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Original Article

Uric acid and blood pressures in low birth weight 7-year-olds

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Abstract

Background Low birth weight (LBW) has been associated with increased cardiovascular diseases, including hypertension, during adulthood. Nephrogenesis impairment in LBW may lead to an increase of uric acid and hypertension.

Objective To assess for a correlation between uric acid and blood pressures in LBW children.

Methods This study was conducted from January to April 2012. A comparative and correlative analytic-observational study with a cross-sectional method was done in children aged 7-8 years, born at Prof. Dr. RD Kandou General Hospital and living in Manado. Forty-eight LBW children and 48 normal birth weight (NBW) children were included in this study. All children underwent uric acid level and blood pressures measurements.

Results Mean uric acid level in LBW children was significantly higher than in NBW children (P=0.001). There was no correlation between uric acid and blood pressures in LBW children(r=0.13, P>0.05 for systolic blood pressure; r=0.05, P>0.05 for diastolic blood pressure).

Conclusions LBW children have higher uric acid levels than NBW children, but no correlation is found between uric acid level and blood pressures. **[Paediatr Indones. 2014;54:114-7.]**

Keywords: *low birth weight, normal birth weight, uric acid, blood pressure*

Low birth weight (LBW) is defined as infants weighing less than 2,500 g at birth.[1,2] Prematurity is a common cause of LBW in Western countries, while intrauterine growth retardation (IUGR) is the most common cause in developing countries. Based on gestational age, LBW can be classified as appropriate for gestational age (AGA) and small for gestational age (SGA).[2] The incidence of LBW is estimated at approximately 6-18%, with higher prevalence in developing countries.[3] Low birth weight prevalence in the USA was about 7.6%.[4] In 2003, it was reported that the prevalence of LBW in Prof Dr. RD Kandou General Hospital, Manado was about 10.83%.[5]

Cardiovascular and metabolic diseases are caused by genetic and enviromental interactions. Low birth weight has been associated with an increased incidence of later cardiovascular diseases, including hypertension. Barker *et al.*[6] first postulated that adult-onset disease had a fetal and early life origin. Decreased nephron number in LBW children is related to hypertension by the increased function of the remaining glomeruli, nephromegaly, glomerular

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hypertension, and glomerular hyperfiltration.[7] These processes lead to glomerulosclerosis, destruction of the remaining nephrons and increased blood pressure.[7,8]

Uric acid is the final product of purine catabolism. It is produced in the liver and eliminated primarily by the kidneys. Uric acid plays a key causal role in the development of hypertension in relation to birth weight.[10,11] A high serum uric acid value (> 6.2 mg/dL or >370 μM/dL) is associated with endothelial dysfunction, a reduction in nitric oxide (NO) levels, and increased risk for the development of hypertension.[9] In addition, normalization of uric acid levels resulted in a reduction of blood pressure.[10] The purpose of this study was to assess for a possible correlation between uric acid level and blood pressures in LBW children.

Methods

This cross sectional study was done from January to April 2012 in children aged 7-8 years who were born at Prof Dr. RD Kandou General Hospital. Subjects had complete medical records including birth weight data, lived in Manado, and did not have any significant illnesses based on physical examination and urinary tests. We excluded chldren with renal diseases, and those with a family history of hypertension, endocrinopathy, or hyperuricemia. There were 48 LBW children and 48 NBW children in this study. The local Medical Ethics Commitees in Manado approved this study, and informed consent was obtained from subjects' parents.

Uric acid levels were measured using quantitative enzymatic colorimetric method with analytic sensitivity of 0.2 mg/dL and a detection range of 0.2-25.0 mg/dL. Blood pressures measurement were performed in standard manners, 3 times wih 3-5 minutes interval using mercury manometer. Of the 3 values obtained we then calculated the mean value.

Descriptive data was analysed by univariate analysis with a mean and standard deviation (SD). Student's T-test was performed to compare mean uric acid levels between the two groups of subjects. Statistical significance was defined as $P<0.05$. Pearson's correlation (r) was performed to assess for a correlation between uric acid and blood pressures. The correlation was considered to be good if $r > 0.8$, and very weak if $r < 0.4$. All statistical results were calculated using *SPSS* software (version 20.0).

Results

A total of 96 children (48 LBW and 48 NBW; 48 boys and 48 girls) with an age range of 7.0-8.9 years were included in the study. **Table 1** shows the characteristics and descriptive analysis of subjects and the parameters examined in this study. Of 48 LBW children, there were 20 boys (42%) and 28 girls (58%) with uric acid levels between 3.6-7.6 mg/dL, while of 48 NBW children, there were 28 boys (58%) and 20 girls (42%) with uric acid levels between 2.0-5.0 mg/dL. Both groups had systolic blood pressure between 90.0-120.0 mmHg and diastolic blood pressure between 50.0-80.0 mmHg.

Table 2 shows the mean uric acid levels of the LBW and NBW groups. Children in LBW group had

Table 1. Subjects' characteristics

Characteristics	Low birth weight (LBW) n = 48	Normal birth weight (NBW) n = 48
Age, years		
Range	7.0-8.25	7.0-8.83
Median	7.5	7.5
Mean (SD)	7.5 (0.3)	7.5 (0.4)
Gender, n (%)		
Males	20 (42)	28 (58)
Females	28 (58)	20 (42)
Birth weight, g		
Range	1,400-2,460	2,500-4,250
Median	2,300	3,100
Mean (SD)	2,182.7 (271.1)	3,224.4 (420.9)
Body weight, kg		
Range	19-30	19-34
Median	21	21
Mean (SD)	21.26 (2.25)	21.40 (2.45)
Uric acid levels, n (%)		
3.6-7.6 mg/dL		
Males	20 (42)	-
Females	28 (58)	-
2.0-5.0 mg/dL		
Males	-	28 (58)
Females	-	20 (42)
Systolic BP, mmHg		
Range	90.0-120.0	90.0-120.0
Median	95.0	90.0
Mean (SD)	95.3 (7.4)	93.4 (6.6)
Diastolic BP, mmHg		
Range	50.0-80.0	50.0-80.0
Median	60.0	60.0
Mean (SD)	61.5 (5.0)	61.1 (4.8)
Mean (SD)	61.5 (5.0)	61.1 (4.8)

significantly higher mean uric acid levels than NBW children.

Pearson's correlation analysis revealed no correlation between uric acid and systolic blood pressures in LBW children (r=0.13, P>0.05), as well as no correlation between uric acid and diastolic blood pressures in LBW children found (r=0.05, P>0.05).

Table 2. Mean uric acid levels of the LBW and NBW groups

Uric acid levels	LBW group	95% CI	NBW group	95% CI	t	P value
Mean uric acid (SD), mg/dL	4.57 (0.67)	4.47 to 4.92	3.92 (0.62)	3.74 to 4.09	4.946	0.001

Discussion

Our study confirmed prior findings that LBW children had higher serum uric acid concentration compared to NBW children. Other studies show that uric acid concentration in 6- to 18-year-old LBW children with primary hypertension was higher than in NBW children as controls [6.7 (SD 1.3) mg/dL vs 3.6 (SD 0.8) mg/dL, respectively, P<0.05].[10,11] This observation was accompanied by an inverse correlation between uric acid and birth weight. Similar results were found by Park *et al*.[14] and Kaneshi *et al*.[15] Low birth weight has been associated with a reduced number of nephrons that predispose to the development of hyperuricemia as a consequence of an increase in proximal tubular reabsorption, which might stimulate uric acid reabsorption.[11]

The favored "nephron-underdosing" hypothesis proposed by Brenner *et al.* in 1988 is that hypertension may result from a congenital reduction in nephron number.[13] Low birth weight correlates with impaired renal development and reduced nephron number at birth. The Framingham Heart study reported that elevated serum uric acid could predict the development of hypertension.[14]

Uric acid may protect endothelial cells from oxidative stress. A high serum uric acid value (> 6.2 mg/dL or 370 μM/dL) is associated with endothelial dysfunction, a reduction in nitric oxide (NO) levels, and increased risk for the development of hypertension.[15] Uric acid is associated with an impairment in plasma NO concentration and with a reduction in both macula densa nitric oxide synthase-1 (NOS-1) and renal endothelial NOS-3, leading to both afferent and efferent arteriole vasoconstriction.[16] Uric acid can enter vascular smooth muscle cells and stimulate a number of factors, including platelet-derived growth factor (PDGF) and mitogen-activated protein kinase (MAPK).[17] These factors induce vascular smooth muscle proliferation and preglomerular arteriolopathy. Once a vascular lesion is established, salt sensitivity can persist and cause renal ischemia that leads to activation of the renin-angiotensin system, renal vasoconstriction and increased sodium reabsorption.[20]

A previous study reported that uric acid had a strong correlation with systolic and diastolic blood pressure in hypertensive LBW children with a mean of age 15 years (r=0.80 for systolic blood pressure and r=0.60 for diastolic blood pressure). An increase of 1 mg/dL serum uric acid correlated with an increase of 14 mmHg systolic blood pressure and 7 mmHg diastolic blood pressure.[10]

We found that uric acid had no correlation with systolic blood pressures (r=0.13) and diastolic blood pressures (r=0.05). Subjects' young age may have affected these results. Other studies suggested that increased uric acid levels increase the risk of hypertension in the future. Alper *et al.* reported a weak correlation between uric acid and systolic and diastolic blood pressures in children between 12-13 years old (r=0.31; P<0.0001 for systolic blood pressures and r=0.29; P<0.0001 for diastolic blood pressures).[21] Jossa *et al*. found that the increment of 1 mg/dL uric acid correlated with the risk of hypertension by 1.23 times at the age of 12 years.[22] Nakanishi *et al*. found a 1.6 times increased risk of hypertension in adolescents with a high level of uric acid.[23] Masuo *et al*. evaluated a linear association between uric acid and systolic blood pressures for 5 years. In their study, an increment of 1 mg/dL of uric acid was followed by increased systolic blood pressure of 23 mmHg in non-obese male adolescents.[24] Selby