Obesity indices as predictive factors for paediatric hypertension: A population-based study in Bali, Indonesia

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Abstract
Introduction: Growing recognition of coexisting obesity and hypertension epidemics in children and adolescents could prevent it from being an insurmountable burden following its trajectory into adulthood.

Objectives: To determine the predictive ability of obesity indices for paediatric hypertension.

Method: In this retrospective cross-sectional study, a multi-stage sampling method was employed to recruit proportional population-based samples across Bali, Indonesia. A total of 436 students aged 6-17 years who had no prior history of hypertension / prolonged use of drugs affecting blood pressure were included in the analysis. Nutritional status assessment warranted a two-step assessment using weight-for-height and body mass index (BMI)-for-age CDC 2000 charts for each gender. Bivariate and multivariate analyses were done to find associated factors. Receiver operating characteristic (ROC) curve analysis was done to assess the predictive ability of waist circumference.

Results: In this study there were 229 children with hypertension. The prevalence of overweight (14.7%) and obesity (40.8%) in hypertensive students was greater than the overall overweight (13.1%) and obesity (32.8%) prevalence. Age, nutritional status and waist circumference were significantly increased in the group with hypertension on bivariate analysis. After multivariate analysis, increasing age (prevalence ratio [PR] 1.106; 95%CI 1.015-1.205) and obesity (PR 2.174; 95%CI 1.371-3.445) were significantly associated with hypertension but not waist circumference. Optimal cut-off points for male (65.5 cm) and female (62.5 cm) waist circumference were obtained.

Conclusions: Obesity status and waist circumference served as promising predictors of hypertension.

(Key words: Paediatric hypertension, Abdominal obesity, Waist circumference, Indonesia)

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Introduction

Over the past two decades, there was a consistent increase in the prevalence of hypertension in children and adolescents with similar age-specific rates. The rise was nearly exponential across each decade of study period, reaching a prevalence of 6% by 2014 with pooled prevalence of 4%[1,2]. Combined prevalence of elevated blood pressure and hypertension summed up to a total exceeding 10% cases which may potentially follow this adverse trajectory into adulthood[3,4]. Additionally, a recent study indicated the long-term impact of elevated blood pressure on cardiovascular disease intermediate markers in adulthood[5].

The concurrent obesity epidemic yields a remarkable contribution to the burden of non-communicable disease in the paediatric population, given its mechanistic relationship with hypertension as a metabolic syndrome cluster[6]. The prevalence of hypertension in obese children and adolescents was markedly higher (15.3%) than the non-obese counterpart[1]. Additionally, proportional increment in the risk of developing hypertension was observed with increasing nutritional status[7]. The seemingly bidirectional association of obesity and hypertension was appraised by a meta-analysis which reported the association between childhood obesity and multiple obesity-related morbidities in adulthood[8].

Although the relationship between obesity and hypertension in childhood and adolescence was well-established[9,10], the data on discriminatory power among obesity indices was lacking[11] and heterogeneous[8,12] in available evidence. Furthermore, the difference in guidelines being adopted to define each disease entity in certain areas, specifically in Indonesia, requires standardized study methods specifically tailored to each population. Addressing the aforementioned research gap is of utmost importance considering its prospective implication on hypertension and obesity guideline development and implementation[13], and lifetime risks adjustment[14,15] in which the contribution from the paediatric population was not commonly accounted for.

Objectives

The primary objectives were to investigate the association between obesity indices with hypertension and identify the optimal cut-off point for waist circumference to predict hypertension.

Method

This study was a provincial, population-based, retrospective, cross-sectional study held in Bali, Indonesia. We used the database from previous study[16] which aimed to investigate blood pressure profile in children and adolescents with distinct methods in terms of study design, eligibility criteria, and outcomes. The study population was considered otherwise healthy because we utilized a sampling frame consisting of general student population.

Ethical issues: Our study fully adhered to the Declaration of Helsinki and its subsequent amendments and was approved by the Ethical Committee of the Medical Faculty of Udayana University/Sanglah General Hospital (No. 1634/UN14.2.2/PD/KEP/2018) Preliminary consent from local school administrators and parents or legal guardians, as well as assent from students were obtained before study commencement.

We employed a multi-stage sampling technique to select regencies, districts, schools, and ultimately students who were eligible for recruitment (Figure 1).

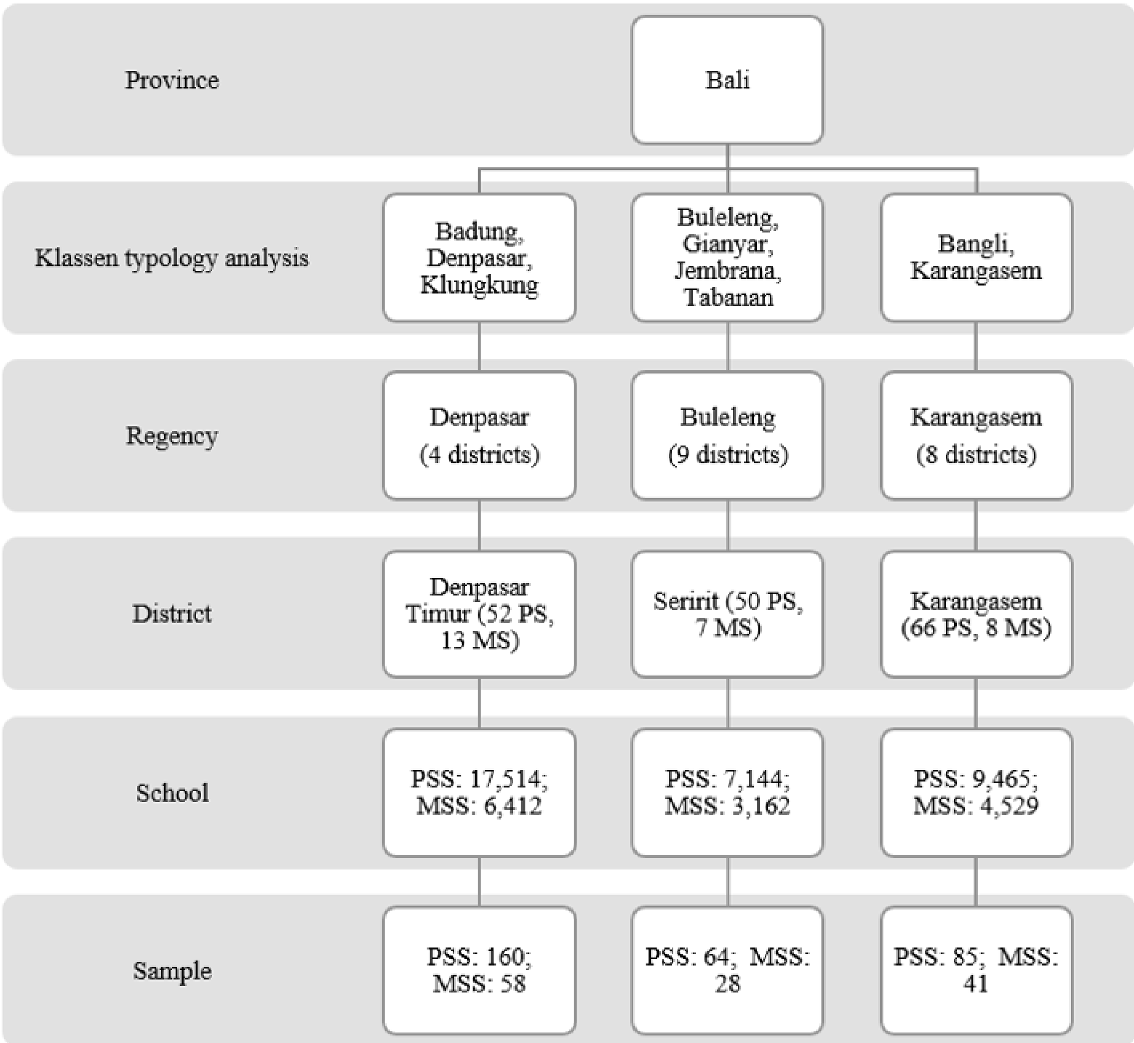


Figure 1: *Schematic flow of multi-stage sampling method*

MS: middle school, MSS: middle school student, PS: primary school, PSS: primary school student

Initially, nine regencies in Bali were classified into three groups of economic growth structure and pattern according to Klassen typology analysis, namely fast-developing and fast-growing area (Badung, Denpasar, Klungkung), fast-developing (Buleleng, Gianyar, Jembrana, Tabanan), and relatively underdeveloped (Bangli, Karangasem)[17]. Simple random sampling was done to choose the regency, district, schools, and students using random number generator and select case feature in IBM SPSS® statistical analysis software. A pre-determined sample size was allocated to proportionally match the ratio of total students in selected districts and subsequently, the ratio of primary and middle school students in each regency based on Ministry of Education and Culture reference data[18]. Estimated sample size was calculated using StatCalc feature in Epi Info™ version 7.2 with 80% statistical power and outcome percentage derived from the previous meta-analysis[1].

The 2019 baseline data were collected from 1,257 students of 18 schools who fulfilled the determined eligibility criteria. We included children aged 6 to 18 years at the time of enrolment, whose parents or legal guardians agreed to provide written informed consent. Subjects who failed to complete the study procedure or had a previous history of prolonged (>2 weeks) use of corticosteroids or other drugs that affect blood pressure were excluded. Data regarding clinical assessment of students and their parents or legal guardians were obtained through a structured interview using questionnaire and direct measurement of key variables. The current analysis focused on sociodemographic characteristics and key variables (i.e. blood pressure, anthropometric measures) of 436 students.

Nutritional and hypertension status assessment involved the measurement of body weight, body height, waist circumference and blood pressure by trained health personnel (doctors) using standardized procedures and calibrated equipment. Weight was measured using flat digital scale (precision 0.1 kg), height was measured using portable stadiometer (precision 0.1 cm), waist circumference was measured using a tape (precision 0.1 cm), and blood pressure was measured using aneroid sphygmomanometer. Body mass index was calculated by dividing weight in kilogrammes with the square of height in metres.

Nutritional status was categorized in compliance with the Indonesian Paediatric Society recommendation on paediatric nutrition care[19]. Generally, all students were subjected to Waterlow criteria for the percentage of median weight-for-height plotted using Centers for Disease Control and Prevention (CDC) 2000 growth charts. Overweight or obesity in students with the percentage of median above 110% would be determined by CDC 2000 body mass index (BMI)-for-age chart (Table 1).

Table 1: ***Nutritional status assessment of over 5 year old children***[19]

Nutritional status	Weight for height (% median)	Body mass index for age
Obese	>120	>95th percentile
Overweight	>110	85th to 95th percentile
Normal	>90	
Underweight	70-90	
Wasted	<70	

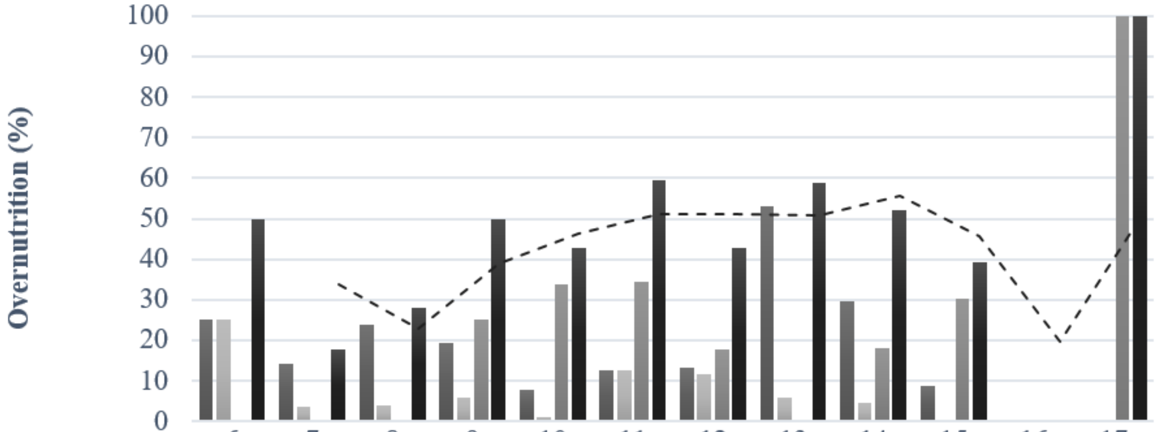
Overweight and obese statuses were collectively termed over-nutrition whilst underweight and wasted were collectively referred to as under-nutrition. Obesity indices consisted of nutritional status to determine obesity in general and waist circumference to determine abdominal obesity. Meanwhile, hypertension status was assessed by categorizing the average of three blood pressure measurementss using clinical practice guideline developed by the American Academy of Pediatrics[20].

Continuous variables were presented in appropriate central tendency and dispersion (i.e., median [interquartile range (IQR)] or mean [± standard deviation (SD)]) depending on the result of Kolmogorov-Smirnov normality test, whereas categorical variables were presented as absolute and relative frequency. Mann-Whitney and Chi-square tests were done preceding multivariable logistic regression analysis incorporating correlated variables with p values less than 0.1. Predictive ability was assessed using receiver operating characteristic (ROC) curve analysis and interpreted accordingly with respect to the indices generated. All statistical analyses were performed using IBM SPSS® version 25 with two-sided p value of <0.05 being considered as statistically significant.

Results

Three regencies and districts were chosen from the first and second cluster sampling. From the total number of students in each district, randomly sampled 1,257 students from 18 schools were included in the initial investigation and 436 of them were included in current analysis (Figure 1). The proportion of students was allotted considering the ratio of students in each district for each level (i.e., primary or middle school).

The overall prevalence of over-nutrition was highest in Denpasar (54.1%), followed by Karangasem (47.2%) and Buleleng (30.1%) regency. A relatively unimodal trend in total prevalence was observed over increasing age with the peak at 11 years, except for higher figures at both extremes of age, which may not represent actual values due to inadequate subjects. Although the peak for Buleleng (12.5%) and Karangasem (34.4%) regencies coincided with that of the total, the peak prevalence for Denpasar (52.9%) was situated at 13 years old (Figure 2).



	6	7	8	9	10	11	12	13	14	15	16	17
Denpasar	25	14.29	24	19.23	7.87	12.5	13.24	52.94	29.54	8.7	0	0
Buleleng	25	3.57	4	5.77	1.12	12.5	11.76	5.88	4.55	0	0	0
Karangasem	0	0	0	25	33.71	34.38	17.65	0	18.18	30.43	0	100
Total	50	17.86	28	50	42.7	59.38	42.65	58.82	52.27	39.13	0	100

Age (years)

Figure 2: ***Prevalence of over-nutrition based on age and regency***

The prevalence of hypertensive individuals exceeded normotensive individuals in obese and overweight students and not in the other nutritional statuses. It was notable that the ratio between hypertensive and normotensive students increased with increasing nutritional status in students with over-nutrition (Figure 3).

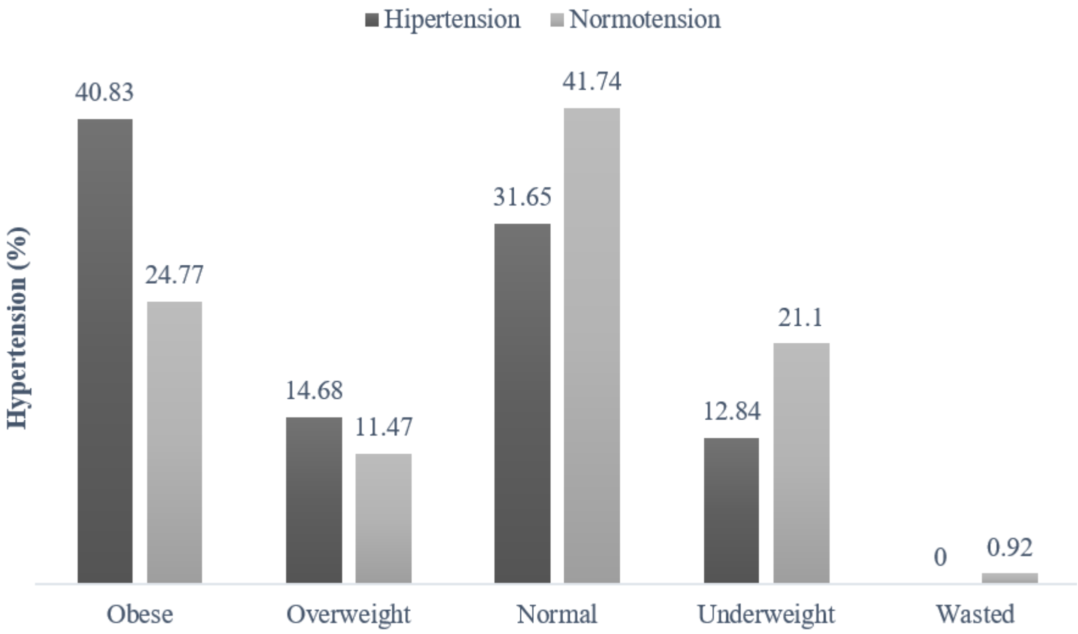


Figure 3: ***Prevalence of hypertension based on nutritional status***

The students had a median age of 11 years (IQR 9-12) and median waist circumference of 65 cm (IQR 59-75). The majority of students were indigenous males with normal nutritional status. Bivariate analysis in Table 2 showed that apart from nutritional status and waist circumference, age was statistically significant and should be included in multivariate analysis.

Table 2: ***Demographics of study subjects***

Variables	Result	p
Gender		0.387
Male - n (%)	237 (54.4)	
Female - n (%)	199 (45.6)	
Age – Median (IQR)*	11 (9-12)	**0.014**
Origin		0.630
Bali - n (%)	418 (95.9)	
Outside Bali - n (%)	18 (04.1)	
Nutritional status		**0.001**
Obese - n (%)	143 (32.8)	
Overweight - n (%)	57 (13.1)	
Normal - n (%)	160 (36.7)	
Underweight - n (%)	74 (17.0)	
Wasted - n (%)	02 (0.5)	
Waist circumference – Median (IQR)*	65 (59-75)	**<0.001**

**Based on Mann-Whitney test; bold indicates p<0.05; IQR: inter-quartile range;*

Binomial logistic regression analysis showed obesity status (PR 2.174; 95%CI 1.371-3.445) and age (PR 1.106; 95%CI 1.015-1.205) as statistically significant factors for hypertension (Table 3). The prevalence ratio for the wasted nutritional status was failed to obtain due to the lack of wasted hypertensive student.

Table 3: ***Multivariable analysis of factors affecting hypertension status***

Variables	Prevalence ratio (PR)	95% confidence interval	p
Age	1.106	1.015-1.205	**0.021**
Nutritional status			
Obese	2.174	1.371-3.445	**0.001**
Overweight	1.688	0.918-3.106	0.092
Normal	Reference	Reference	Reference
Underweight	0.803	0.457-1.412	0.446
Wasted	-	-	0.999
Waist circumference	1.027	0,995-1,061	0.101

bold indicates p<0.05

Waist circumference cut-off value of 65.5 cm provided the most balanced sensitivity (60.6%) and specificity (61.5%) from ROC curve analysis (area under the curve [AUC]=0.640, 95%CI 0.588-0.691, p<0.001). The farthest point from the reference line for male (AUC=0.660, 95%CI 0.591-0.729, p<0.001) with sensitivity (69.9%) and specificity (57%) corresponded to a cut-off value overlapping with that of the overall curve. The ideal cut-off value for female (62.5 cm) with similar sensitivity (62.1%) and specificity (55.8%) in the curve (AUC=0.612, 95%CI 0.533-0.690, p=0.007) was lower than that of overall and male (Figure 4).

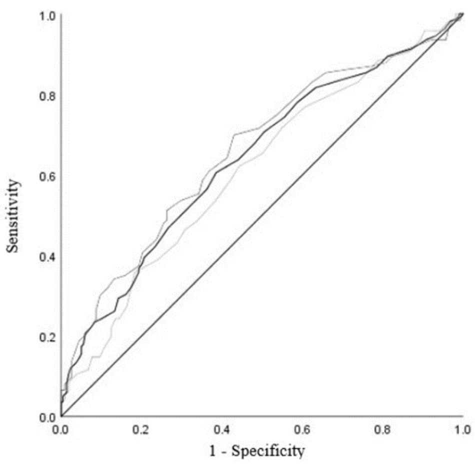


Figure 4. ***ROC curves for the prediction of hypertension by waist circumference***
(Overall, male, and female curves in decreasing opacity, respectively)

Discussion

The rising trend of obesity worldwide is worthy of serious public health attention, chiefly in the younger population. This especially holds true in the provincial scale of Bali because its prevalence of overweight and obesity in children and adolescents (21.9%) by 2018[21] was greater than 2016 global estimates by World Health Organization (18%)[22]. The presence of obesity results in the propensity for numerous comorbidities clustered in metabolic syndrome, including hypertension. Moreover, obesity per se was implicated in the risk of kidney injury, and even at a greater extent when combined with hypertension[23]. Decision to intervene at such a young age requires rigorous research to generate the expected well-grounded evidence.

Earnest efforts to address the long-standing issue of undernutrition in Indonesia had been pursued relentlessly since a dedicated national movement was implemented[24]. Results from the current study showed that the prevalence of over-nutrition was higher than undernutrition, and that its association with hypertension was significant. Despite facing the double burden of malnutrition (i.e. undernutrition and over-nutrition), it was clear from the epidemiological point of view that the scale of over-nutrition related problem outgrew the undernutrition counterpart and the covert tendency of health problems inflicted by over-nutrition should not render it less urgent.

A clear-cut trend of obesity prevalence with increasing age was not found in this study. Conversely, the increasing prevalence with advancing age was observed in an earlier national estimate in the United States (US)[25]. However, the US estimate grouped the subjects into age groups with wide ranges, and it involved younger preschool children (2-5 years). Establishment of prevalence by age would allow for direct comparison with similar obesity-related comorbidities, thus pinpointing the age group at risk to prioritise.

From a previous study in the same site, the prevalence of hypertension in the age group ≤12 years was 47.3% and in the age group >12 years was 62.6%[16]. There appeared to be an arguably exposure-response relationship between hypertension and nutritional status which was amplified with increasing BMI. The supporting rationale was because hypertension was more prevalent exclusively in over-nutrition and the prevalence increased more than twice (i.e. non-linear increase) from overweight to obese. An excellent study with more extensive range of over-nutrition status by Parker *et al*[26] confirmed this relationship precisely with the finding that the risk of developing hypertension consistently increased in obese and severely obese individuals. A more profound quantification was reported in a study by Chorin *et al*[27] which found a concurrent increase in systolic (10 mmHg) and diastolic (3-4 mmHg) blood pressure for every unit increase in BMI of healthy teenagers.

In contrast to the covert characteristic of hypertension, the proposition for the use of waist circumference to screen for central obesity and ultimately hypertension offers the benefit of being an overt characteristic and feasibility in measurement and interpretation. The particular pitfall for this proposition was the absence of standardized cut-off or curves. While the waist circumference cut-off value to predict hypertension remained debatable, the most recent international study[28] proposed to predict adult central obesity by childhood or adolescence waist circumference which corresponded to ≥90th percentile. Pooled age (assuming the median age in this study) and gender-specific cut-off values derived from studies[28-30] associating waist circumference with hypertension in children or adolescents exhibited wide ranges of measure for male (67.1-85.3 cm) and female (68.2-76.1 cm). The optimal cut-off values in this study were below these ranges even with comparable ROC analysis indices, suggesting that the heterogeneity was possibly due to ethnicity.

To the best of our knowledge, by searching for recent studies and comparing with existing systematic review[31], this was the first study in Indonesia that employed two-steps of over-nutrition status determination recommended by the Indonesian Paediatric Society. This study also provided local data to contribute for future waist circumference cut-off value determination.

Our study has several limitations in our methods. Firstly, we did not consider multiple categories of the nominal variable when calculating the minimum sample requirement. Secondly, the current study design did not allow for a chronological analysis of causality.

Conclusions

Nutritional status and waist circumference held the potential to predict hypertension status in children and adolescents.

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