

Evaluation of the Association between Blood Pressure and Birth Weight: A Cross-Sectional Study on 600 Outpatient ChildrenYazdan Ghandi¹, Ali Arjmand Shabestari¹, Fatemeh Dorreh¹, Parsa YousefiChaijan¹ and Taraneh Rezaei^{2*}¹Associate Professor of Pediatrics, Department of Pediatrics, School of Medicine Taleghani Hospital, Amirkabir Hospital, Arak University of Medical Sciences, Arak, Iran***Corresponding Author**

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²Student Research Committee, Arak University of Medical Sciences, Arak, Iran**Submitted:** 2023, Apr 25; **Accepted:** 2023, May 10; **Published:** 2023, May 30**Citation:** Ghandi, Y., Shabestari, A. A., Dorreh, F., YousefiChaijan, P., Rezaei, T. (2023). Evaluation of the Association between Blood Pressure and Birth Weight: A Cross-Sectional Study on 600 Outpatient Children. *J Pediatr Neonatal Biol*, 8(2), 194-200.**Abstract****Background**

Despite the declining global prevalence of preterm birth, it accounts for a certain proportion of births in developing countries. Those born earlier, are prone to have lower birth weight (BW), smaller kidneys, lower glomerular filtration rate, higher blood pressure (BP) and overall poorer future cardio-metabolic health outcomes.

Methods

The current cross-sectional study was conducted on relatively healthy individuals aged 3-18 years with no PMH of any specific diseases, and not in toxic or ill condition. Recruitment was in 2 phases for the participants with high BP at the first visit (regarding a 2-week follow-up BP assessment) and in 1 phase for the normotensive participants.

Results

Among the total 600 participants, the prevalence of elevated BP, grade 1 hypertension (HTN), and grade 2 HTN was 5.2, 5.5, and 2.3%, respectively. The prevalence of children with very low birth weight, low birth weight, and high birth weight was 1.7, 8.7, and 4.5%, respectively. Chi-square analysis showed no statistically significant association between BW and BP (P -value=0.774). There was a statistically significant association between BP and height, weight, and heart rate (HR) (P -value<0.05).

Conclusions

There is no statistically significant interaction between BP and BW. The association illustrated by previous studies may be caused by other underlying factors including weight or by methodological limitations including nor follow-up BP assessment, neither excluding ill, toxic, and hospitalized children. There is a direct relationship between BP and HR, weight, and height. However, the relationship between BP and the two latter is inverted for BP above grade 2 HTN.

Trial Registration

Design of the current study was approved by the ethics committee of the Research Institute for Arak University of Medical Sciences. Ethics Code: IR.ARAKMU.REC.1400.271

Key Words: Blood Pressure, Hypertension, Birth Weight, Heart Rate, Maternal Age, Body Mass Index, Weight, Height, Age, Sex.**1. Background**

The prevalence of preterm birth, a major cause of mortality and morbidity in pediatrics, is decreasing worldwide; however, it accounts for a certain proportion of births in developing countries [1,2]. Those born earlier, are more likely to have lower birth weight (BW), smaller kidneys, lower glomerular filtration rate (GFR), higher risk of nephrocalcinosis, higher systolic and diastolic BP, especially DBP in those with renal calculi, and overall poorer future cardio-metabolic health outcomes [3-6]. Prematurity can make a child prone to hydronephrosis and

obesity, resulting in higher risk of HTN [7-10]. One of the most inspiring clinical observations of the last decade has been the association between low birthweight and hypertension (HTN) in adults [11]. However, conflicting results have been yielded in pediatrics, and further elucidation is needed [3,12]. Previous studies have been limited by age limitations, insufficient numbers to assess age- and sex-specific differences and lack of data on past medical history (PMH), and comorbidities, calling into question the generalizability of those studies to the general population. In the light of the fact that maternal blood pressure-raising

alleles reduce birth weight causing higher later blood pressure in offspring, we aimed to determine whether this association in childhood is similar to adulthood. Furthermore, previous studies have reported that higher BP is observed to be more prevalent among children with higher body mass index (BMI) [13-15]. However, it is recommended to test the hypothesis that age, sex, heart rate (HR), BMI, and maternal age are independent risk factors for higher BP in children. End organ damage including left ventricular hypertrophy or pathologic vascular changes, hyperlipidemia, diabetes mellitus, and nocturnal enuresis are some of major complications of HTN, leading to stronger emphasize in importance of HTN early diagnosis[16-20].

2. Methods and Patients

2.1. Study Design and Population

The current cross-sectional study has been conducted on relatively healthy individuals aged 3-18 years with no PMH of any specific diseases, and not in toxic or ill condition, attending the outpatient pediatric clinic of Amir Kabir hospital, Arak, Iran in spring 2022. The enrollment was carried out in 2 phases for the participants with high BP recorded at the first visit (regarding a 2-week follow-up BP assessment) and in 1 phase for the normotensive recorded participants. Those with missing data regarding BW and maternal age and those with a high BP in the first visit without a 2-week follow-up BP assessment were excluded, leaving a total 600 participants (315 boys) in the current study analysis. The ethics committee of the Research Institute for Arak University of Medical Sciences approved the design of the current analysis (Grant No. 271). The aim and duration of the study and type of cooperation of the participants were explained to them by a medical doctor, and any objective assessments were done in the presence of the parents of the participants and after obtaining written informed consent. The authors declare that they have no conflict of interest.

3. Clinical Measurements

Body measurements of the study participants (weight and height) were recorded with light clothing and shoes removed. BMI percentile-based weight status was assessed and recorded regarding the age and gender of each child. Those with a BMI percentile < 5 were classified as underweight, $5 \leq$ BMI percentile < 85 as normal weight, $85 \leq$ BMI < 95 as overweight, and $95 \leq$ BMI as obese. HR and BP were measured using a digital BP calculator device for children and BP percentile was assessed based on age, gender and height of the child. Maternal age, PMH, and data on BW were collected using a checklist. Illness or toxicity of each participant was determined by a pediatric nephrology subspecialist.

Based on our study design, three measurements of SBP and DBP were taken on the right arm after a 15-min rest in a sitting position without chocolate and caffeine consumption or urination sensation, and at standardized room temperature at the first visit. The mean of the three measurements was considered as BP. Those with affirmed high BP at the first visit, were followed-

up for BP assessment after a 2-week salt-abstinence diet, as the main intervention in children include life-style modification and salt-free diet [21].

4. Definition of Terms

BP was categorized in four classes based on 2023 Nelson Essentials: normal: BP < 90th percentile for age, sex and height; or < 120/80 mmHg for adolescents, elevated BP: 90th percentile \leq BP < 95th percentile; or 120-129/<80 mmHg for adolescents, stage 1 HTN: BP > 95th percentile up to the 95th percentile + 12 mmHg; or 130-139/80-89 mmHg for adolescents, stage 2 HTN: BP \geq 95th percentile + 12 mmHg; or \geq 140/90 mmHg for adolescents. BW was classified in four groups: very low birth weight (VLBW) as $BW \leq 1500$ g, low birth weight (LBW) as $1500 < BW \leq 2500$ g, normal BW as $2500 < BW < 4000$ g and macrosomia or high birth weight as $4000 < BW$. Weight status was classified into 4 groups based on the gender- and age-specific BMI percentile calculated by a general practitioner: underweight: BMI percentile < 5th percentile, healthy weight: 5th percentile \leq BMI percentile < 85th percentile, overweight: 85th percentile \leq BMI percentile < 95th percentile, and obese: 95th percentile \leq BMI percentile. Age- and sex-specific HR assessment was performed for each participant and HR was classified in three groups: bradycardia (below the lower limit of normal for age and sex), normal HR for age and sex, and tachycardia (above the upper limit of normal for age and sex).

5. Outcome

According to the design of the current study, participants with a high BP (either SBP or DBP) at the first outpatient clinic visit were prescribed a salt-free diet for 2 weeks, followed by another BP assessment. All examinations during the initial visit and at the follow-up visit were performed by a certain trained general physician. The collected data were then evaluated by an outcome committee consisting of an epidemiologist, a pediatric nephrology subspecialist, a pediatric cardiology subspecialist, and two general pediatrics to assign and confirm the outcome.

6. Statistical Analysis

Baseline characteristics of the study population are presented as either mean (Std. Deviation) or frequencies (%) continuously- and categorically -distributed variables, respectively. A high BP was affirmed as if the second BP assessed on the follow-up session was above normal BP cutoff points. We controlled our regression analyses for confounding bias due to the potential confounders. The statistical significance level was set at a two-tailed type I error of 0.05. All statistics analyses were performed using STATA version 11.

7. Results

600 participants (315 boys) were evaluated on their BP, BW, weight, height, BMI, HR, maternal age and demographic data. The first two tables represent data on baseline characteristics of the participants.

Table 1. Categorically-distributed Variables		Count	Column N %
sex	Female	285	47.5%
	Male	315	52.5%
BP percentile	NL	522	87.0%
	Elevated	31	5.2%
	Stage 1	33	5.5%
	Stage 2	14	2.3%
Birth Weight	VLBW	10	1.7%
	LBW	52	8.7%
	NL-BW	511	85.2%
	LGA-Macrosomia	27	4.5%
HR	Bradycardia	39	6.5%
	NL	457	76.2%
	Tachycardia	104	17.3%
Weight status	Underweight	68	11.3%
	NL Weight	380	63.3%
	Overweight	80	13.3%
	Obese	72	12.0%

Table 2. Continuously-distributed Variables	Mean	Std. Deviation	Minimum	Maximum
Age	8	3	3	18
height	125	17	86	175
weight	27.7	12.6	11.0	98.0
BMI	17.05	3.67	8.6	40.7
Maternal Age	28	6	15	48

As shown in table 3 and 4, there is no statistically significant association between BP and age, maternal age, and BMI. The mean height and weight are significantly (P -value <0.05) associated with the level of BP. Both mean weight and height are directly associated with BP; however, the association inverts for BP above grade 2 HTN.

Table 3. Continuously-distributed Variables based on BP levels		N	Mean	Std. Deviation	Minimum	Maximum
Age	NL	522	7.52	2.735	3	18
	Elevated	31	8.26	2.955	3	13
	Stage 1	33	8.33	3.332	4	16
	Stage 2	14	7.64	3.522	3	13
	Total	600	7.61	2.804	3	18
height	NL	522	123.97	16.713	87	172
	Elevated	31	128.81	19.885	99	164
	Stage 1	33	131.88	20.236	101	175
	Stage 2	14	122.64	23.503	86	165
	Total	600	124.62	17.346	86	175
weight	NL	522	26.637	11.3482	11.0	98.0
	Elevated	31	33.645	15.4565	15.0	73.0
	Stage 1	33	36.424	16.0254	16.0	68.0
	Stage 2	14	34.071	24.8456	13.0	84.0
	Total	600	27.711	12.6115	11.0	98.0
Maternal Age	NL	522	27.80	5.516	15	48
	Elevated	31	27.94	5.465	18	43
	Stage 1	33	26.73	6.747	15	39
	Stage 2	14	30.43	6.148	19	43
	Total	600	27.81	5.607	15	48

BMI	NL	522	17.092	3.7430	8.6	40.7
	Elevated	31	16.797	2.6424	12.8	23.6
	Stage 1	33	16.297	3.4462	11.5	24.6
	Stage 2	14	17.857	3.7633	13.1	25.1
	Total	600	17.051	3.6781	8.6	40.7

Table 4. Variance analysis of continuously-distributed Variables		Sum of Squares	df	Mean Square	F	Sig.
Age	Between Groups	34.081	3	11.360	1.448	.228
	Within Groups	4674.659	596	7.843		
	Total	4708.740	599			
height	Between Groups	2559.104	3	853.035	2.862	.036
	Within Groups	177672.015	596	298.107		
	Total	180231.118	599			
weight	Between Groups	4765.537	3	1588.512	10.461	.000
	Within Groups	90505.042	596	151.854		
	Total	95270.580	599			
Maternal Age	Between Groups	135.234	3	45.078	1.437	.231
	Within Groups	18697.724	596	31.372		
	Total	18832.958	599			
BMI	Between Groups	30.723	3	10.241	.756	.519
	Within Groups	8072.737	596	13.545		
	Total	8103.460	599			

Fisher's least significant difference test showed that statistically significant (P-value<0.05) mean height difference was only observed between normal BP and stage 1 HTN and statistically significant (P-value<0.05) mean weight difference was seen between normal BP and other stages of BP as represented in table 5.

Table 5. Dependent Variable	(I) BP percentile	(J) BP percentile	Mean Difference (I-J)	Std. Error	Sig.
height	NL	Elevated	-4.839	3.192	.130
		Stage 1	-7.911*	3.099	.011
		Stage 2	1.325	4.676	.777
	Elevated	NL	4.839	3.192	.130
		Stage 1	-3.072	4.319	.477
		Stage 2	6.164	5.560	.268
	Stage 1	NL	7.911*	3.099	.011
		Elevated	3.072	4.319	.477
		Stage 2	9.236	5.507	.094
	Stage 2	NL	-1.325	4.676	.777
		Elevated	-6.164	5.560	.268
		Stage 1	-9.236	5.507	.094
weight	NL	Elevated	-7.0082*	2.2780	.002
		Stage 1	-9.7873*	2.2119	.000
		Stage 2	-7.4345*	3.3373	.026
	Elevated	NL	7.0082*	2.2780	.002
		Stage 1	-2.7791	3.0822	.368
		Stage 2	-.4263	3.9680	.914
	Stage 1	NL	9.7873*	2.2119	.000
		Elevated	2.7791	3.0822	.368
		Stage 2	2.3528	3.9304	.550

	Stage 2	NL	7.4345*	3.3373	.026
		Elevated	.4263	3.9680	.914
		Stage 1	-2.3528	3.9304	.550

As shown in table 6 and 7, there is no statistically significant interaction between BP and sex, BW, and weight status but the interaction between BP and HR was assessed to be significant

(P-value<0.05). Higher BP is more prevalent among those with tachycardia.

Table 6. Categorically-distributed Variables based on BP levels		BP percentile							
		NL		Elevated		Stage 1		Stage 2	
		Count	%	Count	%	Count	%	Count	%
sex	Female	246	47.1%	18	58.1%	12	36.4%	9	64.3%
	Male	276	52.9%	13	41.9%	21	63.6%	5	35.7%
Birth Weight	VLBW	9	1.7%	0	0.0%	1	3.0%	0	0.0%
	LBW	42	8.0%	4	12.9%	4	12.1%	2	14.3%
	NL-BW	446	85.4%	27	87.1%	26	78.8%	12	85.7%
	LGA-Macrosomia	25	4.8%	0	0.0%	2	6.1%	0	0.0%
HR	Bradycardia	36	6.9%	1	3.2%	1	3.0%	1	7.1%
	NL	411	78.7%	14	45.2%	23	69.7%	9	64.3%
	Tachycardia	75	14.4%	16	51.6%	9	27.3%	4	28.6%
Weight status	Underweight	57	10.9%	2	6.5%	8	24.2%	1	7.1%
	NL Weight	334	64.0%	21	67.7%	18	54.5%	7	50.0%
	Overweight	69	13.2%	3	9.7%	5	15.2%	3	21.4%
	Obese	62	11.9%	5	16.1%	2	6.1%	3	21.4%

Table 7. Chi-square analysis of categorically-distributed Variables	Value	df	Asymptotic Significance (2-sided)
Sex	4.640a	3	.200
Birth weight (Fishers exact test)	5.333		0.774
HR	32.629a	6	.000
Condition	10.265a	9	.329

8. Discussion

It has been known that the lower the BW, the smaller the kidneys and the higher SBP and DBP in adults, although the association in different age stages of the childhood showed conflicting results [3, 12]. Herein we demonstrated that there was no statistically significant association between BP and BW. However direct association was observed between BP and HR, weight, and height which was inverted for grade 2 HTN in the 2 latter. The association between BP and BW has been investigated in previous studies with conflicting results [22, 23]. Previous studies had advocated the association between lower BW and higher BP, however, similar association in Iranian children has been matter of debate. Similarly, Kawabe et al. reported a non-significant relationship between BP and BW, and Vohr et al. stated that preterm labor regardless of the BW accounts for the association [12,13]. In contrast, some studies demonstrated that there is an association between BW and BP, either linear or U-shaped [23].

Current study has some notable strengths. First, BP was assessed 3 times by a general physician with digital device and all participants with elevated BP or grade 1 or 2 HTN based on the sex, age and height were followed-up BP assessment

after a 2-week salt-free diet, therefore, BP is confirmed in the participants after the follow-up. Second, hospitalized children, those in ill and toxic condition during outpatient visit and those with PMH of any certain diseases leading to HTN, were excluded by a pediatric nephrologist to decrease the errors in BP affirmation.

Our findings need to be interpreted after its limitations have been taken into account. First, our study may slightly underestimate the association between BP and BW as the data of the participants with definite high BP were included in statistical analysis based on our inclusion and exclusion criteria. However, accurate BP status determination was the solution to previous studies limitations [13,14]. Second, our findings might not be extrapolated to all races. However, it is the common limitation of similar studies because of financial issues [24-26].

9. Conclusion

We had hypothesized whether BW plays independent role in BP estimation in children. Our findings clarify that there is no significant association between lower BW and higher BP. However, it was concluded that HR, height, and weight were directly associated with BP, and the relationship between BP and

height and weight inverted for grade 2 HTN.

9.1. List of Abbreviations

PMH: Past Medical History
BP: Blood Pressure
HTN: Hypertension
BW: Birth Weight
VLBW: Very Low Birth Weight
LBW: Low Birth Weight
HR: Heart Rate
BMI: Body Mass Index

9.2. Declarations

➤ Ethics Approval and Consent to Participate

The design of the current study was approved by the ethics committee of Arak University of Medical Sciences (Ethics Code: IR.ARAKMU.REC.1400.271). Written informed consent was obtained from the parents of all participants.

➤ Consent for Publication

Consent for publication was not required for this study, since the study does not contain any individual data.

➤ Availability of Data and Materials

All data generated or analyzed during this study are included in this published.

➤ Competing Interests

The authors declare that they have no conflicting interests.

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Authors' Contributions

T R, Y Gh and P Y conceived and designed the study and coordinated the manuscript. Y Gh, P Y, F D, A A and T R executed data collection, performed the statistical analysis and prepared the draft of the manuscript. All authors read and approved the final manuscript.

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