

## ORIGINAL ARTICLE

## Blood pressure percentile of different age group of patients with congenital adrenal hyperplasia.

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**Article Citation:** Nisar W, Ibrahim MN, Riaz M, Rai VR, Khoso ZA. Blood pressure percentile of different age group of patients with congenital adrenal hyperplasia. Professional Med J 2025; 32(09):1185-1189. <https://doi.org/10.29309/TPMJ/2025.32.09.9760>

**ABSTRACT... Objective:** To determine the mean blood pressure (BP) of patients with congenital adrenal hyperplasia (CAH) presenting to tertiary care hospital. **Study Design:** Cross-sectional study. **Setting:** Outpatient Department of Pediatrics, National Institute of Child health, Karachi, Pakistan. **Period:** June 2024 to November 2024. **Methods:** A total of 49 children of either sex, aged 5 to 15 years and established cases of CAH were analyzed. Demographic and clinical history of all the children were recorded at enrollment. Systolic and diastolic BP were measured thrice in succession at 1-minute interval, utilizing a mercury sphygmomanometer after the child had rested for a minimum duration of 10 minutes. Data were analyzed on "IBM-SPSS Statistics, version-26.0". P-value <0.05 was used as statistically significant. **Results:** In a total of 49 children, 27 (55.1%) were female. The mean age was  $8.85 \pm 2.87$  years. The mean SBP, and DBP were recorded to be  $120.02 \pm 18.19$  mmHg, and  $78.43 \pm 11.61$  mmHg, respectively. Relatively older age group (11-15 years) was found to have significantly higher SBP ( $128.13 \pm 15.34$  vs.  $116.09 \pm 18.37$  mmHg,  $p=0.028$ ). Bivariate correlation analysis revealed significantly positive correlation ( $p<0.001$ ) of SBP with age ( $r=0.636$ ), height ( $r=0.654$ ), weight ( $r=0.733$ ), and body mass index (BMI) ( $r=0.700$ ). DBP was having significant correlation ( $p<0.001$ ) with age ( $r=0.577$ ), height ( $r=0.645$ ), weight ( $r=0.691$ ), and BMI ( $r=0.606$ ). **Conclusion:** Children with CAH exhibit elevated blood pressure levels, particularly with increasing age, height, weight, and BMI, underscoring the importance of regular cardiovascular monitoring in this population.

**Key words:** Body Mass Index, Blood Pressure, Congenital Adrenal Hyperplasia, Glucocorticoids, Mineralocorticoids.

### INTRODUCTION

Congenital adrenal hyperplasia (CAH) caused by 21-hydroxylase deficiency is an adrenosteroid biosynthetic disorder that presents with defective cortisol synthesis and subsequent increased "17-hydroxyprogesterone (17-OHP)" and adrenal androgen production.<sup>1</sup> The subtypes of CAH, listed from more to less severe, are the classic salt wasting (SW) and simple virilizing (SV), and the non-classic (NC) form. The severe form, often referred to as the classic type, is observed in approximately 1 in 15,000 births globally. In contrast, the milder variant, known as the NC form, is significantly more prevalent, occurring in about 1 in 1,000 births worldwide and as frequently as 1 in 20 births in certain ethnic populations.<sup>2</sup>

Management of CAH is glucocorticoid replacement, while the severe form is generally

treated with mineralocorticoid replacement to prevent SW.<sup>3</sup> Among children with CAH, once-daily hydrocortisone is preferred.<sup>4</sup> The daily neonatal endogenous cortisol production in children, and adolescents is expected to be between 7–9, and 6–8 mg/m<sup>2</sup>/day, respectively.<sup>5</sup> Hydrocortisone, due to its relatively shorter half-life, is unable to assist a normal circadian pattern of cortisol, exposing affected individual to fluctuations of hypercortisolemia despite 'physiologic' doses, potentially resulting in obesity, short stature and insulin resistance.<sup>6</sup> Some researchers have not detected increased risk of hypertension (HTN) in children with CAH, but others noted approximately 20% proportion of children with CAH to have HTN.<sup>7,8</sup> Some researchers with the use of 24-hr ambulatory BP monitoring determined that numerous CAH patients do not have the physiologic nocturnal reduction in SBP.<sup>9</sup>

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Article received on:

06/03/2025

Accepted for publication:

10/05/2025

In another study, the mean SBP among CAH patients was  $112.71 \pm 18.40$  mmHg and mean DBP was  $71.28 \pm 8.9$  mmHg.<sup>10</sup> A study by Nebesio and Eugster revealed the prevalence of HTN as 6.6% among children with CAH.<sup>11</sup>

Data about BP evaluation among children with CAH is limited. Insights into these can drive strategies to monitor such cases regularly so that prompt treatment may be given to children with CAH. Determining the mean BP in children with CAH can help clarify the spectrum of cardiovascular effects in CAH, guide therapeutic adjustments, and improve long-term monitoring strategies in resource-constrained settings. This study was done to determine the mean blood pressure (BP) of patients with CAH presenting to tertiary care hospital.

## METHODS

This cross-sectional study was conducted at the outpatient department of pediatrics, National Institute of Child health, Karachi, Pakistan during June 2024 to November 2024. Approval from Institutional Ethics Committee was obtained (No. IERB-19/2023, Dated: 14-12-2023). Non-probability, consecutive sampling technique was adopted. Using OpenEPI online sample size calculator taking the prevalence of HTN as 6.6% in children with CAH<sup>11</sup>, with 95% confidence level, and 7% margin of error, the sample size was calculated to be 49. Inclusion criteria were children of any gender, 5 to 15 years old and known cases of CAH. Exclusion criteria were maternal history of antenatal dexamethasone. Non consenting parents/guardians who refused for children to be a part of the study were also excluded. CAH was labeled as the serum 17-OHP levels between 2,000 to 4,000 ng/dL and cortisol level  $>18$  mcg/dL on adrenocorticotrophic hormone (ACTH) stimulation test. Written and informed consents were taken from parents/guardians. Demographical and clinical history of all the children were noted at the time of enrollment. Height was measured on wall mounted scale in inches, and weight on a weighing machine in kg. Systolic and diastolic BP were measured thrice in succession at 1-minute interval, utilizing a mercury sphygmomanometer after the child had rested for a minimum duration

of 10 minutes.

Data were analyzed using "IBM-SPSS Statistics, version-26.0". Quantitative data were shown as mean and standard deviation (SD). Frequency and percentages were computed for categorical variables. Effect modifiers were controlled through stratification, and compared with respect to SBP, and DBP. Independent sample t-test was used to compared SBP, and DBP with respect to characteristics of children. Bivariate correlation analysis was conducted to determine Pearson's correlation coefficient ( $r$ ). P-value  $<0.05$  was considered statistically significant.

## RESULTS

In a total of 49 children, 27 (55.1%) were female. The mean age was  $8.85 \pm 2.87$  years, ranging between 5 to 15 years. Residential affiliation of 26 (53.1%) children was rural. Father's and mother's educational status as illiterate were recorded among 16 (32.7%), and 33 (67.3%) children, respectively. All 49 (100%) children were on glucocorticoids / mineralocorticoids. The mean SBP, and DBP were recorded to be  $120.02 \pm 18.19$  mmHg, and  $78.43 \pm 11.61$  mmHg, respectively. Relatively older age group (11-15 years) was found to have significantly higher SBP ( $128.13 \pm 15.34$  vs.  $116.09 \pm 18.37$  mmHg,  $p=0.028$ ). No statistically significant association of any other characteristics was noted with either SBP, or DBP, and the details are given in Table-I.

Bivariate correlation analysis revealed significantly positive correlation ( $p<0.001$ ) of SBP with age ( $r=0.636$ ), height ( $r=0.654$ ), weight ( $r=0.733$ ), and BMI ( $r=0.700$ ). DBP was having significant correlation ( $p<0.001$ ) with age ( $r=0.577$ ), height ( $r=0.645$ ), weight ( $r=0.691$ ), and BMI ( $r=0.606$ ), and the details are shown in Table-II.

## DISCUSSION

The findings of this study have highlighted the cardiovascular risks associated with CAH. The findings revealed that the mean SBP, and DBP were  $120.02 \pm 18.19$  mmHg and  $78.43 \pm 11.61$  mmHg, respectively.

Characteristics		Frequency (%)	SBP in mmHg (Mean±SD)	P-Value	DBP in mmHg (Mean±SD)	P-Value
Gender	Male	22 (44.9%)	119.09±16.13	0.751	75.55±11.51	0.118
	Female	27 (55.1%)	120.78±19.99		80.78±11.37	
Age (years)	5-10	33 (67.4%)	116.09±18.37	0.028	76.33±12.40	0.069
	11-15	16 (32.6%)	128.13±15.34		82.75±8.59	
Residence	Rural	23 (46.9%)	117.96±17.52	0.461	76.96±12.29	0.410
	Urban	26 (53.1%)	121.85±18.93		79.73±11.05	
Father's education	Illiterate	16 (32.7%)	119.94±15.82	0.983	81.13±12.60	0.262
	Literate	33 (67.3%)	120.06±19.47		77.12±11.06	
Mother's education	Illiterate	33 (67.3%)	117.55±20.36	0.174	78.45±12.52	0.982
	Literate	16 (32.7%)	125.13±11.56		78.33±9.59	
On Glucocorticoids / mineralocorticoids		49 (100%)	120.02±18.19	-	78.43±11.61	-

**Table-I. Association of blood pressure with characteristics of children with congenital adrenal hyperplasia**

		Age	Height	Weight	Body Mass Index	Family Monthly Income
Systolic blood pressure	Pearson Correlation	0.636	0.654	0.733	0.700	0.226
	P-value	<0.001	<0.001	<0.001	<0.001	0.119
Diastolic blood pressure	Pearson Correlation	0.577	0.645	0.691	0.606	0.159
	P-value	<0.001	<0.001	<0.001	<0.001	0.274

**Table-II. Correlation analysis between blood pressure measurements and quantitative variables (n=49)**

Elevated BP, particularly systolic HTN, has been reported in children with CAH due to "21-hydroxylase deficiency (21OHD)".<sup>12-14</sup> Roche et al.<sup>15</sup>, suggested that children with CAH often have elevated ambulatory BP levels, with up to 58% exhibiting systolic HTN. Older children aged 11–15 years were observed to have significantly higher SBP compared to younger children ( $p=0.028$ ). Bivariate correlation analysis showed a significant positive relationship of both SBP and DBP with age, height, weight, and BMI. The observed positive correlation between BMI and BP in this study aligns with previous findings that suggest obesity and truncal adiposity as significant contributors to HTN in CAH patients.<sup>16</sup>

The role of glucocorticoid and mineralocorticoid therapy in influencing BP has been well-documented.<sup>17</sup> High doses of glucocorticoids, often used to suppress androgen production, have been implicated in the development of HTN, as noted by Ubertini et al.<sup>18</sup> This study showed that elevated BP across the cohort, may reflect the complex interplay of treatment factors,

including supraphysiological glucocorticoid doses and mineralocorticoid supplementation.<sup>19</sup> The lack of data on specific glucocorticoid doses and salt intake in this study limits a more detailed analysis of their direct impact. Dehkordi et al.<sup>20</sup>, highlighted a positive association between 17-hydroxyprogesterone levels and DBP, further emphasize the potential role of hyperandrogenism in BP regulation among CAH patients. This study did not assess androgen levels, which could provide more insights into this relationship. The significant correlation of BP with anthropometric parameters, including height and weight, is consistent with the observations by Clausen et al.<sup>21</sup>, who reported that growth-related factors influence BP in children with CAH. This underscores the importance of regular monitoring of growth parameters and BP in these patients to mitigate long-term cardiovascular risks. The present study highlights the need for early and consistent BP monitoring in children with CAH to identify and manage HTN effectively.<sup>22</sup> Given the well-established association of childhood HTN with adverse cardiovascular outcomes

in adulthood, incorporating BP screening as part of routine clinical care for CAH patients is essential. Addressing modifiable risk factors, such as obesity, through lifestyle and dietary interventions, could help reduce the burden of HTN in this population.

The findings from this study indicate that children with CAH exhibit BP levels that are significantly influenced by age, height, weight, and BMI. The observed higher SBP in the older age group (11–15 years) underscores the importance of age-related monitoring, as these patients may be at increased risk for early-onset HTN. The strong positive correlations between both SBP, and DBP with anthropometric parameters suggest that as children with CAH grow older and gain weight, there is a parallel increase in their BP. This relationship may reflect the complex interplay between glucocorticoid therapy, metabolic changes, and cardiovascular risk in CAH. Clinically, these findings highlight the need for routine and age-appropriate blood pressure monitoring in CAH patients, particularly those with higher BMI, to detect early signs of HTN. Early identification and management of elevated blood pressure may help prevent long-term cardiovascular complications and allow for better individualization of hormone replacement therapy to balance endocrine control with metabolic and cardiovascular health.

This study has several limitations. The lack of detailed data on glucocorticoid and mineralocorticoid doses, salt supplementation, and androgen levels limits the ability to fully explore the impact of treatment regimens on BP. Future studies with larger cohorts, longitudinal follow-up, and comprehensive data collection are warranted to better understand the complex interactions between CAH, treatment, and cardiovascular health.

## CONCLUSION

Children with CAH exhibit elevated BP levels, particularly with increasing age, height, weight, and BMI, underscoring the importance of regular cardiovascular monitoring in this population. These findings highlight the need for

a multidisciplinary approach to manage CAH, focusing on optimizing treatment regimens and addressing cardiovascular risk factors early in life.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## SOURCE OF FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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## AUTHORSHIP AND CONTRIBUTION DECLARATION

1	<b>Wafa Nisar:</b> Data collection, drafting, responsible for data, approval for publication.
2	<b>Mohsina Noor Ibrahim:</b> Study concept methodology, proof reading, approval for publication.
3	<b>Maira Riaz:</b> Critical revisions, literature review, discussion, approval for publication.
4	<b>Versha Rani Rai:</b> Methodology, critical revisions, literature review, discussion, approval for publication.
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