

The Association of Pediatric Obesity with Nocturnal Non-Dipping on  
24-Hour Ambulatory Blood Pressure Monitoring

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**Abstract**

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Blood Pressure Monitoring

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**Background:** Obesity has been linked with abnormal nocturnal dipping of blood pressure in adults, which in turn is associated with poor cardiovascular outcomes. There are few data regarding blood pressure dipping status in the obese pediatric population.

**Objective:** The goal of this study was to further describe the relationship between obesity and non-dipping status on ambulatory blood pressure monitor (ABPM) in children.

**Design/Methods:** We conducted a cross-sectional study using a database of patients ages 5-21 years who had undergone 24-hour ABPM at Seattle Children's Hospital from January, 2008 through May, 2014. Subjects were grouped by BMI into non-obese (BMI 15th-85th percentile) and obese (BMI >95th percentile) groups.

**Results:** Compared to non-obese subjects (n=161), those who were obese (n=247) had 2.15 times the prevalence of non-dipping, adjusted for race (95% confidence interval = 1.25-3.42). Increasing severity of obesity was not further associated with nocturnal non-dipping.

**Conclusions:** These results suggest that in children, just as in adults, obesity is related to a relatively decreased dipping in nocturnal blood pressure.

## Introduction

The prevalence of hypertension in American children is increasing[1, 2], due in large part to the increasing prevalence of childhood obesity.[3] The use of 24-hour ambulatory blood pressure monitoring (ABPM) has been helpful in diagnosing hypertension in children, as it allows physicians to diagnose white coat hypertension, masked hypertension, and evaluate nocturnal dipping status,[4] which is the percent change from awake to sleeping blood pressures. In adults obesity has been linked with abnormal dipping status on 24-hour ABPM.[5, 6] There are few data regarding abnormal dipping status in the pediatric population. The studies that have been performed have been with smaller numbers of subjects [7-9] or in patient populations with significant medical conditions such as diabetes.[10] The goal of this study was to further describe the relationship between obesity and non-dipping status on ABPM, which may eventually lead to better treatments and prevention methods.

## Methods

### **Data Source**

We conducted a cross-sectional study using a database of patients ages 5-21 years who had undergone a first-time 24-hour ABPM at Seattle Children's Hospital from January, 2008, through May, 2014. Retrospective data collection was approved by the Institutional Review Board at Seattle Children's Hospital.

### **Subject Selection/Methods**

Subjects were selected by querying the electronic medical record to identify all patients who had undergone 24-hour ABPM during the study period. Demographic information collected included subject age, race, gender, past medical history, and current medications at time of ABPM study. Exclusion criteria included past medical history that could affect blood pressure (chronic kidney disease, thyroid disease, congenital heart disease, history of prematurity <34 weeks gestation, etc.), and medications that could affect blood pressures (anti-hypertensives, glucocorticoids, immunosuppressants, stimulants).

All ABPMs were performed using the Spacelabs 90217 ambulatory blood pressure monitor. The monitor was placed by nursing staff in our office at time of clinic visit. Readings were taken every 20 minutes while awake, and every 30 minutes while asleep. The adequacy of the ABPM study was determined by the interpreting physician at the time of ABPM evaluation.

Subjects were grouped into categories based on BMI: lean (15<sup>th</sup>-85<sup>th</sup> BMI percentile), overweight (>85<sup>th</sup> to 95<sup>th</sup> percentile), and obese (>95<sup>th</sup> percentile). [11] We sought to compare the prevalence of nocturnal non-dipping in the lean group vs. the obese group, defined as a decrease in both systolic and diastolic mean nocturnal blood pressure of less than 10% from mean systolic and diastolic awake blood pressure.

We also evaluated the relationship between severity of obesity and prevalence of non-dipping status, using categories described in previous literature [12] that were based on BMI z-scores: obesity category I (BMI z-score 1.6449 to <2), obesity category II (BMI z-score 2 to <2.5), obesity category 3 (BMI z-score  $\geq$ 2.5). Finally, we evaluated the relationship between obesity and the prevalence of isolated nocturnal hypertension or prehypertension.

Hypertension was defined as a mean ambulatory blood pressure greater than the 95<sup>th</sup> percentile for age, sex and height.[13] Prehypertension was defined as mean ambulatory blood pressure less than the 95<sup>th</sup> percentile for age, sex and height, but with a blood pressure load between 25 and 50 percent. Blood pressure load is the percent of individual blood pressure measurements that are greater than the 95<sup>th</sup> percentile for age, sex, and height. Nocturnal prehypertension and hypertension were defined as a patient who met criteria for nocturnal prehypertension or nocturnal hypertension without awake hypertension or awake prehypertension.

### **Statistical Analysis**

Continuous variables were expressed as the mean  $\pm$  standard deviation. Differences in means between continuous outcomes were determined using two-sample t-tests. Our primary analysis of the association of obesity with nocturnal non-dipping was estimated by stratified analysis using prevalence ratio estimates and test-based 95% confidence intervals. Only factors that altered estimates substantially (10% or more) were considered to be confounders and were adjusted for in our analysis. Secondary analyses were also evaluated by stratified analysis using prevalence ratio estimates. STATA (Stata Corp., College Station, TX) version 13.1 was used for statistical analysis.

### **Results**

#### **General Characteristics of Subjects**

1620 total ABPMs were completed during the study period. 248 of these were repeat ABPMs on an individual subject; thus 1372 “first-time” ABPMs were identified. Of these, 98 were of inadequate quality for interpretation. Following application of exclusion criteria, there were 408 subjects included in the primary analysis. Of these 408 subjects, 161 were in the lean group and 247 were in the obese group (Figure 1). Distributions were generally similar for age and gender between the two groups (Table 1). There were differences noted in race, with 49% of subjects in the lean group being Caucasian, compared to 36% in the obese group.

#### **Prevalence of non-dipping**

Mean awake and asleep systolic and diastolic blood pressures are presented in Table 2. Both systolic and diastolic nocturnal dipping were significantly blunted in the obese group compared to the lean group ( $p < 0.0001$ ).

Of the 161 subjects in the lean group, 22 were classified as non-dippers (13.6%) (Table 3). Of the 247 subjects in the obese group, 85 were classified as non-dippers (34.4%). The crude prevalence ratio of non-dipping was 2.51 (95% CI 1.65-3.85) in obese subjects compared to lean subjects. The prevalence ratio adjusted for race was 2.15 (95% CI 1.25-3.42). The prevalence ratio was not affected by adjustment for gender or age of the subjects.

Obesity was found to be significantly associated with isolated nocturnal hypertension. 44 of 247 subjects in the obese group had isolated nocturnal hypertension or prehypertension, compared to 12 of 161 subjects in the lean group. This resulted in a crude prevalence ratio of 2.37 (95% CI 1.51-3.73). This was not affected by adjusting for age, race, or gender.

Increasing severity of obesity was not significantly associated with nocturnal non-dipping status (Table 4). Compared to the reference group of obese category I, subjects in

obese category II had a non-dipping prevalence ratio of 1.28 (95% CI 0.66-2.43) and subjects in obese category III had a prevalence ratio of 1.16 (95% CI 0.61-2.19).

### Discussion

In this study non-dipping status on ABPM was significantly associated with obesity, and obesity was also significantly associated with isolated nocturnal hypertension. We did not find a significant association between non-dipping status and severity of obesity.

In adults, non-dipping status has been shown to predict poor cardiovascular outcomes [14-17], renal outcomes[18, 19], and diabetic outcomes[20]. In adolescent diabetics, nocturnal hypertension and non-dipping have been associated with increased nephropathy[21, 22], increased LVH[23], and increased carotid intimal-media thickness[24]. Non-dipping has also been associated with worsening GFR in children with CKD[25]. However, in the obese but otherwise healthy pediatric population, the data relating nocturnal dipping of blood pressure to health outcomes are scarce.

There are few available data on the prevalence of dipping status in the pediatric population. Previous studies that have looked at the association between obesity and nocturnal dipping have been much smaller. Framme et al. found a similar association as ours [7], with a total of 80 subjects (25 in the lean group and 55 in the obese group). Framme et al., however, found that that obesity only had a significant effect on nocturnal dipping in females, whereas we saw a strong association between obesity and nocturnal dipping in both males (prevalence ratio=2.08, 95% CI=1.16-3.74) and females (prevalence ratio=2.37, 95% CI=1.10-5.11). Their findings may be due to a lack of power in the male group, as their study consisted of 51 females (16 lean and 35 obese) and only 29 males (9 lean and 20 obese). Unfortunately, the authors did not include the direction of the association in males in their article. A recent 2014 study by Westerstahl et al. looked at the relationship between nocturnal dipping and obesity in 76 obese subjects [26]. Comparing to previously established normative ABPM data in children[27], Westerstahl found the prevalence of non-dipping in obese children to be about twice that in children overall. Our data showed a similar prevalence of non-dipping in the obese group compared to this study: 34% in our obese group compared to 40% in the Westerstahl study.

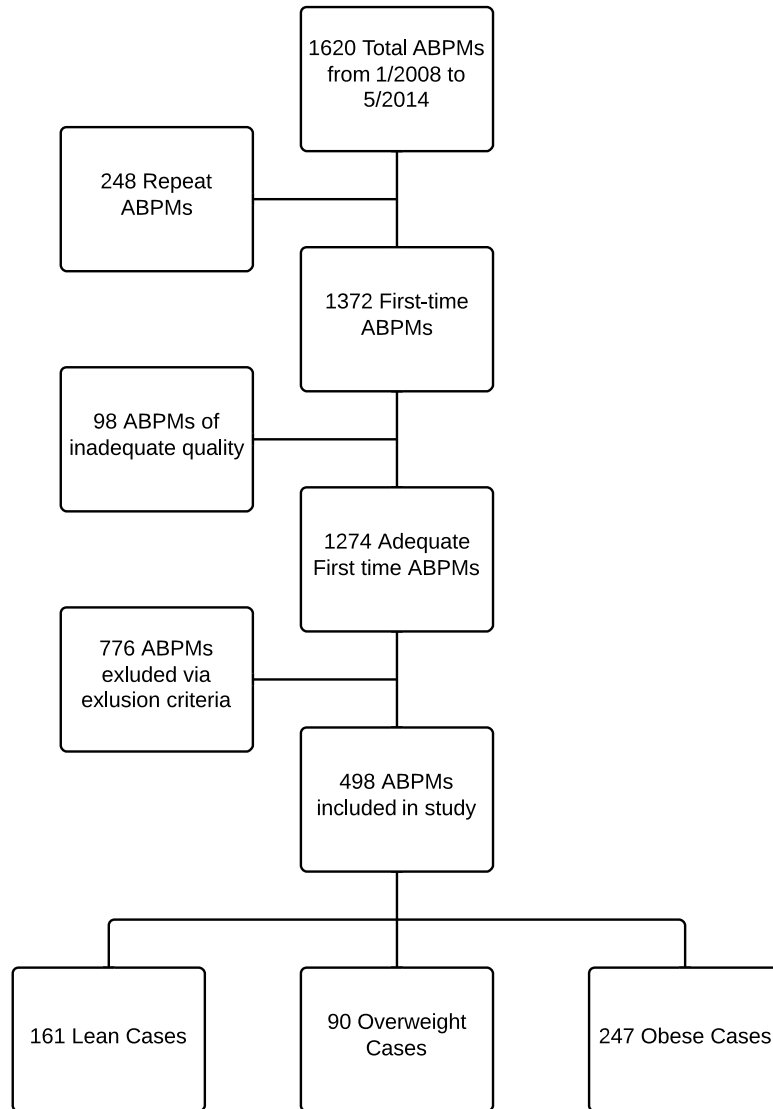
We did not find a significant association between increasing severity of obesity and nocturnal non-dipping. However, we feel this is likely be due to a lack of statistical power, as we had smaller number of subjects in each individual obesity category, and the prevalence ratios for both more obese categories were greater than 1.

The means by which obesity might give rise to nocturnal non-dipping is not known.[28] Activation of the sympathetic nervous system is thought to play a significant role. Compared to lean children, obese children have been shown to have reduced cardiac vagal function[29] and overall increased sympathetic activity[30]. Insulin resistance and impaired glucose tolerance are possible mechanisms by which sympathetic activation occurs[31-33]. Obesity-associated elevation of leptin[34], reduction of adiponectin[35], and alteration of other neuropeptides[28] have also been associated with hypertension. Nocturnal natriuresis, which is increased by hyperinsulinemia and higher leptin levels[36], is also elevated in non-dippers compared to normal dippers[37, 38]. The renin-angiotensin-aldosterone system (RAAS) activity, which is upregulated in obesity[39], also plays a role in circadian blood pressure patterns[40, 41].

This study had several limitations. All subjects in the study were referred to Seattle Children's Hospital for evaluation of hypertension, decreasing the generalizability of our results to the general pediatric population. There is also controversy regarding the reproducibility of nocturnal dipping status, with one study finding that 44% of subjects would alternate between non-dipping and normal dipping status on three repeat ABPMs conducted over 1 year.[42]

In conclusion, our study found an association between obesity and nocturnal non-dipping of systolic and diastolic blood pressure. Whether the diminished blood pressure dipping is related to long-term cardiovascular health outcomes, beyond the association of non-dipping with elevated blood pressure, remains to be determined.

**Figure 1: Study Flow**





**Table 1: Characteristics of Lean and Obese Subjects**

	<b>Lean</b>		<b>Obese</b>	
	N=161	%	N=247	%
<b>Race</b>				
White	79	49.1	89	36.0
Black	10	6.2	13	5.3
Native American/Alaskan	0	0	4	1.6
Asian	19	11.8	22	8.9
Hawaiian/Pacific Islander	0	0	2	0.8
Other	24	14.9	70	28.3
Unknown	29	18.0	47	19.0
<b>Gender</b>				
Male	107	66.5	178	72.1
Female	54	33.5	69	27.9
<b>Age (years)</b>				
	14.6 +/- 3.3		14.2 +/- 2.9	

**Table 2: Comparison of ABPM Findings in Lean and Obese Subjects**

	<b>Lean</b>	<b>Obese</b>	<b>P-value</b>
24-hour SBP (mm Hg)	122.7 +/- 11.0	123.6 +/- 8.6	0.305
24-hour DBP (mm Hg)	70.5 +/- 7.4	68.8 +/- 6.4	0.005
Awake SBP (mm Hg)	129.6 +/- 11.6	129.5 +/- 10.3	0.644
Awake DBP (mm Hg)	76.5 +/- 8.0	73.8 +/- 7.1	<0.001
Asleep SBP (mm Hg)	110.2 +/- 9.8	113.0 +/- 8.9	0.006
Asleep DBP (mm Hg)	59.5 +/- 6.5	60.1 +/- 6.1	0.976
SBP Noct. Dipping (%)	15.1 +/- 4.6	12.4 +/- 5.6	<0.001
DBP Noct. Dipping (%)	22.2 +/- 6.0	18.5 +/- 7.0	<0.001

**Table 3: Prevalence Ratio of the Association Between Obesity and Non-dipping Status, Adjusted for Race**

	<b>Non-dipping</b>		<b>Prev. Ratio</b>	<b>95% CI</b>
	<b>Yes</b>	<b>No</b>		
<b>Lean</b>	22 13.7	139 86.3	1.00	Ref
<b>Obese</b>	85 34.4	162 65.6	2.15	1.25-3.42

**Table 4: Prevalence Ratio of the Association Between Obesity Severity and Non-dipping Status, Adjusted for Race**

	<b>Non-dipping</b>		<b>Prev. Ratio</b>	<b>95% CI</b>
	<b>Yes</b>	<b>No</b>		
<b>BMI Cat. I</b>	10 25.0	30 75.0	1.00	Ref
<b>BMI Cat. II</b>	36 39.1	56 60.1	1.28	0.66-2.43
<b>BMI Cat. III</b>	39 33.9	76 66.1	1.16	0.61-2.19

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