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Clinical characteristics and factors affecting quality of life in children with congenital adrenal hyperplasia

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Abstract: **Background**: Congenital Adrenal Hyperplasia (CAH) is a group of disorders characterized by impaired adrenal steroid hormone synthesis, with a wide spectrum of clinical manifestations. The prognosis of CAH depends on factors, such as clinical phenotype, treatment and management. **Objectives**: To analyze the factors influencing the quality of life in children with CAH. **Methods**: This retrospective study included 30 CAH patients divided into good prognosis (n=13) and poor prognosis (n=17) groups. Clinical characteristics, genetic mutations, treatment compliance, medication regimens and complications were analyzed by t-tests and logistic regression. **Results**: The good prognosis group presented better compliance (92.31% vs. 47.06%, P=0.017) and hormonal control (84.62% vs. 35.29%, P=0.01). The prevalence of the salt-wasting (SW) type of CAH was higher in the poor prognosis group (70.59% vs. 23.08%, P=0.038), while the simple virilizing (SV) type was higher in the good prognosis group (53.85% vs. 17.65%). The poor prognosis group received a higher hydrocortisone dose (16±3mg/m^2/day) compared to the good prognosis group (12±4mg/m2/day, P=0.025). Complications such as hypertension (P=0.017), hyperpigmentation (P=0.026) and urinary incontinence (P=0.017) were more prevalent in the poor prognosis group. **Conclusion**: In children with CAH, the quality of life is significantly affected by treatment compliance, hormonal control, and the presence of complications.

Keywords: Congenital adrenal hyperplasia; Hormonal control; 21-Hydroxylase deficiency; Pediatric endocrinology; Quality of life; Treatment compliance

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INTRODUCTION

Congenital adrenal hyperplasia (CAH) is a group of genetic disorders caused by defects in the steroidogenic pathway, resulting in impaired cortisol biosynthesis. The most common form, 21-hydroxylase deficiency, accounts for about 95% of CAH and follows an autosomal recessive inheritance pattern (Auer *et al*., 2023; Claahsen-van *et al*., 2022; Ferreira *et al*., 2021). Its global incidence ranges from 1 in 10,000 to 1 in 20,000 live births, though it is higher in certain populations due to consanguinity and genetic drift. In the United States, the incidence is approximately 1 in 15,000 live births, highlighting its significance as a public health concern (Musa *et al*., 2020).

Children with CAH face various clinical challenges, depending on the severity of the enzyme defect, and ranging from aldosterone deficiency to androgen excess (Murphy *et al*., 2021; Nordenstrom *et al*., 2023). The most severe form, salt-wasting CAH (SW-CAH), causes marked cortisol and aldosterone deficiency, which can lead to life-threatening hyponatremia and hyperkalemia in untreated patients. Simple virilizing CAH (SV-CAH) and non-classic CAH (NC-CAH) present with milder phenotypes. However, proper clinical management was significant to prevent virilization for normal growth and development (Prete A *et al*., 2021).

Effective management of CAH hinges on early diagnosis, generally achieved through newborn screening programs that detect elevated 17-hydroxyprogesterone (17-OHP) (Daniel *et al*., 2021; Gunawardana *et al*., 2024). Treatment involves lifelong glucocorticoid replacement and mitigate cortisol deficiency to suppress adrenal androgen overproduction. Mineralocorticoids and salt supplementation are also necessary for patients with SW-CAH. Despite these measures, disease control remains challenging, with fluctuating hormone levels affecting both physical and psychosocial health (Gusmano *et al*., 2023; Hou *et al*., 2024; Kobayashi and Fujiu, 2024).

Quality of life (QoL) has become an critical outcome measure in chronic diseases, including CAH. Children with CAH may experience compromised QoL due to the chronic nature of the disease, the burden of regular medication and the psychosocial stress associated with visible symptoms such as ambiguous genitalia or virilization. Previous studies have indicated that treatment adherence, hormonal control and the presence of complications significantly affect QoL in these patients. (Lasaite *et al*., 2022; Lawrence *et al*., 2023; Shafaay *et al*., 2023). In this context, the present study aimed to delineate the clinical characteristics of children with CAH due to 21-hydroxylase deficiency and identify key factors impacting their QoL. These factors were vital for developing targeted interventions to improve prognosis. The study is notable for its comprehensive approach, examining multiple potential influences on QoL, including subtype, treatment compliance, hormonal control, medication dosage and complications such as hypertension, hyperpigmentation and urinary incontinence.

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MATERIALS AND METHODS

Study design

This retrospective study included 30 pediatric patients diagnosed with CAH who were admitted to the hospital between June 2021 and June 2023. Data on patient demographics, medication regimens and complications, were collected to analyze the factors influencing the quality of life in children with CAH. Additionally, Clinical diagnostic information was also gathered to describe the clinical characteristics of these patients.

As this retrospective study used only de-identified patient data, it posed no risk to the participants or their medical care. All patients have signed informed consent at the time of their CAH diagnosis. The study protocol was approved by the hospital's Ethics Review Committee, ensuring compliance with ethical and regulatory guidelines for retrospective studies.

Inclusion and exclusion criteria

Inclusion Criteria: Patients were eligible if they were in the neonatal, infant, toddler, childhood, or adolescent stage, had no prior history of mental illness, and were able to cooperate with treatments and examinations. Diagnosis of CAH due to 21-hydroxylase deficiency followed the "Consensus on the Diagnosis and Treatment of CAH with 21-Hydroxylase Deficiency" by the Endocrinology, Genetics and Metabolism Group of the Pediatric Branch of the Chinese Medical Association (Kocova *et al*., 2021). Additionally, participants were required to be free from severe acute complications, such as adrenal crisis.

Exclusion Criteria: Patients were excluded if they exhibited unstable vital signs, including significant fluctuations in heart rate, body temperature, or blood pressure. Those with comorbid conditions that severely impacted their quality of life were also excluded. In addition, participants who failed to cooperate or discontinued treatment during the study period were excluded.

Grouping methods

Patients were categorized based on their QoL scores. For children aged 4 years and older, QoL was assessed using the Pediatric Quality of Life Inventory (PedsQL). For children younger than 4 years, caregivers completed the Toddlers and Preschoolers Quality of Life (TAPQOL) scale.

The PedsQL is a widely recognized instrument that evaluates the quality of life in children and adolescents. It encompasses various versions tailored to distinct age brackets, including an infant version, a children's version, and a youth version. The PedsQL scores are typically standardized and divided into several subdimensions, which encompass Emotional Functioning, Social Functioning, School Functioning, and Physical Functioning, ultimately contributing to an overall quality of life score. The scoring range spans from 0 to 100 points, with a score of 100 indicating optimal quality of life. The scale demonstrates strong reliability, as evidenced by a Cronbach's alpha of 0.88 (Raghunandan *et al*., 2023).

The TAPQOL is specifically designed to assess the quality of life in children under 4 years old. This questionnaire was completed by parents or primary caregivers to evaluate the quality of life of young children. The TAPQOL incorporates questions covering various domains, such as Activities of Daily Living, Social Interaction, Emotional and Behavioral Functioning, Cognitive Development, Physical Functioning, Pain/Discomfort and Sleep Patterns. Scores for each subdimensions are standardized on a scale from 0 to 100 points, with higher scores reflect a better quality of life. The TAPQOL demonstrates good reliability, with a Cronbach’s coefficient above 0.7 (Diaz-Garcia *et al*., 2023).

Based on the quality of life scores, participants were classified into two groups. Those scoring 60 or below were assigned to the poor prognosis group (n=17), while those scoring above 60 were classified into the good prognosis group (n=13).

Clinical type of CAH

The term "clinical types" refers to the various forms of CAH, categorized by their clinical manifestations and the specific enzyme deficiencies involved (Dreves *et al*., 2023). The following 3 types were included in the current study:

(1) SW-CAH: This is the most severe variant of CAH, typically resulting from a deficiency in 21-hydroxylase. Patients with this type are unable to produce sufficient cortisol and aldosterone, leading to excessive salt loss in their urine, which can pose life-threatening risks if untreated.

(2) SV-CAH: This form, also caused by 21-hydroxylase deficiency, is less severe than the SW type. Patients generally do not experience salt-wasting issues but may exhibit symptoms of virilization, such as ambiguous genitalia in females and accelerated growth in males.

(3) NC-CAH: This milder form of 21-hydroxylase deficiency often presents later in life and is characterized by symptoms such as hirsutism (excessive hair growth), acne and infertility. Consequently, it may go undiagnosed until adulthood.

Clinical testing

A fasting venous blood sample of 2 ml was collected for the analysis of 17-OHP and the CYP21A2 gene testing.

Hormonal Control (17-OHP): The concentration of 17-OHP was measured using an enzyme-linked immunosorbent assay (ELISA). It was essential to adhere strictly the operational guidelines provided in the human 17-OHP ELISA quantitative detection kit (product number K-1423-50×2N; Hunan Kangqing Biotechnology Co., Ltd; China). A well-controlled result indicated that the 17-OHP level falls within or close to the normal range. In contrast,

a poorly controlled result indicated a level significantly above the normal range, suggesting inadequate or unsatisfactory treatment.

Table 1: Analysis of Clinical Symptoms in 30 Patients

Clinical Manifestation	Number of Cases
Abnormal vulvar morphology	13
Hyperpigmentation of external genitalia	3
Mammary areola hyperpigmentation	3
Cutaneous hyperpigmentation	2
Precocious puberty	3
Nausea and vomiting	2
Hypospadias	1

CYP21A2 Gene Testing: Genomic DNA was extracted from the blood samples using a DNA extraction kit (item number: 56404; QIAGEN). The CYP21A2 gene region was amplified using a polymerase chain reaction (PCR) instrument (Eppendorf Mastercycler, Germany), and the resulting PCR products were subjected to Sanger sequencing. Subsequently, copy number analysis of the CYP21A2 gene was performed using the SALSA MLPA kit (item number ME024-025R; MRC Holland). The analysis was followed by sequence alignment using Clustal Omega v1.2.4 to identify variants, which were validated through the public database NCBI. Finally, a detection report was generated.

Statistical analysis

Measurement data were presented as either the mean ± standard deviation or the median and interquartile range, depending on whether the data followed a normal distribution. Categorical data was expressed as frequency and percentage. To compare continuous variables between two groups, unpaired t-tests were used. Both univariate and multivariate logistic regression analyses were performed to calculate the odds ratio (OR) and 95% confidence interval (CI) for each parameter treated as a continuous variable. Statistical significance was defined as a p-value less than 0.05. All statistical analyses were conducted using SPSS version 19 (SPSS Inc., Chicago, IL, USA) and R software version 3.0.2 (Free Software Foundation, Inc., Boston, MA, USA).

RESULTS

Analysis of clinical symptoms in 30 patients

Among the 30 children diagnosed with CAH, the most common clinical manifestation was abnormal vulvar morphology, observed in 13 cases (Table 1). Hyperpigmentation of the external genitalia and mammary areola was reported in 3 cases. Additionally, 2 children exhibited cutaneous hyperpigmentation. Precocious puberty was documented in 3 patients, while nausea and vomiting were noted in 2 patients. Hypospadias was observed in a single case.

CYP21A2 gene mutation analysis in 30 children with congenital adrenal hyperplasia

In our cohort of 30 children with CAH, genetic analysis revealed distinct mutation profiles across different clinical subtypes (Tables 2-4). Among the 15 patients with the simple virilizing type, the most frequent mutation was c.518T>A, identified in 13 cases. The mutations c.208G>T and c.710T>A were each found in 3 patients. Less common mutations included c.1070G>A and the heterozygous deletion CYP21A1P/CYP21A2_CH-9, each documented in 1 patient. For the 27 patients with the salt-wasting type, the most prevalent mutations were c.293-13C>G (12 cases) and c.955C>T and c.1069C>T, each present in 11 cases. The heterozygous deletion CYP21A1P/CYP21A2_CH-1 was observed in 9 patients. Additional mutations, such as c.923dup and c.713T>A, appeared in 3 cases each, while other mutations were identified at lower frequencies. Among the 16 patients with the non-classic type, the mutation c. *13G>A was predominant, found in 10 patients. Other notable mutations included c.188A>T in 4 patients and c.719T>A in 3 patients, alongside several other less common variants. The impact of specific mutations on the quality of life was variable and did not show statistically significant differences among the groups.

Comparison of general information between two prognosis groups

In our cohort of 30 children with CAH, the comparison between the good prognosis group (n=13) and the poor prognosis group (n=17) revealed several significant differences (Table 5). The average age at diagnosis was similar between the two groups, with the good prognosis group diagnosed at 91±32 days and the poor prognosis group at 95±33 days (P=0.741). Body mass index (BMI) was also comparable between the groups (18.6±2.3 vs. 18.4±2.6; P=0.833).

The distribution of the final sex of rearing distribution showed no significant difference (P=0.46), with males constituting 46.15% and 64.71% and females constituting 53.85% and 35.29% in the good and poor prognosis groups, respectively. Consanguinity was noted in 30.77% of the good prognosis group and 35.29% of the poor prognosis group (P=1.0), while a positive family history was present in 15.38% and 17.65% of the good and poor prognosis groups, respectively (P=1.0).

Table 2: Analysis of CYP21A2 gene single virulent mutation (15 participants)

Mutation Type	Frequency
c.518T>A	13
c.208G>T	3
c.710T>A	3
c.1070G>A	1
CYP21A1P/CYP21A2_CH-9 (heterozygous deletion)	1

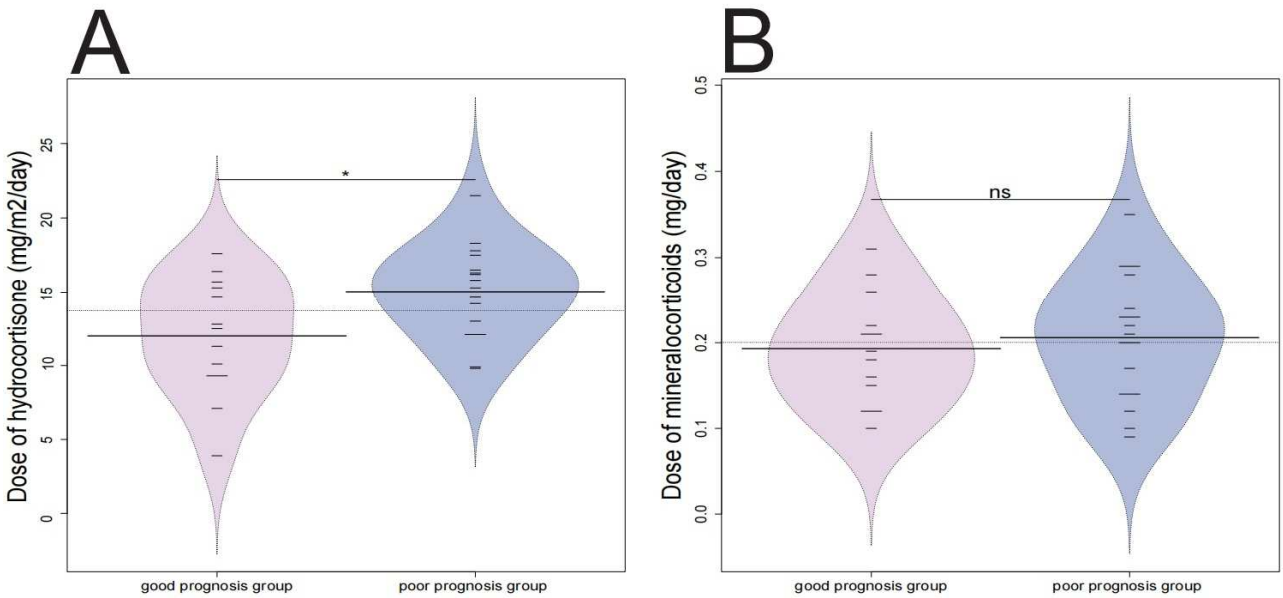

Fig. 1: Analysis of medication usage between two prognosis groups. (A) Dose of hydrocortisone (mg/m^2/day) of good prognosis group and poor prognosis group. (B) Dose of mineralocorticoids (mg/day) of good prognosis group and poor prognosis group.

Notably, compliance with treatment was significantly higher in the good prognosis group (92.31%) compared to the poor prognosis group (47.06%) (P=0.017). Hormonal control based on 17-OHP levels was better in the good prognosis group, with 84.62% demonstrating well-controlled levels vs. 35.29% in the poor prognosis group (P=0.01). Surgical correction rates for clitoroplasty/ vaginoplasty did not differ significantly between the two groups (P=1.0). The clinical type of CAH showed significant variability (P=0.038), with the salt-wasting type was more prevalent in the poor prognosis group (70.59%) than in the good prognosis group (23.08%), whereas the simple virilizing type was more common in the good prognosis group (53.85%) than in the poor prognosis group (17.65%). The non-classic type was relatively infrequent in both groups (23.08% in the good prognosis group and 11.76% in the poor prognosis group).

Analysis of medication usage between two prognosis groups

A comparative analysis of medication usage between the good prognosis group and the poor prognosis group revealed significant differences in the dose of hydrocortisone administered (Fig. 1). The good prognosis group received a mean dose of 12±4 mg/m^2/day, whereas the poor prognosis group received a higher mean dose of 16±3mg/m^2/day (P=0.025). Conversely, there was no significant difference in the dose of mineralocorticoids, with the good prognosis group receiving 0.19±0.06mg/day and the poor prognosis group receiving 0.21±0.07mg/day (P=0.62). These findings suggest that higher doses of glucocorticoids were associated with a poorer prognosis in children with CAH.

Table 3: Analysis of salt loss mutation of CYP21A2 Genotype (27 persons).

Mutation Type	Frequency
c.955C>T	11
c.293-13C>G	12
c.1069C>T	11
CYP21A1P/CYP21A2_CH-1 (heterozygous deletion)	9
c.1280G>A	2
c.292+1G>A	1
c.*3349G>A	1
c.923dup	3
CYP21A1P/CYP21A2_CH-5 (heterozygous deletion)	1
CYP21A1P/CYP21A2_CH-8 (heterozygous deletion)	1
CYP21A1P/CYP21A2_CH-3 (heterozygous deletion)	1
c.713T>A	3
c.332_339del	1

Analysis of complications between two prognosis groups

In the analysis of complications among children with CAH, significant differences observed between the good prognosis group and the poor prognosis group (Table 6). Hypertension was significantly more prevalent in the poor prognosis group (52.94%) compared to the good prognosis group (7.69%) (P=0.017). Similarly, hyperpigmentation was more frequent in the poor prognosis group (58.82%) than in the good prognosis group (15.38%) (P=0.026). Urinary incontinence was observed in 52.94% of the poor prognosis group but only in 7.69% of the good prognosis group (P=0.017). No statistically significant differences

were observed regarding the prevalence of precocious puberty (15.38% vs 17.65%, P=1), hirsutism (7.69% vs 23.53%, P=0.355), or short stature (15.38% vs 17.65%, P=1) between the two groups. These results highlight the association of certain complications with poorer prognosis in children with CAH.

Table 4: Analysis of Atypical mutation of CYP21A2 genotype (16 persons)

Mutation Type	Frequency
c.*13G>A	10
c.188A>T	4
c.719T>A	3
c.844G>T	2
c.*740C>T	2
c.*1215C>T	2
c.*1351G>C	2
c.2588_2707del	2
c.-126C>T	2
c.-113G>A	2
c.-110T>C	2
c.-103A>G	2
c.165dup	1
TNXA/TNXB CH-1	1

Correlation analysis of factors affecting the quality of life in 30 children with CAH

Correlation analysis of factors affecting the quality of life in 30 children with CAH revealed several significant associations (Table 7). Poor compliance with treatment was negatively correlated with quality of life (rho=-0.476, P=0.008), as was poor hormonal control based on 17-hydroxyprogesterone levels (rho=-0.493, P=0.006). The clinical type of CAH also showed a negative correlation (rho=-0.425, P=0.019). Conversely, the dose of glucocorticoids was positively correlated with quality of life (rho=0.369, P=0.045).

Among complications, hypertension (rho=0.476, P=0.008), hyperpigmentation (rho =0.439, P=0.015), and urinary incontinence (rho =0.476, P=0.008) were all associated with poorer quality of life. These findings indicate that better treatment compliance and hormonal control were linked to improved quality of life, whereas higher doses of glucocorticoids and the presence of complications such as hypertension, hyperpigmentation and urinary incontinence were associated with reduced quality of life in these children.

Logistic regression analysis of influencing factors of quality of life in 30 children with CAH

Univariate logistic regression analysis identified several factors significantly affecting the quality of life in 30 children with CAH (Table 8). Poor compliance with treatment (OR=0.074, 95% CI: 0.004-0.506, P=0.023), inadequate hormonal control based on 17-OHP (OR=0.099, 95% CI: 0.012-0.521, P=0.012), and the clinical type of CAH (OR=0.317, 95% CI: 0.091-0.896, P=0.043) were associated with lower quality of life. In cantrast, higher doses of glucocorticoids were linked to worse outcomes (OR=14.024, 95% CI: 1.462-254.407, P=0.040). Complications such as hypertension (OR=13.500, 95% CI: 1.975-274.960, P=0.023), hyperpigmentation (OR=7.857, 95% CI: 1.511-62.090, P=0.024) and urinary incontinence (OR=13.500, 95% CI: 1.975-274.960, P=0.023) were also significantly with lower quality of life. Multivariate logistic regression analysis (Table 9) further refined these associations. Compliance with treatment (OR=0.157, 95% CI: 0.023-0.925, P=0.043), hormonal control based on 17-OHP (OR=0.209, 95% CI: 0.046-0.943, P=0.032), hypertension (OR=4.704, 95% CI: 1.103-20.155, P=0.037) and urinary incontinence (OR=4.964, 95% CI: 1.138-21.536, P=0.036) remained significant predictors.

Hyperpigmentation (P=0.062) and glucocorticoids dose (P=0.110) showed trends towards significance, while the clinical type of CAH was no longer a significant predictor in the multivariate model (P=0.097). These findings underscore the critical role of treatment compliance, effective hormonal control, and management of complications in improving the quality of life for children with CAH.

DISCUSSION

The present study investigates the clinical characteristics and factors influencing the QoL in 30 pediatric patients diagnosed with CAH due to 21-hydroxylase deficiency. Our findings highlight several significant determinants of QoL, including treatment compliance, hormonal control, clinical type of CAH, glucocorticoid dosage and the presence of complications such as hypertension, hyperpigmentation and urinary incontinence. These results underscore the complexity of managing CAH and improving the QoL for affected children. The significant association between treatment compliance and better QoL was one of the most clinically relevant findings. Non-compliance with treatment regimens negatively impacts the hormonal balance, leading to unstable 17-OHP levels, which can exacerbate CAH symptoms and complications.

Non-compliance may result from multiple factors, including socioeconomic barriers, limited insufficient caregiver education, or inadequate healthcare system support. A multifaceted approach that includes patient education, regular follow-up, and integrated support systems could substantially improve treatment adherence and, in turn, QoL. Previous studies have demostrated that effective communication and trust between healthcare providers and patients enhance adherence to treatment protocols, thereby improving clinical outcomes (Liu *et al*., 2022; Maher *et al*., 2023).

Table 5: Comparison of general information between two groups

Indexs	Good prognosis group (n=13)	Poor prognosis group (n=17)	t/χ2	P
Age at diagnosis (days)	91±32	95±33	0.333	0.741
BMI	18.6±2.3	18.4±2.6	0.212	0.833
Final sex of rearing [n(%)]			/	0.46
- *Male*	6(46.15%)	11(64.71%)		
- *Female*	7(53.85%)	6(35.29%)		
Consanguinity [n(%)]			/	1
-+*ve*	4(30.77%)	6(35.29%)		
--*ve*	9(69.23%)	11(64.71%)		
Positive family history [n(%)]			/	1
-*Yes*	2(15.38%)	3(17.65%)		
-*No*	11(84.62%)	14(82.35%)		
Compliance with treatment [n(%)]			/	0.017
-*Yes*	12(92.31%)	8(47.06%)		
-*No*	1(7.69%)	9(52.94%)		
Hormonal control (17-OHP) [n(%)]			/	0.01
-*Well*	11(84.62%)	6(35.29%)		
-*Poor*	2(15.38%)	11(64.71%)		
Surgical correction [n(%)]			/	1
-*Clitoroplasty/Vaginoplasty done*	3(23.08%)	5(29.41%)		
- *Not done yet*	10(76.92%)	12(70.59%)		
Clinical type of CAH [n(%)]			/	0.038
-*SW*	3(23.08%)	12(70.59%)		
-*SV*	7(53.85%)	3(17.65%)		
-*NC*	3(23.08%)	2(11.76%)		

Hormonal control, as reflected by 17-OHP levels, was another pivotal factor affecting QoL. Poor control of 17-OHP suggests an inadequate dosage or timing of administered corticosteroids, resulting in insufficient suppression of adrenal androgen production. Reduced cortisol levels trigger increased adrenocorticotropic hormone (ACTH) secretion, driving excessive androgen production and leads to virilization and other adverse effects. Effective dose adjustments and ongoing monitoring are therefore essential for optimizing hormonal control. This emphasizes the importance of individualized treatment plans that are regualy reviewed and tailored to each patient's dynamic requirements (Schröder MAM *et al*., 2022; Mallappa A and Merke DP, 2022; S L *et al*., 2023). Interestingly, our data revealed that higher doses of glucocorticoids were paradoxically associated with poorer QoL. This may be attributed to the adverse effects of over-treatment, including Cushingoid features, growth suppression, obesity and metabolic complications. These findings highlight the necessity of a delicate balance in glucocorticoid dosing. Alternative approaches, such as using hydrocortisone to mimic the natural diurnal rhythm of cortisol or employing newer agents with fewer side effects, could assisst mitigate these detrimental outcomes (Fylaktou *et al*., 2022).

The clinical type of CAH also emerged as a significant determinant of QoL, with SW-CAH patients exhibiting poorer QoL compared to those with SV or NC types. The life-threatening nature of the SW-CAH requires rigorous management to prevent adrenal crises, which, if not effectively managed, can result in severe morbidity or even mortality. This higher disease burden, combined with more complex treatment protocols, naturally impacts the QoL adversely. Stringent monitoring and prompt management of adrenal crises through mineralocorticoid replacement and sodium supplementation are therefore essential. Additionally, genetic counseling and early neonatal screening can facilitate timely diagnosis and treatment initiation, potentially improving long-term outcomes for children with SW-CAH (Dreves *et al*., 2023; Miller and White, 2022).

Complications such as hypertension, hyperpigmentation, and urinary incontinence were more prevalent in the poor prognosis group and were significantly associated with lower QoL. Hypertension in CAH patients may result from prolonged glucocorticoid therapy or an underlying dysregulation of the renin-angiotensin-aldosterone system. Long-term cardiovascular monitoring and early intervention strategies should be prioritized to reduce the negative impact of hypertension on QoL.(White PC, 2022; Tian Y *et al*., 2023). Hyperpigmentation, primarily resulting from excessive ACTH stimulation, also significantly affected QoL. This is because hyperpigmentation can be psychologically distressing and socially stigmatizing, particularly for children and adolescents. Optimal hormonal control can adress the physical manifestation and alleviate psychological distress, thereby improving overall QoL (Kurzyńska *et al*., 2022).

Table 6: Analysis of complications between two prognosis group

Indexes	Good prognosis group (n=13)	Poor prognosis group (n=17)	P
Hypertension [n (%)]	1 (7.69%)	9 (52.94%)	0.017
Hyperpigmentation [n (%)]	2 (15.38%)	10 (58.82%)	0.026
Urinary incontinence [n (%)]	1 (7.69%)	9 (52.94%)	0.017
Precocious puberty [n (%)]	2 (15.38%)	3 (17.65%)	1
Hirsutism [n (%)]	1 (7.69%)	4 (23.53%)	0.355
Short stature [n (%)]	2 (15.38%)	3 (17.65%)	1

Table 7: Correlation analysis of factors affecting the quality of life in 30 children with congenital adrenal hyperplasia

	rho	P value
Compliance with treatment [n (%)]	-0.476	0.008
Hormonal control (17-OHP) [n (%)]	-0.493	0.006
Clinical type of CAH [n (%)]	-0.425	0.019
Dose of glucocorticoids (mg/m2/day)	0.369	0.045
Hypertension [n (%)]	0.476	0.008
Hyperpigmentation [n (%)]	0.439	0.015
Urinary incontinence [n (%)]	0.476	0.008

Table 8: Single factor logistic regression analysis of influencing factors of quality of life in 30 children with congenital adrenal hyperplasia

	Coefficient	Std Error	Wald	P Value	OR	CI Lower	CI Upper
Compliance with treatment [n (%)]	-2.603	1.149	2.266	0.023	0.074	0.004	0.506
Hormonal control (17-OHP) [n (%)]	-2.311	0.921	2.509	0.012	0.099	0.012	0.521
Clinical type of CAH [n (%)]	-1.148	0.568	2.021	0.043	0.317	0.091	0.896
Dose of glucocorticoids (mg/m2/day)	2.641	1.288	2.051	0.040	14.024	1.462	254.407
Hypertension [n (%)]	2.603	1.149	2.266	0.023	13.500	1.975	274.960
Hyperpigmentation [n (%)]	2.061	0.913	2.258	0.024	7.857	1.511	62.090
Urinary incontinence [n (%)]	2.603	1.149	2.266	0.023	13.500	1.975	274.960

Another important factor was the role of genetic variations in influencing the severity and presentation of CAH symptoms, which indirectly impacts QoL. The variable mutation profiles across different CAH types and their association with clinical severity indicate that personalized medical approaches based on genetic profiling could enhance treatment precisiom. Research into genotype-phenotype correlations can guide the development of tailored therapeutic interventions that better address individual patient needs, ultimately fostering improved QoL outcomes (Adriaansen *et al*., 2022; Dabas *et al*., 2020; Glazova *et al*., 2023).

Additionally, comorbid mental health conditions, although not included in this study's criteria, were essential factors to consider when evaluating QoL in CAH patients. The chronic nature of CAH and the lifelong requirement for medical management can create significant psychological stress, contributing to anxiety, depression, and other mental health issues. Integrated care models that include endocrinologists and mental health professionals can provide comprehensive care aimed at improving both physical and psychological well-being (Merke *et al*., 2021; Claahsen-van *et al*., 2021; Auchus *et al*., 2022). The present study also emphasizes the importance of regular follow-up and multidisciplinary care in managing CAH effectively. Teams comprising endocrinology, genetics, nephrology, and psychological support services must collaborate to optimize patient outcomes. Periodic assessments using QoL instruments such as PedsQL and TAPQOL provide valuable insights into the patient well-being and help guide tailor interventions (Fraga *et al*., 2024; Merke and Auchus, 2020; Liu *et al*., 2022; Barbot *et al*., 2022).

While the present study provides valuable insights into the clinical characteristics and factors affecting quality of life in children with CAH, it has several limitations. First, the sample size was small, which may introduce certain errors in the results. The cohort of 30 patients limits the generalizability of our findings and may not capture the full spectrum of CAH phenotypes and their impact on quality of life. Second, the retrospective design may introduce recall bias potentially affecting the accuracy of collected data. Finally, the absence of a control group and reliance on self-reported QoL measures may reduce the robustness of our conclusions. Future studies with larger, more diverse populations and prospective designs are needed to validate these findings and provide a more comprehensive understanding of the determinants of quality of life in patients with CAH. CAH is a rare disease that profoundly affects the hormone levels in both female and male children

Table 9: Multivariate logistic regression analysis of influencing factors of quality of life in 30 children with congenital adrenal hyperplasia

	Coefficient	Std Error	Wald	P Value	OR	CI Lower	CI Upper
Compliance with treatment	-1.853	0.915	4.104	0.043	0.157	0.023	0.925
Hormonal control (17-OHP)	-1.563	0.721	4.586	0.032	0.209	0.046	0.943
Clinical type of CAH	-0.835	0.495	2.754	0.097	0.434	0.151	1.235
Dose of glucocorticoids	1.421	0.893	2.547	0.110	4.126	0.765	22.267
Hypertension	1.548	0.732	4.369	0.037	4.704	1.103	20.155
Hyperpigmentation	1.148	0.612	3.486	0.062	3.152	0.937	10.757
Urinary incontinence	1.602	0.763	4.374	0.036	4.964	1.138	21.536

and is highly associated with precocious puberty and advanced bone age. The gene expression, pathogenesis and mechanisms of CAH remain incompletely understood.. Moreover, the clinical symptoms and risk factors of CAH require further investigation.. This study by reporting the symptoms and linical examination results of 30 children with CAH, provides important empirical evidence that contributes to a better understanding of this rare disease. Timely identification and reporting of rare diseases by hospitals are essential for advancing research and improving treatment strategies. Based on our findings, strategies that enhance treatment compliance, provide personalized hormonal management, enable early genetic diagnosis and ensure comprehensive multidisciplinary care are critical for improving QoL in children with CAH. Future research could focus on developing novel therapeutic agents with fewer side effects, exploring gene therapy approaches. and integrating mental health support into routine care. These advances could substantially refine the management of CAH, ultimately improving QoL for affected children and their families.

CONCLUSION

In summary, the quality of life in children with CAH is shaped by a complex interplay of treatment adherence, hormonal control, glucocorticoid dosing, CAH clinical type, and the presence of complications. Among these faxtors, clinical type may represent the primary intrinsic determinant, while complications constitute a significant external influence.

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Authors' contributions
Shiyi Xu and Hui Liu: Conception and design or analysis and interpretation of the data; Zhen Li, Qingxian Fu and Qiuting Lin: Drafting of the paper and revising it critically for intellectual content. All authors approved the final version of the article and agreed to be accountable for all aspects of the work.

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Data availability statement
The datasets used and/or analyzed during the current study were available from the corresponding author on reasonable request.

Ethical approval
The study was approved by Fujian Children's Hospital (Fujian Branch of Shanghai Children's Medical Center); College of Clinical Medicine for Obstetrics & Gynecology and Pediatrics (2024ETKLRK09006).

Conflict of interest
Declare that they have no conflict of interest

Consent to participate
All patients have signed informed consent

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