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# Clinical assessment and early intervention for deviations in children's growth and development

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**Abstract**: **Background**: Chinese adults' and children's heights have grown over two decades, but many parents remain unaware of the main factors affecting their children's height. **Objectives**: This study analyzed clinical and early pharmacological interventions for preventing and treating growth disorders and promoting normal growth in children with deviations. **Methods**: This study involves a non-randomized intervention. A retrospective study of 120 children examined at our hospital from March 2023 to February 2025 were divided into four groups based on height and development: short stature group (SS, n=28), less short stature group (LSS, n=32), early development group (ED, n=41) and central precocious puberty group (CPP, n=19). The SS group and LSS group received oral lysine, inositol, vitamin $B_{12}$ solution + γ-aminobutyric acid (GABA) and the ED group and CPP group received oral Zhi Bai Di Huang Wan and all children were given health guidance. Clinically relevant information, such as baseline information, height growth values, and growth factor levels before and after treatment, was collected and compared among the four groups of children, and pre-treatment factors affecting children's height growth outcomes were also analyzed. **Results**: Before treatment, the four children's groups differed significantly ($P < 0.05$). After 3 and 6 months, all children's heights increased, with the fastest growth in the LSS group. Logistic regression showed sex and age before treatment were key factors affecting height. ROC curves revealed AUCs for sex, age and the model of 0.599(95% CI: 0.497-0.701), 0.774(95%CI: 0.686-0.861) and 0.818 (95% CI: 0.735-0.900). **Conclusion**: Clinical analysis and early intervention for children with growth deviations detected during school physical exams can restore normal growth, slow early bone age advancement, improve height outcomes and prevent or treat growth disorders.

**Keywords**: Clinical characteristics; Growth deviation; Pharmacologic intervention; Treatment effects

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## INTRODUCTION

As the health impact of traditional diseases brought about by hunger and economic backwardness declines due to social progress and improved medical care, growth and development indicators have become a high priority in the global and Healthy China strategy (Hokken-Koelega *et al.*, 2023). The United Nations Children's Fund in 2015 pointed out five key indicators about children's long-term health, the first of which is height in adulthood. The Healthy China 2030 strategy mentions (Gao *et al.*, 2021), to reduce the growth retardation rate of children under the age of 5 from 8.1% in 2013 to less than 5% in 2030. As Chinese society progresses and develops, parents' height expectations for their children are increasing. Research indicates that genetic factors are the primary determinants of height (Luo and Song, 2022). These factors determine an adolescent's growth potential, significantly influencing physical appearance, body shape, physiological functions, timing of sexual maturation, developmental characteristics, potential and growth trajectory. However, genetics is not the sole determinant of height. While heredity establishes the possibility for height development, the successful realization of this potential depends on environmental factors. Therefore, it is entirely possible to scientifically intervene in height development while adhering to its objective principles. By actively creating an optimal growth environment, children's height potential can be maximized. However, the reality is not as satisfactory as it should be. According to statistics from the China Health Commission, the total number of short-statured children between the ages of 4 and 15 years old is about 7 million (Dong *et al.*, 2020). In addition to these short children who are in urgent need of treatment, there are 39 million ordinary families who are not satisfied with their children's height and hope to make their children reach their ideal height through various means. At present, children's substandard height has become an urgent problem in China. Based on this, this study analyzes the clinical characteristics and early intervention treatment of children with growth deviation and analyzes the influence of children's basic conditions before treatment on their height outcomes.

## MATERIALS AND METHODS

### *General information*

A retrospective analysis was conducted on children who underwent physical examinations at our hospital from March 2023 to February 2025. A random sampling method was used to select 120 cases. The children were categorized into 4 groups according to their height range and

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developmental degree: short stature group (SS, n=28), less short stature group (LSS, n=32), early developmental group (ED, n=41) and central precocious puberty group (CPP, n=19). Age (months), height (cm), BMI ($kg/m^2$), family history of dwarfism and pre-treatment bone age (years) were collected from the four groups of children. *Inclusion criteria*: (1) Ages 5-8 years old; (2) Heights less than P25 (Height standards refer to the percentile tables for height and weight of children and adolescents aged 0-18 years, based on the growth standards for children under 7 years old published by the National Health Commission of the People's Republic of China (2023); (3) Developmental advancement (advanced bone age or early development of sexual organs); (4) Complete follow-up data. *Exclusion criteria* were (1) Comorbid underlying diseases, such as respiratory diseases; (2) Allergy to the drugs used in the study; and (3) Children with growth advancement but predicted to have unaffected final height in adulthood.

***Grouping methods***

Short stature group (SS Group): Children with growth deviations and short stature (height < P10), i.e., individuals of the same race, sex and age who are 1.28 standard deviations below the mean height of the normal population in a similar living environment (- 1.28 SD).

Less short stature group (LSS Group): Heights between P10-P25, heights less than normal child height (P25) and greater than the range of growth deviations and children of short stature (P10).

Early development group (ED Group): For children with early bone age (bone age more than 1 year older than actual age) or early development of sexual organs (the development of secondary sexual characteristics before the age of 8 years for females and 9 years for males; in this study, “breast development before the age of 8 years for females and testicular development before the age of 9 years for males, with a testicular volume of ≥4 ml” were taken as the subjects of the study), but have not met the diagnostic criteria of CPP. However, the diagnostic criteria for CPP have not yet been met.

Central precocious puberty group (CPP Group): Children diagnosed with CPP according to the 2022 Expert Consensus Diagnostic Criteria for the Diagnosis and Treatment of Central Precocious Puberty (Subspecialty Group of Endocrinologic and the Society of Pediatrics, 2023): (1) Premature onset of secondary sexual characteristics: Development of secondary sexual characteristics before age 8 in girls and before age 9 in boys. Initial manifestations include breast nodules in girls and increased testicular volume in boys. (2) Advanced bone age: Bone age exceeds chronological age by 1 year or more. (3) Enlarged gonads: Pelvic ultrasound reveals increased uterine and ovarian volume in girls, with multiple follicles >4 mm in diameter visible within the ovaries; testicular volume ≥4 ml in boys. (4) Hypothalamic-pituitary-gonadal axis (HPGA) activation: Serum gonadotropins and sex hormones reach pubertal levels.

***Treatment method***

All children were treated with oral vitamin D (Sinopharm Holding Starshark Pharmaceutical (Xiamen) Company, DAC H35021450); take 2 tablet once daily, in combination with reasonable diet and exercise as the general interventions and based on the general interventions, the following therapeutic measures were further synthesized: the SS and LSS groups were given oral lysine inositol Vitamin $B_{12}$ oral solution (Jichuan Pharmaceutical Group Company, DAC H32026226) + γ-aminobutyric acid treatment, oral lysine inositol Vitamin $B_{12}$ 5 ml at once, 3 times per day, solid drink containing γ-aminobutyric acid ingredient 100mg/packet, 1 packet per day; the ED and CPP groups were given oral Zhibai DiHuangWan treatment (Jiuzhitang Company, DAC Z20023069), take 12 pills twice daily. Among these, the CPP group lacked pre-treatment growth rate data, making it impossible to assess whether the patient had rapid-onset CPP. Therefore, GnRHa treatment was temporarily withheld.

***Indicator collection***

Collect baseline data for all children, including age, gender, height, weight, BMI and family history of short stature. Height measurements were taken at baseline, 3 months post-treatment and 6 months post-treatment. Bone age assessment was conducted by quantifying children's bone age using the Chinese Wrist Bone Age Standard (China 05) based on X-ray readings of their wrists. This method involves assigning maturity scores to 20 wrist bones (13 bones in the RUS system and 7 in the CARPAL system). The total score was compared against a standard database to match the corresponding bone age value (total bone age score = Σ(maturity score of each bone) × weighting coefficient).

***Sample size calculation***

This study included 8 variables. Based on the 10 events per candidate predictor parameter (10 EPP) principle, a sample size of 80 cases was required. Accounting for a 20% dropout rate, a minimum of 100 cases needed to be enrolled. The final sample size enrolled in this study was 120 cases, consistent with the sample size calculation results.

***Statistical analysis***

In this study, SPSS 26.0 was used for data analysis and statistical processing and the Shapiro-Wilk (SW) test was used to test the normality of the relevant data; data that met the normal distribution were described by $\bar{x}\pm s$ and those that did not were described by interquartile spacing [M(p25, p75)] and the measurement data were described by [n(%)]; perform tests for homogeneity of variance on each indicator. Comparisons between groups were made using one-way analysis of variance (ANOVA) and the rank sum test of nonparametric test (Wilcoxon rank sum test) was

used for non-normal distribution; statistical comparison of categorical data was performed by $x^2$ test; Logistic regression model was used to study and explore the influencing factors related to dichotomous outcomes. The AUC value of the ROC curve characterizes the classification and predictive performance of indicators and predictive models. $P<0.05$ indicated that the difference was statistically significant; GraphPad Prism 8.0.2 was used to plot the children's growth curve.

## RESULTS

***Comparison of general information***

Comparison of the general information of the children in the four groups revealed significant differences in all indicators ($P < 0.05$) (Table 1).

***Child growth curve***

The heights of the children in the four groups pre-treatment, 3 months and 6 months after treatment are shown in table 2. All the children's heights increased to different degrees, among which the LSS group had the largest growth rate, while the ED group had the smallest growth rate, and the growth curves of the children in the four groups are shown in fig. 1.

***Logistic regression analysis of relevant pretreatment factors affecting height growth outcomes in children***

The height growth values of the children 6 months after the treatment were dichotomized, with whether the growth value was >3.2 cm (median) as the dependent variable [("growth value >3.2 cm"=1 (n=59), "growth value ≤3.2 cm"=0 (n=61)] and the sex of the children before the treatment (1=female, 0=male), age, height and weight and bone age as independent variables for one-way regression analysis. Including variables with $P < 0.05$ from the univariate regression in the multivariate regression analysis revealed that gender and age are independent factors influencing children's height growth (Table 3).

***ROC curve***

Construct a predictive model based on sex (1=female, 0=male) and age and plot the ROC curve. Analysis of each indicator is shown in table 4. The results showed that the AUCs of sex, age and prediction model were 0.599 (95%CI: 0.497-0.701), 0.774(95%CI: 0.686-0.861) and 0.818 (95%CI: 0.735-0.900), respectively, as shown in the fig. 2.

***Therapeutic safety***

No children receiving treatment experienced adverse reactions.

## DISCUSSION

Growth deviations in clinical practice emphasize "early detection, early screening and early intervention" (Liu *et al.*, 2025a). The younger the child, the more active the proliferation and differentiation of the cartilage layer of the epiphysis is (Mastromauro and Chiarelli, 2022), the more room and potential a child has to grow, the more responsive he or she will be to intervention treatments (Yang *et al.*, 2023). Lysine inositol Vitamin $B_{12}$ oral solution is an amino acid vitamin drug that contains lysine, which can effectively promote the production and metabolism of proteins, but also repair the body's damaged tissues and cells, improve the immunity of children and effectively strengthen the body's ability to fight diseases (Sun *et al.*, 2023). γ-aminobutyric acid (GABA) is a non-protein amino acid, which has the function of promoting the secretion of growth hormone by the pituitary gland and influences and promotes the secretion of growth hormone by the pituitary gland through bi-directional regulation (Zhang *et al.*, 2024). The drug acts as a neuroleptic, with its ability to deepen and prolong deep sleep, increased sleep time helps children's brain development and strengthens their memory ability and also has a positive effect on ensuring the quality of sleep and when the quality and duration of sleep are ensured (Bavato *et al.*, 2025) The children's height growth will also be improved. Central precocious puberty is defined as the development of secondary sexual characteristics in children presenting before the normal age, but without organic pathology (Liu *et al.*, 2025c).

Chinese traditional medicine believes that the kidneys are the foundation of the innate nature and the relationship between the abundance or decline of kidney Qi and the growth and development of the organism is very important. Precocious puberty has the characteristics of the kidneys that are often deficient, the spleen is often insufficient and the liver is often surplus (Liu *et al.*, 2025b). According to its different pathogenesis, treatment should be based on the principles of liver detoxification, spleen strengthening, phlegm elimination, yin nourishment and fire reduction (Ma *et al.*, 2023). Zhi Bai Di Huang Wan used in this study has the effect of nourishing Yin and clearing heat (Wang *et al.*, 2024). It can be used to treat central precocious puberty that does not meet the criteria for injectable drug therapy.

In the present study, the children who came to the hospital for the entrance medical examination, showing growth deviation, were grouped and their general information was analyzed and it was found that there was a significant difference in all the indices of the four groups of children. In the SS and LSS groups, there were more boys than girls in the ED and CPP groups and it was also found that the BMI index of the ED group was significantly higher than that of the other three groups, which, in combination with previous studies, suggests that obesity may be a causative factor in the early development of children and its higher than CPP group may be because the height of children in ED group was significantly lower than that of children in CPP group (Li *et al.*, 2024).

**Table 1**: Comparison of general information [n(%)].

| Variable | SS (n=28) | LSS (n=32) | ED (n=41) | CPP (n=19) | *t/F* | *P* |
|---|---|---|---|---|---|---|
| Sex | | | | | 14.365 | 0.002 |
| *Male* | 18(64.29) | 18(56.25) | 14(34.15) | 3(15.79) | | |
| *Famale* | 10(35.71) | 14(43.75) | 27(65.85) | 16(84.21) | | |
| Age (months) | 75.14±8.37 | 76.44±7.24 | 69.02±6.79 | 79.79±8.06 | 12.374 | <0.001 |
| Height (cm) | 110.09±4.11 | 115.48±3.83 | 110.25±3.14 | 113.74±3.42 | 17.164 | <0.001 |
| HtSDS (point) | -1.43±0.11 | -0.74±0.12 | -1.12±0.13 | -1.02±0.12 | 164.589 | <0.001 |
| Weight (kg) | 17.16±1.34 | 19.79±1.35 | 18.65±1.25 | 19.16±1.19 | 21.738 | <0.001 |
| BMI (kg/m$^2$) | 14.16±0.87 | 14.83±0.54 | 15.34±0.63 | 14.80±0.35 | 18.629 | <0.001 |
| Bone age (years) | 6.61±0.74 | 6.75±0.67 | 6.32±0.61 | 7.37±0.50 | 11.838 | <0.001 |
| Family history of short stature | | | | | 10.110 | 0.018 |
| *Yes* | 3(10.71) | 0(0.00) | 0(0.00) | 0(0.00) | | |
| *No* | 25(89.29) | 32(100.00) | 41(100.00) | 19(100.00) | | |

**Table 2**: Height of children at different treatment times

| Group | Pre-treatment | 3 months | 6 months | growth rate (cm/month) | *F* | *P* |
|---|---|---|---|---|---|---|
| SS(n=28) | 110.09±4.11 | 111.27±4.15 | 113.20±4.27 | 0.52±0.09 | 3.955 | 0.023 |
| LSS(n=32) | 115.48±3.83 | 116.87±3.83 | 119.23±3.65 | 0.62±0.10 | 8.057 | <0.001 |
| ED(n=41) | 110.25±3.14 | 111.56±3.29 | 112.85±3.42 | 0.43±0.12 | 6.437 | 0.002 |
| CPP(n=19) | 113.74±3.42 | 115.89±3.63 | 117.41±3.19 | 0.61±0.12 | 5.717 | 0.006 |
| *F* | 17.164 | 17.164 | 23.546 | 21.382 | | |
| *P* | <0.001 | <0.001 | <0.001 | <0.001 | | |

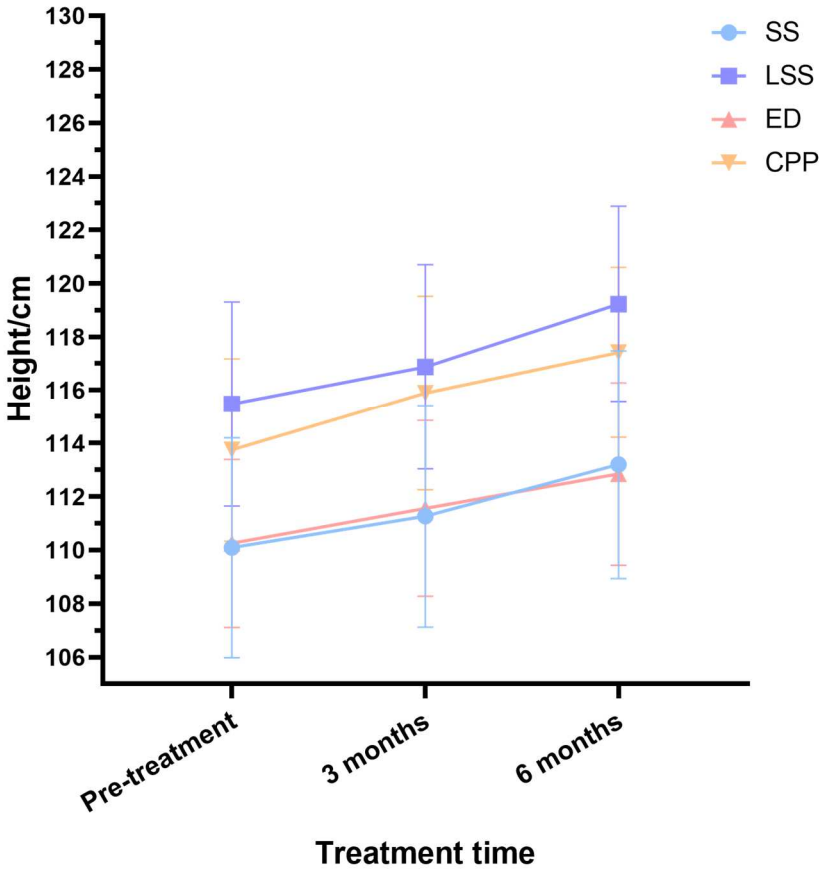


**Fig. 1**: Child growth curve

**Table 3**: Logistic regression analysis of factors influencing height growth outcomes in children

| Variable | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | *P* | OR | 95% CI | *P* |
| Sex | 0.443 | 0.212~0.924 | 0.030 | 0.375 | 0.156~0.900 | 0.028 |
| Age(months) | 0.874 | 0.823~0.927 | 0.001 | 0.858 | 0.791~0.929 | 0.001 |
| Height(cm) | 0.895 | 0.818~0.979 | 0.015 | 1.026 | 0.897~1.174 | 0.707 |
| Weight(kg) | 1.028 | 0.820~1.289 | 0.809 | | | |
| Bone age(years) | 0.807 | 0.490~1.330 | 0.401 | | | |

**Table 4**: ROC curve analysis

| Variable | AUC | 95%CI | Cut-off point | Sensitivity (%) | Specificity (%) |
|---|---|---|---|---|---|
| Sex | 0.599 | 0.497-0.701 | 0.50 | 81.36 | 68.85 |
| Age (months) | 0.774 | 0.686-0.861 | 75.50 | 54.24 | 65.57 |
| Predictive model | 0.818 | 0.735-0.900 | 0.45 | 86.44 | 72.13 |

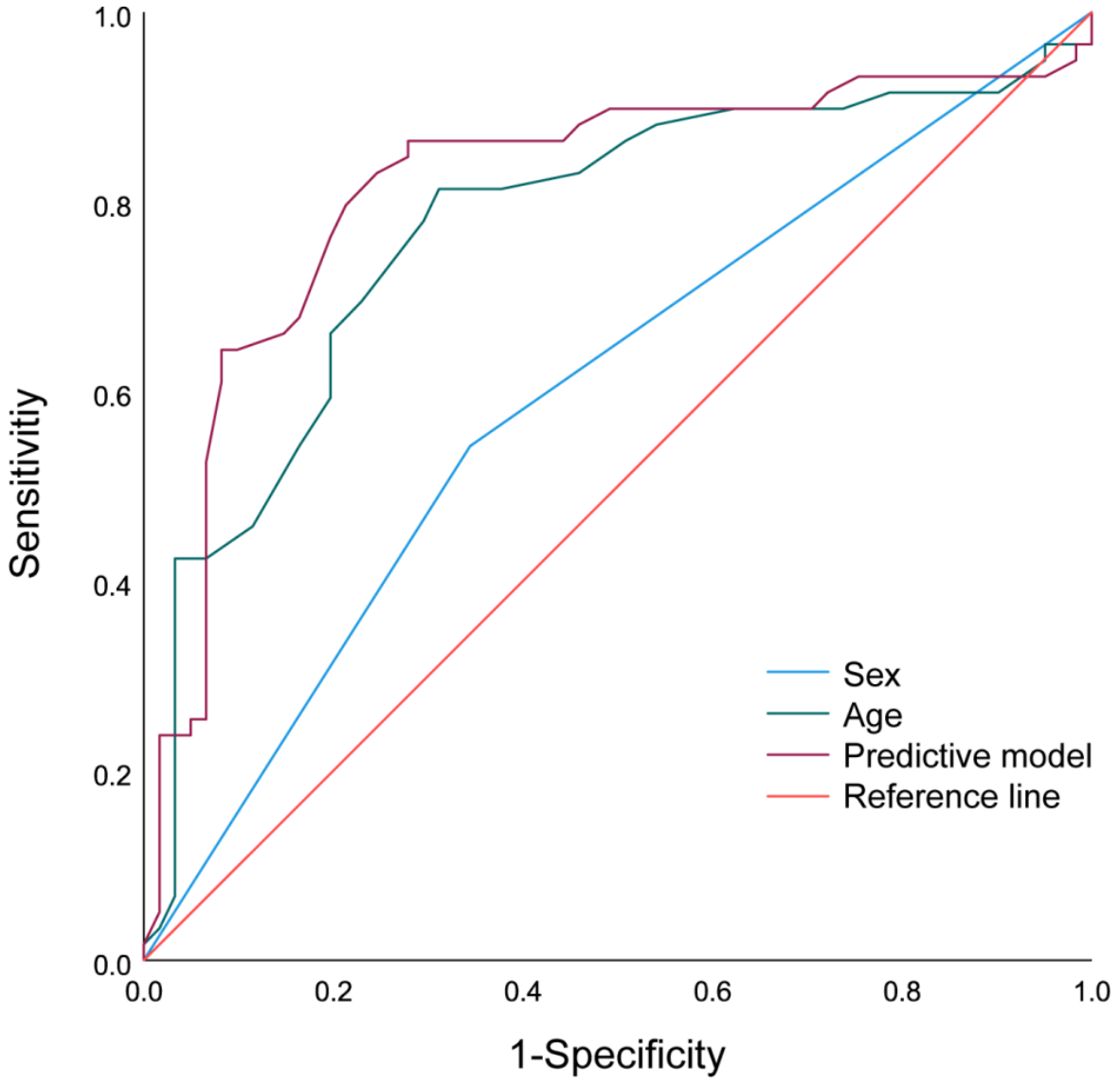


**Fig. 2**: ROC curve

The heights of the four groups of children increased to different degrees before treatment, 3 months and 6 months after treatment, with the LSS group having the largest growth rate and the ED group having the smallest growth rate, suggesting that lysine inositol vitamin $B_{12}$ oral solution combined with γ-aminobutyric acid has a better therapeutic effect on children with short stature and that Zhibai Dihuangwan has a better therapeutic effect on ED compared with CPP. The reason might be that the BMI of children in the ED group is higher than that of the other three groups (Zevin and Eugster, 2023). A single Zhi Bai Di Huang Wan is generally effective in its treatment. In this study, none of the children receiving treatment experienced adverse reactions, indicating that the treatment regimen used in this study is safe and feasible.

Logistic regression analysis revealed that sex and age before treatment were correlates of the outcome of height growth in children, which is consistent with the clinical emphasis on early detection and early intervention. The results of plotting ROC curves showed that the AUCs of gender and age were 0.599 (95% CI: 0.497~0.701) and 0.774 (95% CI: 0.686~0.861) respectively and the AUC of the prediction model constructed based on these two factors was 0.818 (95% CI: 0.735~0.900), which indicated that these two factors had a better effect in predicting This suggests that these two factors are effective in predicting children's height growth outcomes and can be applied to clinical practice to adjust interventions as early as possible and promptly, so that children can achieve better height outcomes.

In summary, screening children for growth deviations during school entrance physicals, followed by clinical analysis and early intervention, can restore normal growth and development in children. Simultaneously, it effectively slows the bone age growth rate in children with premature development, thereby improving height growth outcomes at 6 months and preventing growth disorders.

## CONCLUSION

Clinical analysis and early intervention for children with growth deviations during school entrance exams can normalize growth, slow bone age progression in premature development, improve height gain at 6 months and prevent or treat growth disorders. However, this study also has certain limitations. It is a single-center, retrospective analysis with a single source of samples and a relatively small sample size. Therefore, the regression model may exhibit some over fitting. Additionally, it did not adjust for clinically relevant confounding factors, which may introduce some bias in the results. Future multi-center, prospective studies could further explore the factors influencing growth deviation in children, providing additional data references for early detection and intervention in clinical practice.

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None

***Authors' contributions***
Guangqun Tang: Developed and planned the study, performed experiments and interpreted results. Edited and refined the manuscript with a focus on critical intellectual contributions; Juan Wan, Jianying Liu: Participated in collecting, assessing and interpreting the data. Made significant contributions to date interpretation and manuscript preparation; Maojia Zhu, Rui Liu: Provided substantial intellectual input during the drafting and revision of the manuscript.

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***Data availability statement***
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

***Ethical approval***
This experiment was approved by Ziyang Central Hospital Ethics Committee. [Ethical approval number: 2024 (203)]. The included children had the consent of their guardians and signed an informed consent form before treatment. This study was performed in adherence with the STROBE guidelines. See Supplementary file for the STROBE checklist.

***Conflict of interest***
The authors declare that they have no conflict of interest.

***Consent to participate***
We obtained signed informed consent forms from every participant.

***Supplementary data***
https://www.pjps.pk/uploads/2026/04/SUP1775907322.pdf

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