

The Relationship Between Thyroid Hormone Levels and Height in Children with Down Syndrome at Dr. M. Djamil General Hospital, Padang

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ABSTRACT

Background: Hypothyroidism and linear growth disorders are common health issues among children with Down syndrome. Thyroid hormones play a crucial role in the process of linear growth through both direct and indirect mechanisms.

Objective: To analyze the relationship between hypothyroidism and height in children with Down syndrome.

Methods: This study employed a *cross-sectional* design, utilizing medical records data on thyroid hormone levels (FT4 and TSH) and height measurements of children with Down syndrome at Dr. M. Djamil General Hospital in Padang from January 2023 to July 2025. Sampling was conducted using *total sampling*, and the data were analyzed using *Fisher's exact test* ($p < 0.05$).

Results: Of the 40 subjects, 20% were hypothyroid and 80% were euthyroid. Normal height was observed in 65% of subjects, and short stature in 35% of subjects. Hypothyroid subjects with short stature showed a 50% higher frequency compared to euthyroid subjects with short stature 31.2%; however, after analyzing the relationship between height and thyroid hormone levels, a *p-value* of 0.416 was obtained, indicating no association between hypothyroidism and height in children with Down syndrome.

Conclusion: This study found no association between thyroid hormone levels and height in children with Down syndrome. Linear growth disorders in children with Down syndrome are multifactorial and not solely due to hypothyroidism.

Keywords: Down syndrome, hypothyroidism, height, linear growth

INTRODUCTION

Down syndrome is the most common chromosomal disorder in children, with a global incidence of 1:800–1,000 live births and 1:600 live births in Indonesia, with a continuing upward trend.¹ The condition most often results from nondisjunction during meiosis, producing trisomy 21.^{2,3} Resulting overexpression of genes on chromosome 21 disrupts cellular development and function, predisposing affected individuals to a spectrum of medical complications, including endocrine disorders.³

Hypothyroidism is the most common endocrine complication in Down syndrome, with reported prevalence ranging from 4% to 24%.^{2,4} Children with Down syndrome are estimated to have a 30-fold greater risk of developing hypothyroidism compared to the general population.⁵ In addition to endocrine dysfunction, children with Down syndrome

experience significant linear growth impairment from the prenatal period. Mean birth length is 0.5–1 standard deviation (SD) below that of typically developing infants, and by age three, approximately 30% fall below the 3rd percentile for length.¹

Thyroid hormones play a crucial role in a child's height by directly stimulating tissue growth through growth factors or indirectly by regulating the production of growth hormone (GH).^{6–8} In hypothyroidism, a child's linear growth rate slows significantly due to thyroid hormone deficiency and a reduced effect on growth factors and GH synthesis.^{6,8}

Many studies have been conducted in developed countries, but research in Indonesia remains limited, particularly regarding the relationship between hypothyroidism and height in children with Down syndrome. This study aims to examine the relationship between hypothyroidism and height in children with Down syndrome at Dr. M. Djamil General Hospital in Padang, with the goal of improving early screening and preventing linear growth disorders, thereby optimizing linear growth in children with Down syndrome.

MATERIALS & METHODS

This was an observational analytical study with a *cross-sectional* design that utilized secondary data from the medical records of paediatric patients with Down syndrome who were treated at the Paediatric Endocrinology Clinic of Dr. M. Djamil General Hospital in Padang from January 2023 to July 2025. The study has been approved by the Research Ethics Committee of Dr. M. Djamil General Hospital in Padang under number DP.04.03/D.XVI.XI/439/2024.

The study population consisted of all children with Down syndrome receiving

treatment at the Pediatric Endocrinology Clinic of Dr. M. Djamil General Hospital in Padang. Sampling was conducted using total sampling. Inclusion criteria were children with Down syndrome who were newly diagnosed and had not yet received thyroid hormone therapy. Exclusion criteria included children with Down syndrome who had congenital heart disease, celiac disease, musculoskeletal abnormalities, and malnutrition, as these conditions can independently affect height.

The independent variable is thyroid hormone levels, categorized as hypothyroid and euthyroid.⁹ The dependent variable is height, categorized using a growth curve specific to Down syndrome.¹⁰ Short stature is defined as height below the 3rd percentile or -2 SD according to age and sex.

Statistical Analysis

Data analysis was performed using SPSS software. Univariate analysis is presented as frequencies and percentages for categorical variables. Bivariate analysis used Fisher's exact test to assess the relationship between thyroid hormone levels and height. A p-value of <0.05 was considered statistically significant.

RESULT

During the study period, 213 children with Down syndrome were treated at the Pediatric Endocrinology Clinic, consisting of 135 existing patients and 77 newly diagnosed patients. Of these 77 new patients, 21 children were excluded due to malnutrition and 16 due to congenital heart disease. Consequently, 40 subjects met the study criteria and were included in the analysis, comprising 8 hypothyroid children and 32 euthyroid children.

Table 1. Characteristics of study subjects

Category	n	%
Sex		
Male	22	55.0
Female	18	45.0
Age Group		
Infant (≤12 months)	25	62.5

Child (>12 months)	15	37.5
Thyroid Function		
Hypothyroid	8	20.0
Euthyroid	32	80.0
Height (DS-specific growth chart)		
Normal stature (>P3 or >-2SD)	26	65.0
Short stature (≤P3 or ≤-2SD)	14	35.0

Table 1 shows that the study subjects were predominantly male (55%), with the majority aged ≤12 months (62.5%). The prevalence of hypothyroidism was 20% (8 out of 40 subjects), and the majority of subjects (80%)

were euthyroid. A total of 65% of the subjects had normal stature based on the Down syndrome-specific growth curve, while 35% exhibited short stature.

Table 2. Relationship between thyroid hormone levels and height in children with Down syndrome

Thyroid Function	Normal Stature		Short Stature		p value
	n	%	n	%	
Hypothyroid	4	50.0	4	50.0	0.416*
Euthyroid	22	68.8	10	31.2	

**Fisher's exact test*

Table 2 shows that 50% of hypothyroid subjects with short stature were identified, a higher percentage than the 31.2% of euthyroid subjects with short stature. However, *Fisher's exact test* yielded a p-value of 0.416, indicating that there is no statistically significant association between thyroid hormone levels and height in children with Down syndrome.

DISCUSSION

This study involved 40 children with Down syndrome. The gender distribution showed a male-to-female ratio of 1.2:1, which is consistent with epidemiological data from several previous studies indicating a slightly higher prevalence among males.¹¹ The predominance of the infant age group (≤12 months) at 62.5% in this study aligns with epidemiological data on hypothyroidism in Down syndrome, where the prevalence of hypothyroidism is higher during the first year of life. Van Trotsenburg et al., in a prospective cohort study of 196 infants with Down syndrome, found that 25–40% of children with Down syndrome had elevated TSH levels between the ages of 2 weeks and 24 months.^{12,13} This is due to the maturation of the hypothalamic-pituitary-thyroid (HPT) axis in Down syndrome, which occurs more

slowly compared to typical children, even up to 2 years of age.¹⁴

The prevalence of hypothyroidism in this study was 20%, consistent with the range reported in various studies (4–54%). This wide variation is influenced by differences in diagnostic criteria, screening methods, age groups, and population characteristics.^{14–16} The majority of hypothyroidism cases in Down syndrome are subclinical, with Pierce et al. finding that approximately 60–70% of cases have TSH levels between 5–10 μIU/mL.¹⁷ As many as 65% of subjects had normal stature, which is related to the predominance of the infant age group in this study. Children with Down syndrome begin to experience significant linear growth impairment as early as 6 months of age, and this deficit increases progressively with age.^{10,18}

This study found no significant association between thyroid hormone levels and height in children with Down syndrome (p = 0.416). These results are consistent with several studies. Konishi et al., in a *cross-sectional* study of 301 children with Down syndrome, found that although there was an increase in TSH, there was no correlation between hypothyroidism and height.¹⁹ Cattoni et al., in a retrospective study of 583 patients with Down syndrome, also found that elevated

TSH was not associated with reduced height.²⁰ Rifal et al. from Dr. Soetomo General Hospital in Surabaya reported that the majority of children with Down syndrome who had hypothyroidism at diagnosis still had height within the normal range.²¹

The absence of an association in this study can be explained by several mechanisms. First, most subjects were ≤ 12 months old, at which point maternal thyroid hormone reserves still provide partial protection, so the impact of hypothyroidism on growth has not yet fully manifested. Fort et al. demonstrated that the impact of congenital hypothyroidism on height is most pronounced after 6–12 months of age.²² Second, this study used a cross-sectional design that measured thyroid status and height at a single time point, thus failing to capture the dynamics of changes in growth velocity. Third, the grouping did not account for the severity of hypothyroidism. A study by AlAaraj et al. showed that the effects on linear growth were primarily observed in the group with TSH > 12 mIU/L.²³

On the other hand, several longitudinal studies show different results. Van Trotsenburg et al., in a double-blind randomized clinical trial involving 196 neonates with Down syndrome, demonstrated that the group receiving thyroxine therapy had linear growth 1.1 cm greater than the placebo group at 24 months of age.¹³ Kowalczyk et al. found a significant correlation between annual growth velocity and TSH levels ($r = -0.34$; $p < 0.05$), with children who started therapy earlier showing better growth velocity.⁵ The discrepancy between the results of this study and those of the aforementioned studies is most likely due to differences in study design, subject age characteristics, and growth assessment methods (height at a single time point versus growth velocity). Overall, linear growth disorders in children with Down syndrome are multifactorial, involving the intrinsic genetic abnormality of trisomy 21, dysregulation of the GH-IGF-I axis, hypotonia, cardiovascular and

gastrointestinal comorbidities, and thyroid dysfunction.^{16,24}

CONCLUSION

There was no significant association between thyroid hormone levels (hypothyroidism) and height in children with Down syndrome at Dr. M. Djamil General Hospital, Padang ($p = 0.416$). Linear growth disorders in children with Down syndrome are multifactorial and are not solely caused by hypothyroidism. It is recommended that a longitudinal study be conducted with stratification of hypothyroidism severity and monitoring of linear growth velocity to obtain a more comprehensive picture of the relationship.

Declaration by Authors

Ethical Approval: Approved

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