(14.7%)	0.100
	No	24(68.6%)	11(31.4%)	

Our findings revealed an association between hydrocortisone dose BMI SDS and BMI. We may note that obese children took more than 15.0mg/m²/day of hydrocortisone (*p*=0.08, *p*=0.0027). A similar finding

was found in research done in the United States, where almost half of the participants had a BMI rating above the 95th percentile.[18]

To avoid increased weight gain and early adiposity rebound in CAH children, the HC dose must be carefully adjusted, especially throughout early childhood.[19] On a daily dose of hydrocortisone of 12.0mg/m^2, 35.69% were found to be controlled clinically, but Only 26.3% of patients receiving a higher dose of >15mg/m^2/day achieved clinical control. Those who were controlled clinically had an average age of 17.7x25.8months. Those who were not under control had an average age of 5.5x5.8months. In our study, the age was 7.40±2.34 years. Positive family history of CAH was 67.7%, prenatal death occurred in 50.7%, and a highly significant difference was found with BMI. History of abortion was found in 47.8% and found a highly significant difference with short sutures. A highly significant difference was noted in BMI in comparison with parental consanguinity. Our results are comparable with national and international studies.[18,20]

CONCLUSION

A significant effect of congenital adrenal hyperplasia was documented on the growth of children.

Conflict of Interest: None.

Author Contribution

Following authors have made substantial contributions to the manuscript as under:

AQ & VRR: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

RM & SM: Data acquisition, data analysis, data interpretation, approval of the final version to be published.

TML & MNI: Critical review, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Hindmarsh PC, Geertsma K. Congenital Adrenal Hyperplasia: A Comprehensive Guide: Academic Press; 2017, [Internet] available at:https://www.elsevier.com/books/congenital-adrenal-hyperp - lasi/hindmarsh/978-0-12-811483-4
2. Turcu AF, Auchus RJ. The next 150 years of congenital adrenal hyperplasia. J Steroid Biochem Mol Biol 2015; 153(1): 63-71. doi: 10.1016/j.jsbmb.2015.05.013.
3. Fleming L, Van Riper M, Knafl K. Management of Childhood Congenital Adrenal Hyperplasia-An Integrative Review of the Literature. J Pediatr Health Care 2017; 31(5): 560-577. doi: 10.1016/j.pedhc.2017.02.004.
4. Witchel SF. Genetics and Pathophysiology of Congenital Adrenal Hyperplasia. Adrenal Disorders: Springer; 2018, [Internet] available at: https://link.springer.com/chapter/10.1007/978-3-319-62470-9_5
5. Mazziotti G, Giustina A. Glucocorticoids and the regulation of growth hormone secretion. Nat Rev Endocrinol 2013; 9(5): 265-276. doi: 10.1038/nrendo.2013.5.
6. Kühn ER, Geelissen SM, Van der Geyten S, Darras VM. The release of growth hormone (GH): relation to the thyrotropic- and corticotropic axis in the chicken. Domest Anim Endocrinol 2005; 29(1): 43-51. doi: 10.1016/j.domaniend.2005.02.022.
7. Collaer ML, Hindmarsh PC, Pasterski V, Fane BA, Hines M. Reduced short term memory in congenital adrenal hyperplasia (CAH) and its relationship to spatial and quantitative performance. Psychoneuroendocrinology 2016; 64(1): 164-73. doi: 10.1016/j.psyneuen.2015.11.010.
8. Bretones P, Riche B, Pichot E, David M, Roy P, Tardy V, et al. Growth curves for congenital adrenal hyperplasia from a national retrospective cohort. J Pediatr Endocrinol Metab 2016; 29(12): 1379-1388. doi: 10.1515/jpem-2016-0156.
9. Mendes C, Vaz Matos I, Ribeiro L, Oliveira MJ, Cardoso H, Borges T. Hiperplasia Congénita da Suprarrenal por Deficiência de 21-Hidroxílase: Correlação Genótipo-Fenótipo [Congenital adrenal hyperplasia due to 21-hydroxylase deficiency: genotype-phenotype correlation]. Acta Med Port 2015; 28(1): 56-62.
10. Sarafoglou K, Forlenza GP, Yaw Addo O, Kyllo J, Lteif A, Hindmarsh P, et al. Obesity in children with congenital adrenal hyperplasia in the Minnesota cohort: importance of adjusting body mass index for height-age. Clin Endocrinol (Oxf) 2017; 86(5): 708-716.
11. White PC. Update on diagnosis and management of congenital adrenal hyperplasia due to 21-hydroxylase deficiency. Curr Opin Endocrinol Diabetes Obes 2018; 25(3): 178-184.
12. Alzanbagi MA, Milyani AA, Al-Agha AE. Growth characteristics in children with congenital adrenal hyperplasia. Saudi Med J 2018; 39(7): 674-678. doi: 10.15537/smj.2018.7.22193.
13. Claahsen-van der Grinten HL, Dehzad F, Kamphuis-van Ulzen K, de Korte CL. Increased prevalence of testicular adrenal rest tumours during adolescence in congenital adrenal hyperplasia. Horm Res Paediatr 2014; 82(4): 238-244. doi: 10.1159/000365570.
14. Lajic S, Karlsson L, Nordenström A. Prenatal Treatment of Congenital Adrenal Hyperplasia: Long-Term Effects of Excess Glucocorticoid Exposure. Horm Res Paediatr 2018; 89(5): 362-371. doi: 10.1159/000485100.
15. Weismiller DG. Expanded Newborn Screening: Information and Resources for the Family Physician. Am Fam Physician 2017; 95(11): 703-709.
16. Tsuji A, Konishi K, Hasegawa S, Anazawa A, Onishi T, Ono M, et al. Newborn screening for congenital adrenal hyperplasia in Tokyo, Japan from 1989 to 2013: a retrospective population-based study. BMC Pediatr 2015; 15: 209. doi: 10.1186/s12887-15-529-y.
17. El-Maouche D, Arlt W, Merke DP. Congenital adrenal hyper-plasia. Lancet 2017; 390(10108): 2194-2210. doi: 10.1016/S0140-6736(17)31431-9. Erratum in: Lancet. 2017; 390(10108): 2142.
18. Stikkelbroeck NM, Van't Hof-Grootenboer BA, Hermus AR, Otten BJ, Van't Hof MA. Growth inhibition by glucocorticoid treatment in salt wasting 21-hydroxylase deficiency: in early infancy and (pre)puberty. J Clin Endocrinol Metab 2003; 88(8): 3525-3530. doi: 10.1210/jc.2002-030011.
19. Hashemipour M, Ghasemi M, Hovsepian S. A case of congenital lipoid adrenal hyperplasia. Int J Prev Med 2012; 3(7): 510-514.
20. Johannsen TH, Mallet D, Dige-Petersen H, Müller J, Main KM, Morel Y, et al. Delayed diagnosis of congenital adrenal hyper plasia with salt wasting due to type II 3beta-hydroxysteroid dehydrogenase deficiency. J Clin Endocrinol Metab 2005; 90(4): 2076-2080. doi: 10.1210/jc.2004-1374.