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CLINICAL CHARACTERISTICS IN FEMALE CHILDREN WITH CONGENITAL ADRENAL HYPERPLASIA DUE TO 21-HYDROXYLASE DEFICIENCY UNDERGOING GENITAL RECONSTRUCTION SURGERY

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ABSTRACT

Objective: To describe some clinical characteristics of female children with congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency who underwent feminizing genitoplasty.

Subjects and Methods: A retrospective descriptive study was conducted on 103 female patients with CAH due to 21-hydroxylase deficiency who underwent feminizing external genital reconstruction performed by the same surgeon between 2020 and 2025 at the National Children's Hospital.

Results: From January 2020 to December 2025, 103 female patients with CAH due to 21hydroxylase deficiency underwent feminizing external genital reconstruction by the same surgeon. 72% of patients were diagnosed during the neonatal period, predominantly presenting with the salt-wasting form. The simple virilizing form accounted for 28% of cases. The disease showed familial occurrence, with nearly one-quarter of patients having affected siblings. The mean age at surgery was 37 ± 35 months (range: 6–211 months). External genital abnormalities classified as Prader stages 2 and 3 were most common, accounting for 65% of cases. Severe forms with a high urogenital sinus (Prader stages 4 and 5) accounted for 25%.

Conclusion: In female children, CAH due to 21-hydroxylase deficiency most commonly presents as the salt-wasting form, is typically diagnosed in the neonatal period, and most frequently manifests with Prader stage 2 or 3 genital abnormalities.

Keywords: Congenital adrenal hyperplasia, genitoplasty, prader

1. INTRODUCTION

Congenital adrenal hyperplasia (CAH) is an autosomal recessive genetic disorder characterized by a partial or complete deficiency of an enzyme involved in the synthesis of adrenal cortex hormones. CAH due to 21-hydroxylase deficiency is the most common, accounting for over 90% of cases. Globally, the incidence is approximately 1 in 3000 to 1 in 4000 live births. The deficiency of adrenal cortex hormones, specifically cortisone, leads to increased secretion of adrenocorticotropic hormone (ACTH) by the pituitary gland, adrenal hyperplasia, increased intermediate metabolites, and increased androgens, causing clinical symptoms. The disease can affect both male and female infants. It is often diagnosed early in the neonatal period due to manifestations of acute adrenal crisis at varying degrees, accompanied by genital virilization in females. Treatment requires a combination of glucocorticoid (GC) and mineralocorticoid (MC) hormone replacement therapy at doses sufficient to balance corticotropin-releasing hormone (CRH) and adrenocorticotropic hormone (ACTH), along with genital feminization surgery. To contribute to the study of CAH in female children undergoing genital surgery, we conducted the research "Some clinical characteristics in female children with CAH due to 21-hydroxylase deficiency who underwent female genital reconstruction surgery."

2. METHODS

This retrospective descriptive study included 103 female patients with CAH due to 21-hydroxylase deficiency who underwent female-oriented external genitalia reconstruction by the same surgeon between January 2020 and December 2025 at the National Children's Hospital.

2.1. Research Subjects

- Selection criteria:

+ The female patient was diagnosed with CAH due to 21-hydroxylase deficiency.

+ Underwent feminizing genitoplasty.

+ Complete medical records are available.

- Exclusion criteria:

+ The patient was diagnosed with gender development disorder.

+ Patients with genital abnormalities due to other pathologies, not caused by CAH due to 21-hydroxylase deficiency.

+ Incomplete medical records.

2.2. Research Methods

This retrospective descriptive case series we used a convenience sampling method including all patients who met the inclusion criteria and did not meet the exclusion criteria. Data were collected from medical records and follow-up records. The data were collected from the study case sample and analyzed using statistical software.

2.3. Research ethics

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The research complies with regulations; all information is encrypted and secured, and is used solely for scientific research purposes. The data collection process does not interfere with treatment or affect the rights of patients.

3. RESULTS

From January 2020 to December 2025, 103 female children with 21-hydroxylase deficiency underwent female genital reconstruction surgery performed by the same surgeon. 72.8% of patients were diagnosed in the neonatal period, with the predominant manifestation being the salt-wasting form (71%). Simple virilizing form accounted for 29%. The disease was familial, with nearly a quarter of patients having siblings with the disease. The average age at surgery was 37±35 months, the youngest being 6 months and the oldest 211 months. External genital abnormalities were most common with Prader stages 2 and 3, accounting for 65%, while severe forms with high urogenital sinuses (Prader stage 4 and 5) accounted for 25%.



A, B, C: Prader stage 4 with clitoral hypertrophy and elevated urogenital sinus; D, E, F: Severe virilization of the genitalia in untreated CAH children; G, H, I: Post-operative images of female genital reconstruction surgery.

Figure 1. Before and after images of genital reconstruction surgery in female children with CAH

4. DISCUSSION

Congenital adrenal hyperplasia (CAH) is an autosomal recessive genetic disorder caused by a disorder in the synthesis of adrenal cortex hormones due to a partial or complete deficiency of the enzyme involved in adrenal cortex hormone synthesis. CAH due to a deficiency of the enzyme 21-hydroxylase (21-OH) is the most common, accounting for over 90% of cases. Worldwide, the general incidence is 1 in 3000 to 1 in 4000 live births. The disease can affect both male and female children. Depending on the degree of enzyme deficiency, patients will exhibit varying degrees of severity, such as masculinization in female fetuses during the fetal period, leading to ambiguous genitalia after birth; severe salt and water loss, and ultimately death. [1]. Clinical manifestations of the disease are commonly found in two forms: salt-wasting and simple virilizing form, with salt-wasting being more frequent and often manifesting early in the neonatal period. In salt-wasting form, the 21-OH enzyme is absent or present in small amounts, resulting in low cortisol and aldosterone levels despite consistently high ACTH and renin activity. Children will exhibit acute adrenal insufficiency, and female genital virilization. After treatment of the adrenal insufficiency episode, if not treated adequately and consistently, patients will exhibit chronic adrenal insufficiency due to decreased aldosterone and cortisol, such as fatigue, skin darkening, chronic dehydration, and susceptibility to stress-induced adrenal insufficiency. In simple virilizing form, the 21-OH enzyme is only partially deficient, so the adrenal cortex can still respond to increased renin activity by increasing aldosterone secretion. As a result, patients do not have electrolyte imbalances but only simple virilizing form, and the disease is often detected late [2, 3].

Our study found that most cases were diagnosed in the neonatal period, with signs of acute adrenal crisis. 72% of children had the salt-wasting form, and 28% had the simple virilizing form form. Most patients were diagnosed early due to manifestations of acute adrenal insufficiency syndrome, accompanied by external genital abnormalities.

The manifestation of virilization of the external genitalia in female infants begins during the fetal period and is detected after birth, as a consequence of high androgen levels during pregnancy [2]. Characteristic symptoms include:

- In severe cases, the clitoris is enlarged and resembles a penis.

- The two labia majora are fused together and have rugation resembling a scrotum.

- Common urogenital sinus: the urethra and vagina are separate but drain into the urogenital sinus.

-The internal female reproductive system normally includes the uterus, fallopian tubes, and ovaries; it does not contain the structures of the Wolffian duct.

- 46XX chromosome.

Classification of the degree of external genitalia masculinization based on Prader's classification [4]:

- Stage 1: Isolated clitoral hypertrophy, normal vaginal and urethral separation, normal vestibular region.

- Stage 2: Clitoral hypertrophy, closely situated urethra and vagina, narrow vestibule.

- Stage 3: Similar to Stage 2 but with a common urogenital canal, fused labia majora, and scrotal-like rugation.

- Stage 4: Penile-like clitoris, high urogenital sinus, and scrotalized labia majora.

- Stage 5: Complete virilization, resembling normal male external genitalia, with nonpalpable gonads (no testicles in the scrotum).

In our study, the predominant incidence was Prader stages 2,3, accounting for 65% of cases.

Prader stage 1 accounted for only 10%. Patients with severe virilization and high urogenital sinus (Prader stages 4,5) accounted for 25% of cases.

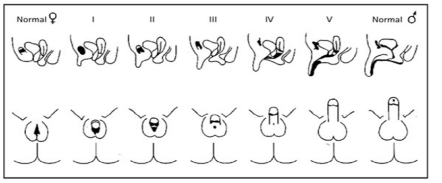


Figure 2. Classification of the degree of genital masculinization in female children with CAH

The consequences of cortisol and aldosterone deficiency and excess androgen severely affect height development, sexual function, reproduction, and quality of life of patients as they grow up. For children with CAH, if not detected early and treated appropriately, they will experience changes in the genitals towards masculinization, changes in appearance such as darkened skin, development of secondary male sexual characteristics: muscles, rough features, pubic hair growth, acne... directly affecting the child's psychology. Furthermore, these symptoms will appear when a CAH patient does not control the disease well, meaning the child still has excess androgen, and high testosterone levels also make the child's emotions more prone to outbursts and anger than other children. The authors all agree that the quality of life (QoL) of female CAH patients is more affected by the disease, especially the masculinization in females [3, 5]. Treatment of CAH requires multidisciplinary collaboration. Lifelong treatment involves hormone replacement therapy and genital feminization surgery. The goal of surgery is to reshape the external genitalia to resemble female genitalia. Currently, there are many reports on the timing of surgery and post-operative care. Most studies have found that early genital reconstruction surgery to match genetic sex can help reduce anxiety in children and their parents, giving them greater psychological stability. Most patients who undergo early surgery have good results, and both patients and their families are satisfied. Most authors agree that surgery should be performed in the early years of life, usually before 2 years of age [6, 7]. In our study, the average age of surgery was 37±35 months, the youngest being 6 months and the oldest 211 months. However, some studies suggest that early genital reconstruction surgery does not yield the desired results and affects the child's QoL in adulthood. Some authors argue that genital surgery in childhood can lead to feelings of inferiority in women with CAH, which are affected by the surgical process itself. Although there is not complete consensus on the age of surgical intervention, most studies suggest that early surgery offers more benefits [8].

5. CONCLUSION

In female infants with CAH, the salt-wasting form is more common. Most patients are diagnosed early in the neonatal period. The most common degree of genital virilization is Prader stage 2 or 3. Severe virilization occurs in approximately one-quarter of cases. Reconstructive surgery is performed early in the first few years of life. Longitudinal studies are needed to assess the long-term effects and benefits of genital reconstruction surgery in female infants with CAH.

REFERENCES

[1] Ibrahim H, Lachkar AA, Bidault V, Delcour C, Paye-Jaouen A, Peycelon M, and El-Ghoneimi A. Genito-Urinary Reconstruction in Female Children With Congenital Adrenal Hyperplasia: Favorable Surgical Outcomes Can Be Achieved by Contemporary Techniques and a Dedicated Multidisciplinary Management. Journal of Pediatric Surgery 2024 Sep; 59:1851–8. DOI: 10.1016/j.jpedsurg.2024.05.009

[2] Sturm RM, Durbin-Johnson B, and Kurzrock EA. Congenital Adrenal Hyperplasia: Current Surgical Management at Academic Medical Centers in the United States. Journal of Urology 2015 May; 193:1796–801. DOI: 10.1016/j.juro.2014.11.008

[3] Shalaby M, Chandran H, Elford S, Kirk J, and McCarthy L. Recommendations of Patients and Families of Girls with 46XX Congenital Adrenal Hyperplasia in the United Kingdom Regarding the Timing of Surgery. Pediatric Surgery International 2021 Jan; 37:137–43. DOI: 10.1007/s00383-020-04780-3

[4] Kudela G, Gawlik A, and Koszutski T. Early Feminizing Genitoplasty in Girls with Congenital Adrenal Hyperplasia (CAH)—Analysis of Unified Surgical Management. International Journal of Environmental Research and Public Health 2020 May; 17:3852. DOI: 10.3390/ijerph17113852

[5] Abosena W, Almetaher HA, El Attar AA, Nofal AH, and Elhalaby EA. Outcomes of One-Stage Feminizing Genitoplasty in Children with Congenital Adrenal Hyperplasia and Severe Virilization. Pediatric Surgery International 2024 Mar; 40:72. DOI: 10.1007/s00383-024-05638-8

[6] Zainuddin AA, Grover SR, Soon CH, Nur Azurah AG, Mahdy ZA, Wu LL, Rasat R, Harun F, Chia WY, and Shamsuddin K. Malaysian Females With Congenital Adrenal Hyperplasia: Surgical Outcomes and Attitudes. Frontiers in Pediatrics 2019 Apr; 7:144. DOI: 10.3389/ fped.2019.00144

[7] Fisher RS, Espeleta HC, Baskin LS, Buchanan CL, Chan YM, Cheng EY, Coplen DE, Diamond DA, Nokoff NJ, Palmer BW, Poppas DP, Scott Reyes KJ, Tishelman A, Wolfe-Christensen C, Mullins LL, and Wisniewski AB. Decisional Regret about Surgical and NonSurgical Issues after Genitoplasty among Caregivers of Female Infants with CAH. Journal of Pediatric Urology 2022 Feb; 18:27–33. DOI: 10.1016/j.jpurol.2021.10.001

[8] Erginel B, Ozdemir B, Karadeniz M, Poyrazoglu S, Keskin E, and Soysal FG. Long-Term 10-Year Comparison of Girls with Congenital Adrenal Hyperplasia Who Underwent Early and Late Feminizing Genitoplasty. Pediatric Surgery International 2023 Jun; 39:222. DOI: 10.1007/s00383-023-05498-8