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ORIGINAL ARTICLE

Various Clinical Manifestations of Congenital Adrenal Hyperplasia in Children

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ABSTRACT

The study's objectives was to determine the frequency of various clinical manifestations of congenital adrenal hyperplasia in children.

Materials & Methods: The research methodology is descriptive and cross sectional. The event was held at the Department of Pediatric Medicine at DHQ Hospital in Faisalabad. The study will last from September 29th to March 28th, 2019. A total of 90 children with congenital adrenal hyperplasia of age 0-10 years of either gender were included. After taking informed written consent from all children's parents, different clinical presentations (ambiguous genitalia, simple virilising and salt wasting) were noted in each patient.

Results: Mean age of children was 4.84 ± 1.78 years. Out of the 90 patients, 62 (68.89%) were male and 28 (31.11%) were females with male to female ratio of 2.2:1. Mean duration of symptoms was 5.79 ± 2.59 days. In this study, I have found the ambiguous genitalia in 27 (30.0%), simple virilising in 17 (18.88%) and salt wasting in 59 (65.56%) children with congenital adrenal hyperplasia.

Conclusion: This study has shown that the salt wasting is the most common clinical presentations of congenital adrenal hyperplasia in children followed by ambiguous genitalia and simple virilising.

Keywords: Congenital adrenal hyperplasia, ambiguous genitalia, salt wasting.

INTRODUCTION

Most occurrences of childhood adrenal insufficiency are caused by congenital adrenal hyperplasia (CAH), and 21-hydroxylase deficiency is the most common form of this condition, accounting for around 95% of cases with an incidence of 1 in 9,000 to 1 in 20,000 births.[1] Deficiency in the enzyme 21-hydroxylase in the adrenal glands is the most frequent form of CAH, which is caused by mutations in the CYP21A2 gene.[2]

Cortisol and aldosterone cannot be synthesised in this condition because of a deficiency in an enzyme that transforms 17-OHP and progesterone. According to CAH, the degree of symptoms is determined by which hormones the enzyme block affects. As a result, typical 21-hydroxylase deficiency causes an overproduction of adrenal androgens and an underproduction of cortisol. 17-hydroxyprogesterone, a diagnostic hormone, is unusually high when the 21-hydroxylase enzyme is deficient. Virilization is a common sign of high androgen production. [3] 21-hydroxylase insufficiencies in females without salt-wasting has also been recorded in a non-classic variant, with genitalia that are normally normal in appearance at delivery.[4]

Patients with 21-hydroxylase insufficiency inherit inactivating mutations of different severity in both CYP21A2 alleles, causing decreased synthesis and release of cortisol and aldosterone as well as high levels of adrenal androgens.[5] Reduced levels of circulating cortisol, especially in individuals with more severe manifestations, increase the likelihood of an early salt-wasting crisis and a later adrenal crisis (AC). [6]

CAH is commonly classified into three types: Traditional types of CAH include salt-wasting (SW) and simple virilizing (SV), with late-onset (LAH) often being labeled a "non-classical" variant (NC).[7] There are serious consequences for neonates with SW-CAH because of the difficulty in maintaining sodium balance, whereas SV-CAH is more likely to cause female infertility. Adults with small height due to premature epiphyseal maturation and early pubescence are among the most common symptoms in older children.[8] Researchers found that the most common symptoms in this condition were: ambiguous genitalia (23.5% of cases), salt wasting (5.9%), simple virilizing (13.7% of cases), and ambiguous genitalia (with salt wasting) (51 percent).[9]

This study evaluated the incidence of different clinical manifestations of congenital adrenal hyperplasia in local children. This research will help us better understand how common congenital adrenal hyperplasia is in children. This study will assist clinicians establish a management regimen for these patients to prevent complications, morbidity, and mortality.

MATERIALS & METHODS

The study's objectives are to determine the frequency of various clinical manifestations of congenital adrenal hyperplasia in children. The research methodology is descriptive and cross sectional. The event was held at the Department of Pediatric Medicine at DHQ Hospital in Faisalabad. The sampling technique used was non-probability and consecutive sampling.

The following criteria were used to select the sample: all children with congenital adrenal hyperplasia (as defined by the operating definition), duration of symptoms >24 hours, age 0-10 years, and both genders. Patient with H/o heart disease (assessed on medical record), Chronic renal failure (assessed on history and s/creatinine >1.5 mg/dl), Children with type I diabetes and complications such as diabetic ketoacidosis, children with type I diabetes and celiac disease, mucocutaneous candidiasis, Addison's disease, hypoparathyroidism, and Cushing's disease were excluded from the study.

A total of 90 children who met the inclusion criteria and were admitted to the Department of Pediatric Medicine at DHQ Hospital, Faisalabad, were chosen with the approval of the institution's ethical review committee. After taking informed written consent from all children parents, different clinical presentations (ambiguous genitalia, simple virilising and salt wasting) were noted in each patient (as per-operational definition) by the researcher herself. All this data including (age, gender, duration of symptoms, parental consanguinity, place of living, family history of CAH and different clinical presentations was recorded on a specially designed proforma.

SPSS 20.0 was used to do the statistical analysis. A mean and standard deviation for each of the quantitative variables were computed and displayed. Qualitative factors were analyzed for frequency and percentages. Effect modifiers were controlled through stratifications and post-stratification chi square was applied to see their effect on presentation. P-value ≤ 0.05 was taken as significant.

RESULTS

Mean age of children was 4.84 ± 1.78 years. Out of the 90 patients, 62 (68.89%) were male and 28 (31.11%) were females with male to female ratio of 2.2:1 (Figure I). Mean duration of symptoms was 5.79 ± 2.59 days. Distribution of patients according to parental consanguinity, place of living and family history of CAH is shown in Table I respectively. In this study, I have found the ambiguous genitalia in 27 (30.0%), simple virilising in 17 (18.88%) and salt wasting in 59 (65.56%) children with congenital adrenal hyperplasia. (Table I). Stratification of clinical presentations with respect to age and gender is shown in Table II respectively. Stratification of clinical presentations with respect to duration of symptoms and parental consanguinity is shown in Table II respectively. Table II have shown the stratification of clinical presentations with respect to place of living and family history of CAH.

Table 1: Distribution of patients according to age, cousin marriage, living, family history and various clinical presentations

According to duration of disease (n=90)	≤7	72	80.0
	>7	18	20.0
	Total	90	100.0
According to parental consanguinity (n=90).	parental consanguinity	No. of Patients	%age
	Yes	52	57.78
	No	38	42.22
	Total	90	100.0
According to place of living (n=90).	Place of living	No. of Patients	%age
	Rural	57	63.33
	Urban	33	36.67
	Total	90	100.0
According to family history of CAH (n=90)	Family history of CAH	No. of Patients	%age
	Yes	32	35.56
	No	58	64.44
	Total	90	100.0
Clinical presentations of CAH	Clinical presentations	Frequency	Percentage
	Ambiguous genitalia	27	30.0
	Salt wasting	59	65.56
	Simple virilising	17	18.88

Table 2: Stratification of clinical presentations with age, gender, duration of symptoms, cousin marriage and family history

with respect to age.			0-5 years (n=53)	6-10 years (n=37)	P-value
	Ambiguous genitalia	Yes	17	10	0.157
		No	36	27	
	Salt wasting	Yes	38	21	0.142
		No	15	16	
	Simple virilising	Yes	11	06	0.588
		No	42	31	
with respect to gender.			Male (n=62)	Female (n=28)	P-value
	Ambiguous genitalia	Yes	20	07	0.487
		No	42	21	
	Salt wasting	Yes	43	16	0.259
		No	19	12	
	Simple virilising	Yes	09	08	0.115
		No	53	20	
			≤7 days (n=72)	>7 days (n=18)	P-value
with respect to duration of symptoms.	Ambiguous genitalia	Yes	24	03	0.168
		No	48	15	
	Salt wasting	Yes	45	14	0.222
		No	27	04	
	Simple virilising	Yes	16	01	0.106
		No	56	17	
with respect to parental consanguinity.			Yes (n=52)	No (n=38)	P-value
	Ambiguous genitalia	Yes	15	12	0.780
		No	37	26	
	Salt wasting	Yes	32	27	0.348
		No	20	11	
	Simple virilising	Yes	13	04	0.083
		No	39	34	
with respect to place of living.			Rural (n=57)	Urban (n=33)	P-value
	Ambiguous genitalia	Yes	16	11	0.600
		No	41	22	
	Salt wasting	Yes	40	19	0.225
		No	17	14	
	Simple virilising	Yes	09	08	0.324
		No	48	25	
with respect to family history of CAH.			Yes (n=32)	No (n=58)	P-value
	Ambiguous genitalia	Yes	08	19	0.442
		No	24	39	
	Salt wasting	Yes	21	38	0.992
		No	11	20	
	Simple virilising	Yes	09	08	0.096
		No	23	50	

DISCUSSION

CAH refers to a series of recessively inherited enzyme defects that affect adrenal steroid synthesis, resulting in low cortisol and aldosterone levels and increased androgens in the bloodstream of those with the condition.[10] Every 18 000 live births are affected in the UK, however not all instances are detected in the first year after conception.[15] There is presently no CAH screening for newborns in the UK, however the National Screening Committee is considering this.[11]

CAH can be divided into three distinct categories: salt-wasting (SW), simple virilizing (SV), and non-classical (late-onset) (NC). While in infants, SW-CAH can lead to life-threatening crises owing to the inability to maintain salt balance, the most common manifestation of SV-CAH is the sexualization of women. In older children, early pubescence and fast development contribute to premature epiphyseal maturation, which results in a low height in adulthood.[12] If left unchecked, an overabundance of androgens in the body can lead to early virilization, pubic hair growth in females, irregular menstrual cycles, and infertility in both sexes.[11] The consequences of excess testosterone on the female brain have dominated research into its psychological influence to far;[13] however, reduced quality of life has been demonstrated for adults with CAH. CAH has a long-term effect on health, despite the fact that steroid replacement treatment can prevent adrenal crises and normalize development.[14] Despite the fact that the epidemiology of babies has been thoroughly documented,[15] Only a few cases have been documented of older children with CAH presenting clinically, yet they nonetheless suffer from preventable complications.

This research was done to see how often different types of clinical manifestations of congenital adrenal hyperplasia occur in children. The mean age of the children was 4.84 1.78 years. In all, 62 (68.89 percent) of the 90 patients were male, and 28 (31.11 percent) were female. A total of 27 (30.0 percent) children with congenital adrenal hyperplasia had ambiguous genitalia, whereas only 17 (18.88 percent) had simple virilizing, and 59 (65.56 percent) had salt wasting. A research found that 23.5% of participants had ambiguous genitalia, 5.9% had ambiguous genitalia plus salt wasting, 13.7% had simple virilizing, and 5.9% had salt wasting as part of their clinical presentation (51 percent).[9]

The British Pediatric Surveillance Unit actively monitored all children under the age of 16 with a newly diagnosed CAH between August 2007 and August 2009. Testing for CAH revealed 144 cases, of which 132 (92 percent) showed 21-hydroxylase deficiency, from 12 different labs. More than half of the youngsters were Asian (36%) and almost half were boys (43%) who were between the ages of three and seven. For children under the age of 16, the rate of new diagnoses per 100,000 was 0.6 (95 percent CI 0.50 to 0.71). It was projected that 5.48 babies per 100,000 were diagnosed in the first year of life, with the vast majority of them (77; 89 percent) showing up in the first month. Only one in three female students showed signs of sexually transmitted infections. On or after 14 days of age, 18 (67%) of the 27 neonates with salt-wasting crises were diagnosed.[15]

In addition to peripheral precocious puberty, some adolescents with CAH also suffer central precocious puberty (CPP) due to the early maturity of the hypothalamic-pituitary-gonadal axis (HPG).[16] Non-salt-losing CAH was also seen in three of the male patients with an advanced bone age. Hyperandrogenism, whether it occurs on an ongoing or intermittent basis, may activate the hypothalamic-pituitary axis, resulting to CPP. [16] Boys, in particular, who do not lose salt are at greater danger since their osseous

maturation may not be detected until they are three to seven years old, five years or more ahead of their chronological age.[17] As hydrocortisone medication slows the generation of adrenal androgens, it allows pituitary gonadotropins to be released from the hypothalamus if the right amount of hypothalamic maturation is already present.[17]

Cah is mainly shown to be salt-losing, with a 2.7:1 ratio of simple virilizing and salt-losing CAHs being identified in another study. Those who claimed that classic salt wasting phenotype accounts for 75% of all instances of classic CAH are in accord with this. Developed-country research[18] In terms of prevalence, the SW kind of the disease was shown to be almost twice as prevalent as SV type of the disease. However, research from Singapore and India have shown a similar trend.[19] revealed a 1:1.6 and a 1:1.8 illness ratio for SW and SV types, respectively. This revealed that a significant number of people with SW kind of sickness, particularly men, probably died before diagnosis; this is especially true.[20]

CONCLUSION

This study has shown that salt wasting is the most common clinical presentations of congenital adrenal hyperplasia in children followed by ambiguous genitalia and simple virilising. So, we recommend that early identification of these presentations should be taken into consideration for early diagnosis of congenital adrenal hyperplasia for taking management in order to reduce its complications as well as morbidity and mortality.

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