ORIGINAL ARTICLE

Our Current Practice of Congenital Adrenal Hyperplasia Management: Where Do We Stand?

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ABSTRACT

Aim: To improve the management of congenital adrenal hyperplasia in females and make recommendations regarding gender assignment and genitoplasty surgery in our setup.
Methods: The study was carried out in department of pediatric Urology and Endocrinology, Children hospital and ICH Multan from 1st January, 2009 to December, 2018. We did retrospective analysis of records of 25 patients with ambiguous genitalia and diagnosed as a case of CAH. The clinical data, investigations surgeries performed and there outcome were reviewed.
Results: Out of twenty five patients, thirteen (52%) were diagnosed as salt wasters and twelve (48%) were having simple virilization. Our ten patients (40%) were incorrectly assigned male sex at presentation. The fourteen (56%) patients had low vaginal confluence and about eleven (34%) patients had high vaginal confluence.
Conclusion: Children with CAH should be diagnosed early and every possible effort should be made to assign correct gender. Early genital surgery helps in medical, psychological and social wellbeing of child in our setup.
Keywords: CAH=Congenital adrenal hyperplasia. Vaginal confluence.

INTRODUCTION

Congenital adrenal hyperplasia is the most common disorder of adrenal gland resulting in adrenal insufficiency in the new born. Its incidence reported is 1 in 15-20,000 live birth worldwide [1]. Congenital adrenal hyperplasia (CAH) the most frequent etiology[2], is a group of autosomal recessive disorders occurs due to the defect in any of the five enzymes needed for the biosynthesis of cortisol from cholesterol by the adrenal gland. This deficiency of hydrocortisone causes compensatory increase in the secretion of adrenocorticotrophic hormone resulting in increase in the formation of testosterone the active androgen responsible for virilization in females.

Genital ambiguity is considered as social problem in our setup and these children are considered stigmata for the family. Therefore, every effort should be made to correctly assign the gender and to start appropriate medical treatment as early as possible. We present here our experience of management of CAH in twenty five female patients so that we may improve our current practices of gender assignment and treatment both medical and surgical in order to save the child from both social and medical complications.

MATERIAL AND METHOD

This study was carried out in Children hospital & The ICH Multan from 1st January, 2011 to 31st December 2018. The records of all the patients presented with ambiguous genitalia was reviewed retrospectively. Only those patients with a XX karyotype and were diagnosed as cases of CAH were included in the study. Others who had pure urogenital sinus, XY karyotype, under masculinized male or true hermaphrodites were excluded from the study. All the patients were examined and managed initially by the endocrinology and medical departments. After doing karyotyping and base line investigation, medical therapy was started. Then patients were referred to urology department for evaluation and genitoplasty. In urology department, history, examination and baseline investigations of all the patients were noted in pre designed proforma. Imaging studies like ultrasound, genitography, CT or MRI scan if needed were done. Examination under anesthesia (EUA) and urethrocystoscopy were performed in all the patients. Masculinization status was classified according to Prader scoring system. Length of common sinus and level of confluence of vagina in common channel with relation to external sphincter were noted.

After complete assessment, the results were shared with the parents of the patients. Surgical therapy was offered to all the parents and the outcome of surgery regarding cosmetic, functional and post-operative complications were explained to the parents. After consent surgery was planned individually for every patient. Complications both minor and major were noted. Cosmetic outcome was noted based on Likert scale: 1=good, 2=satisfied, 3=dissatisfied, 4=very dissatisfied[3].

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RESULTS

Total 25 patients having age from one to twelve years were included in the study. The mean age was 3 years and the median age was 2 years. Primary gender assignment by the parents was male in ten patients (40%) while the remaining fifteen patients were raised as females (60%).
Our 12(48%) out of 25 patients had both cortisol and aldosterone deficiency and were taking both tablet hydrocortisone and florinef. While 23(52%) patients had cortisol deficiency alone and were taking hydrocortisone . Patients were distributed into two groups according to their age at presentation. Those who presented early age less than 4 years were included in group I and those who

presented late having age more than 5 were included in group II. The treatment performed and its outcome of both the groups was compared. In group I there were 19 patients and in group II there were 6 patients.

Clinical presentation, masculinization status by Prader scorring and surgery performed in both the groups is shown in table I, and outcome of surgery with complications and cosmetic score of both groups is shown in table II.

Table I

Groups according to age	Primary gender assigned by family	Pradder score	Surgery performed
GROUP I Age 1-4 y 19 pts 76%	A: Female 13 68% B: Male 6 31%	II 2 10% III 6 31% IV 7 37% V 4 21%	A: 5/13 38% B: 2/6 33% Total: 7/19 36%
GROUP II Age 5-12 y 6 pts 24%	A Female 2 33% B: Male 4 66%	II 0 III 1 16% IV 1 16% V 4 66%	A: 2/2 100% B: 1/4 25% Total: 3/6 50%

Table II

Groups	Total operated patients	Complications	Cosmetic scorring
I 19/25 Patients 76%	7/19 36%	No 3(42%) Minor 4(57%) Major 0	V. Dissatisfied 0 Dissatisfied 2(28%) Satisfied 3(42%) Good 2(28%)
II 6/25 Patients 24%	3/6 50%	No 0 Minor 3(100%) Major 0	V. Dissatisfied 0 Dissatisfied 0 Satisfied 1(33%) Good 2(66%)

DISCUSSION

Congenital adrenal hyperplasia is a group of heritable disorders of adrenal cortex. Mutations in at least five various genes resulting in enzymatic defects can lead to this disorder. It may lead to decrease in production of cortisol and aldosterone and excess in production of androgens. The relatively large secretion of androgens in the fetal life cause virilization of female and abnormal development in male. The disease can be sporadic or may run in the families. Positive family history, previous still birth, unexplained neonatal deaths in family or maternal drugs intake may prompt antenatal screening of these high risk group. Prenatal diagnosis of CAH can be made by utilizing invasive technique at 14th week or by noninvasive techniques[4] before 9th week of pregnancy respectively[5]. Prenatal dexamethasone treatment can avoid genital ambiguity in the female fetus. Studies shows the prenatal corticosteroid therapy reduces virilization in females[6] and has 80 to 85% success rate[7]. In our society there is poor referral and deficit antenatal diagnostic facilities which lead to late presentation of CAH. None of our patients had antenatal diagnosis and only two patients (8%) had positive family history.

Neonatal screening for CAH by 17 OH progesterone levels is a useful tool for early detection[8]. Neonates may presents in the medical emergency department with the complaints of excessive vomiting, dehydration within 2 to 3 weeks after birth[9]. Excessive vomiting may lead to electrolyte imbalance and shock[10]. Examination of genitalia may reveal abnormal development. Neonatal presentation with ambiguous genitalia is also rare in our society. Neonate with ambiguous genitalia is taken as stigma by the parents and the genital ambiguity of the child is concealed. In our study 11 out of 23 patients (48%) with only gender ambiguity were referred to the tertiary care unit for proper evaluation at the average age of 7.5 years. Proper mineralocorticoid therapy can save neonate life. Hydrocortisone correct effects of the enzyme deficiency and prevent further virilization and allow normal growth and development[11].

Whenever a child with ambiguous genitalia is born, the child should be referred to specialized center for proper investigations. Gender assignment team comprising of pediatric urologist/surgeon, endocrinologist, and neonatologist should properly investigate the child and assign correct gender. Early gender assignment is the important factor and goal of management. Physical examination, karyotyping, hormonal profile, imaging studies all helps in achieving this goal. Several studies have shown that early gender assignment and medical treatment has psychological and social impact on the growth and development of child. Psychological support should be offered to both the parents and family of the child[12]. Proper counselling of the parents and reassurance decreases the anxiety of the parents. Early surgical treatment should be offered[13] and these results should discussed.

In our study all the patients were referred after two years of age and six were referred even after five years. The delay in seeking specialized facilities in patients with genital ambiguity can be attributed to ignorance, poverty, and lack of understanding of disease. In our country majority of the deliveries are conducted at rural centers by traditional birth attendants. Delay in referral and lack of knowledge results in wrong gender assignment to the child. In our study ten females 40 % were wrongly assigned male gender and were raised like that. The rest were also doubtful about the gender. Our average age of presentation and referral to specialized centers for surgical treatment are much delayed as compared to the developed countries of the world.

There were lot of controversies regarding technique of surgery and its timing[14]. Goals of genitoplasty are proper genital appearance and the good adult sexual or

reproductive functions. Clitoral recession used to be the standard part of treatment of all surgeries for ambiguous genital in females. The trend in the western society is changing from clitoral resection[15] to minimal surgery of clitoris[16] and even preservation of corporal tissue so that if child may wish to change gender in later life it will be helpful. In our society however the enlarge clitoris is still cosmetically unacceptable by the family.

We adopted corporal recession in all our surgeries by preserving neurovascular bundles and if glans was enlarged it was covered partially by preputial skin so as to make it cosmetically acceptable[17].

In some of our patients with delayed presentation group II, due to lack of early hormonal therapy females were more masculinized with significant clitoral hypertrophy and greater androgenic effects. The excessive masulinization cause hindrance in their proper plan of management. Change of gender from male to female is a sensitive issue in conservative society like ours. Strong desire to have a boy in the family greatly affects the decision making process. Also accepting a mix gender child(hijara) is considered a social shame and parents are not willing to accept the realities specially presenting late. In our study parents of seven (28%) patients refused surgery as they were reluctant for female gender reassignment.

Initially two stage repair was performed with surgery of clitoris in first stage and vaginoplasty at later stage. This procedure had higher rate of complications like vaginal stenosis and less cosmetic acceptance. Almost every patient need a revision surgery after puberty. Over the years surgical techniques improved. Currently a single stage repair is recommended. Both clitoral recession and vaginoplasty are done in single sitting. This technique has the added advantage of using preputial skin for labial reconstruction. Vaginoplasty has also evolved from simple cutback to perianal flap placement and partial or total urogenital sinus mobilization[18]. These maneuver not only improve the cosmetic outcome but also results in good functional preservation[19].

Similarly level of confluence of vagina to the urogenital sinus adds further complexity to the repair procedure. High level of confluence require total mobilization of urogenital sinus and complications rate are also very high. Some centers recommend surgery at puberty for high vaginal confluence so as to decrease the incidence of vaginal stenosis[20]. For low confluence and associated hydrometrocolpos, early surgery below one year of age was recommended. In our study average age of surgery is 3 years in low and 4 years in high vaginal confluence which is higher as compared to international standards. But our complications rate is well below as compared to rest of the centers[21,22].

Lot of gender advocacy groups are now favoring delayed genitoplasty in patients with CAH[23]. Also there is a trend to preserve the corporal bodies so that future genital surgery after gender reassignment becomes easy. But in country like ours these children are not very much socially acceptable in school and society so the trend continues to be the traditional one of assigning gender and surgery as early as possible. How it affects the sexual and psychological outcome is yet to be determined.

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