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Metabolic Biomarkers Behind Stunting: The Role of Serum Leptin and Adiponectin in Early Childhood Growth

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Abstract

Background: Stunting is a nutritional problem that often affects children worldwide. Leptin and adiponectin are essential in modulating bone metabolism and, consequently, skeletal growth and height. This study aims to analyse leptin and adiponectin levels in stunted children and normal children and to determine the threshold values of leptin and adiponectin as early biomarkers of stunting.

Methods and Results: A case-control study was conducted in the working area of Kota Ruteng Primary Health Center Care, in Manggarai Regency, East Nusa Tenggara, Indonesia, from September to December 2024. The subjects were randomly selected from children aged 24-60 months. A total of 80 children, including 38 boys and 42 girls, were enrolled and divided into a stunting group (n=40) and a non-stunting group (n=40).

Multivariate analysis demonstrated that age 2–3 years, premature birth, low birth weight, and height were significant determinants of stunting, while leptin and adiponectin were independently associated with increased risk. ROC analysis showed that leptin had moderate discriminatory ability (AUC = 0.630; cut-off <2.18 ng/mL), whereas adiponectin yielded an AUC of 0.266 with a cut-off <29.5 ng/mL

Conclusion: Stunted children have higher leptin levels, and their height and adiponectin levels are lower than those of non-stunted children. Leptin and adiponectin levels can be used as early biomarkers of stunting.(**International Journal of Biomedicine. 2026;16(1):78-82.**)

Keywords: stunting • leptin • adiponectin • child growth • early childhood

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Abbreviations

HAZ, height-for-age z-score; **LAZ**, length-for-age z-score; **LBW**, low birth weight.

Introduction

Infancy and childhood are periods of rapid growth, requiring a high intake of energy-rich foods. Inadequate food intake, both in terms of quality and quantity, leads to stunting.[1] Stunting has a severe impact on children's future, such as cognitive impairment, chronic diseases, and even mortality.[2] The causes of stunting are multifactorial, including malnutrition, infection, and chronic inflammation.[3]

In addition to growth hormone, adipokines (leptin and adiponectin) also influence child growth and development, energy regulation, and glucose homeostasis.[4] Leptin and adiponectin play a role in regulating metabolic function and growth rate in children, such as weight and height.[5] Most previous studies have examined the relationship between leptin and adiponectin and obesity, such as cohort studies in Korea,[6] Brazil,[7] and Spain.[8] Conversely, there is still little research evidence examining leptin and adiponectin in stunted children, such as in the Philippines[9] and Bangladesh,[10] in different populations, such as fetuses, one-month-old, and 6-month-old children, and the results are still controversial, so further research is needed.

Although adipokines such as leptin and adiponectin are known to influence growth, there is still a significant gap in understanding their specific relationship with stunting in children in underdeveloped areas. Most studies have focused on urban populations or developed countries, making research in rural and marginalized communities a priority, as stunting is most prevalent in these areas. Addressing this gap could provide valuable insights into preventing and managing stunting in vulnerable populations. The relationship between serum leptin and adiponectin levels and stunting in children aged 24–60 months is still poorly understood. Given their role in regulating metabolism and growth, these adipokines may be valuable biomarkers for predicting stunting. This study aims to explore the relationships among leptin, adiponectin, and stunting in children aged 24–60 months, and to identify the threshold values of leptin and adiponectin that can serve as predictive biomarkers for stunting.

Methods

Study Population

This study was a case-control study in children aged 24-60 months in the working area of the Kota Ruteng Primary Health Center Care, Manggarai, Indonesia, spread across eleven sub-districts (Laci, Carep, Compang Carep, Bangka Nekang, Karot, Mbaumuku, Pitak, Pocomal, Satar Tacik, Tadong, and Watu) from September to December 2024. The subjects were randomly selected, with a sample size of 80 (40 stunted and 40 normal children). The inclusion criteria for the case group in this study were: parents willing to serve as research respondents and children with a height-for-age z-score < -2SD. The inclusion criteria for the control group were parents willing to serve as research respondents and children with height-for-age z-scores ≥ -2SD. This study excluded children with parental heights (father and mother) ≤145 cm, children with congenital abnormalities, and children who were ill at the time of the study.

Anthropometric Measurements

Respondents' body weight was measured using a SECA 334 standing baby scale or a SECA 813 standing scale (Hamburg, Germany) and recorded in grams. Respondents' height/length was measured using a SECA 416 infantometer or SECA 213 stadiometer (Hamburg, Germany) and recorded in centimeters. HAZ/LAZ of each respondent was calculated based on height/length, using the WHO child growth standards. Stunting was determined if the HAZ/LAZ z-score was less than -2SD.

Blood Chemistry Measurements

Blood samples were collected and processed by a professional laboratory. 5 mL of venous blood was collected from respondents into EDTA tubes, centrifuged for 10 minutes at 4000 rpm, and immediately quenched. Aliquots were stored at -20°C until analysis. All biomarkers were analyzed using commercially available enzyme-linked immunosorbent assay (ELISA) kits from Diagnostic Biochem Canada (DBC) according to the manufacturer's instructions. Leptin ELISA Kit (CAN-L-4260, DBC, Inc., London, Canada) and adiponectin ELISA kit (CAN-APN-5000, DBC, Inc., London, Canada). Results were read using an ELSA microplate reader series 17539 in the Institute of Tropical Diseases, Airlangga University, Surabaya. Concentrations were calculated against standards for each biomarker.

Predictive Analytics Approach

To enhance the analytical value, logistic regression results and ROC curves were used to identify predictive thresholds for implementation in digital health dashboards or decision-support systems. The model's performance indicators (AUC, sensitivity, and specificity) were assessed to evaluate their potential for stunting risk classification.

Statistical analysis

Statistical analysis was performed using IBM SPSS version 20.0. The normality of the data distribution was tested using the Shapiro-Wilk test for continuous data (P>0.05). Baseline characteristics were summarized as frequencies and percentages for categorical variables and mean ± standard deviation (SD) for continuous variables. Bivariate analysis used the Chi-Square test or Fisher's Exact Test for categorical variables, while continuous variables used the independent t-test for normally distributed data or the Mann–Whitney U test for non-normal distributions. Variables with P-value < 0.25 at the bivariate stage were then entered into a multivariate logistic regression model. The probability value of P-value <0.05 was considered statistically significant. Receiver operating characteristic (ROC) curves were used to determine leptin and adiponectin cut-off values in predicting stunting.

Results

There were 80 children in total, 40 of whom experienced stunting and 40 healthy children, consisting of 38 boys and 42 girls. The characteristics of the respondents are summarized in Table 1. There was a difference in age between groups (P=0.000). Stunted children significantly had a history of premature birth (P=0.018) and low birth weight (P=0.002). As expected, stunted children experienced a significant decrease in body weight (10.56±1.92 vs. 14.18±2.11 kg; P=0.000) and a significantly shorter height (83.69±6.74 vs. 95.47±6.20 cm; P=0.000) compared to the control group. Leptin levels (2.234±1.978 vs 1.278 ± 0.928 ng/mL; P=0.045) were higher in stunted children than in controls. In contrast, compared to controls, adiponectin levels (26.822±10.194 vs 37.939±15.624 ng/mL; P=0.000) were lower in stunted children.

Table 1.

Demographic characteristics and biochemical parameters.

Characteristics	Group		*P*-value
	Stunting (n=40)	Normal (n=40)	
Age 2-3 years >3 – 5 years	 18 (45.0%) 22 (55.0%)	 19 (47.5%) 21 (52.5%)	0.000[a]
Birth History Premature Normal	 6 (15.0%) 34 (85.0%)	 0 40 (100.0%)	0.018[b]
Birth Weight LBW Normal	 10 (25.0%) 30 (75.0%)	 0 40 (100.0%)	0.002[b]
Body Weight, kg	10.56 ± 1.92	14.18 ± 2.11	0.000[c]
Height, cm	83.69 ± 6.74	95.47 ± 6.20	0.000[c]
Leptin (ng/mL)	2.234 ± 1.978	1.278 ± 0.928	0.045[c]
Adiponectin (ng/mL)	26.822 ± 10.194	37.939 ± 15.624	0.000[c]

[a] *Chi-square test;* [b] *Fisher's Exact Test;* [c] *Mann-Whitney U.*

The multivariate model was developed using the Forward Wald method. The Hosmer–Lemeshow goodness-of-fit test indicated that the model fit the data well (P=0.879). Multivariate logistic regression (Table 2) showed that children aged 2–3 years had a higher risk of stunting (OR=0.302; *P*=0.006), while premature birth remained a significant predictor (OR=0.455; *P*=0.001). Low birth weight indicated a tendency toward increased risk (OR=0.786; *P*=0.019), and height demonstrated a protective effect (OR=0.683; *P*=0.045). Leptin (OR=2.728; *P*=0.025) and adiponectin (OR=4.925; *P*=0.001) were both significantly associated with elevated stunting risk. These findings indicate that birth characteristics, anthropometric status, and metabolic biomarkers collectively influence stunting in children.

Table 2.

Logistic regression risk factor with stunting.

Variables	*P*-value	OR	95% CI	
			Lower	Upper
Age >3 – 5 years (Reff) 2-3 years	0.006	0.302	0.027	1.044
Birth History Normal (Reff) Premature	0.001	0.455	0.334	1.506
Birth Weight Normal (Reff) LBW	0.019	0.786	0.404	1.214
Body Weight, kg	0.991	1.0302	1.044	1.062
Height, cm	0.045	0.683	0.470	2.065
Leptin (ng/mL)	0.025	2.728	1.072	4.784
Adiponectin (ng/mL)	0.001	4.925	0,882	6.970

OR = Odds Ratio; CI = Confidence Interval.

Based on the area under the curve (AUC), leptin can predict stunting with an AUC of 0.630 (95% CI=0.509-0.0752). The cut-off value of leptin in detecting stunting is <2.18 ng/mL (sensitivity 37.5% and specificity 85.0%, *P*=0.045) (Figure 1). Based on the area under the curve (AUC), adiponectin can be predicted at 0.266 (95% CI=0.158-0.375). The cut-off value of adiponectin in detecting stunting is <29.5 ng/mL (sensitivity 32.5% and specificity 67.5%, *P*=0.000) (Figure 2).

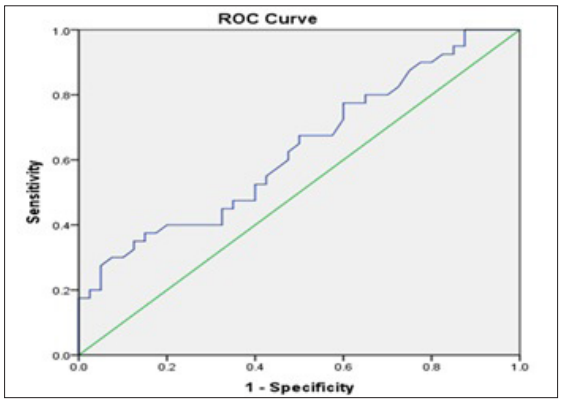

Figure 1. *The ROC curve for the diagnostic accuracy of leptin in detecting stunting.*

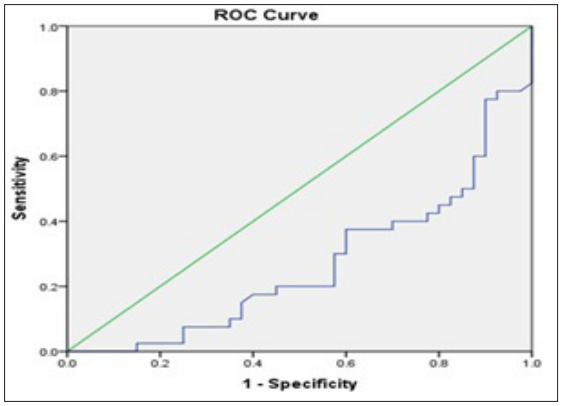

Figure 2. *The ROC curve for the diagnostic accuracy of adiponectin in detecting stunting.*

Discussion

Premature births and LBW children experience short stature in the first 5 years of life and experience a 10% decrease in height until adulthood. This is caused by abnormalities in growth hormones, such as insulin-like growth factor (IGF), and by the accumulation of network adipose tissue.[11] In addition, children with premature births will experience the phenomenon of catching up on growth in infancy, so that the accumulation of fat mass is faster than muscle mass in childhood.[12] Leptin circulation in the blood can regulate food intake and nutrient metabolism, impacting nutritional status. Leptin regulates glucogenesis and gluconeogenesis, maintains metabolic homeostasis, suppresses appetite, and increases energy expenditure.

Adequate, stable energy balance generally maintains healthy leptin levels. The average leptin levels of stunted children aged 6-8 years were higher than those of non-stunted children.[13,14] Our study supports this data, as leptin levels were higher in stunted children.

The cut-off value of leptin in stunted children was <2.18 ng/mL. This finding supports the evidence that low leptin levels are closely associated with impaired linear growth. The role of leptin in growth regulation is more complex than its function as an indicator of fat mass; it also acts as an energy-metabolism regulator and influences bone development, including the epiphyseal growth plate, which is essential for height gain.[15] A low cut-off value may reflect deficits in adipose tissue and energy reserves, conditions that can disrupt hormonal signaling required for linear growth and reduce the potential for catch-up growth in stunted children.[16] Therefore, future interventions aimed at improving leptin levels may contribute to more effective stunting prevention and management.

Adiponectin also plays a critical role in metabolic regulation, energy homeostasis, and the link between fat metabolism and bone health. Disruptions in fat oxidation are associated with an increased risk of fat accumulation, thereby increasing vulnerability to a high-fat diet among stunted adolescents.[17] Low-fat and energy intake during childhood can reduce growth factors, such as IGF hormones, and loss of fat mass can result in low adiponectin levels.[18]

The establishment of an adiponectin cut-off value of <29.5 ng/mL in the present study suggests that children aged 24–60 months with reduced adiponectin levels may be at increased risk of stunting. This relationship is biologically plausible, as adiponectin plays a central role in regulating energy homeostasis, insulin sensitivity, and lipid metabolism, all of which are integral to linear growth and bone tissue development. Lower circulating adiponectin may impair anabolic pathways involved in chondrocyte maturation, osteoblast activity, and overall skeletal growth, thereby contributing to growth faltering.[19,20] These findings support the potential use of adiponectin as an adjunctive biomarker for early identification of stunting risk. Incorporating adiponectin measurement into routine screening could complement conventional anthropometric assessment, particularly in regions with high stunting prevalence or in settings where standardized equipment for height and weight measurement is limited. This biomarker-based approach may enhance the detection of growth disturbances at earlier stages, allowing for more timely and targeted interventions.

The strengths of this study include its focus on a specific population of stunted children and its contribution of significant regional data to the worldwide literature on stunting. The strategic use of leptin and adiponectin as biomarkers is a reasonable approach to understanding the mechanisms underlying child stunting. Using ROC curves to find optimal cut-off values adds complexity, but, more importantly, ROC analysis helps identify the threshold that maximizes overall sensitivity and specificity. Meanwhile, this study also has several limitations. First, data collection in this study was conducted on a single occasion without a follow-up period, which can introduce bias in the observations because it cannot account for seasonal variations or changes in children's lifestyles over time. Observations conducted over a longer period can yield more representative results. Second, this study is a single-center study with a small sample size. It was also performed at a community health center. Finally, this study did not measure body fat mass in stunted children, so it cannot identify the causes and risk factors that affect leptin and adiponectin levels.

Conclusion

Leptin levels are significantly higher in stunted children, while adiponectin levels are considerably lower than in non-stunted children. Low adiponectin levels are more likely to stymie than high leptin levels. The findings demonstrate the potential to integrate leptin and adiponectin biomarker analysis into predictive-analytic frameworks for early stunting detection.

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Ethical Statement

This study received approval from the Health Research Ethics Committee of the Faculty of Medicine, Airlangga University, Surabaya, with No. Ref 203/EC/KEPK/FKUA/2024.

Competing Interests

The authors declare that they have no conflicts of interest.

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