

Plasma homocysteine and blood pressure in small for gestational age children

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Abstract

Background Homocysteine is associated with endothelial damage and hypertension. Increased plasma homocysteine levels are often accompanied by cardiovascular impairment, including hypertension. Small for gestational age children have been found to have morbidity and mortality in cardiovascular diseases.

Objective To assess for a possible association between homocysteine level and blood pressure in small for gestational age children.

Methods This observational study was undertaken from December 2011 to April 2012 in Prof. Dr. R. D. Kandou Hospital, Manado, North Sulawesi, on children who were born small for gestational age in year 2004-2005. Data was analyzed by T-test to compare homocysteine levels in small for gestational age and normal birth weight children. Regression analysis and simple coefficient test were used to assess for an association between homocysteine levels and blood pressure in children who were small for gestational age at birth.

Results The mean homocysteine level in small for gestational age children was significantly higher than that of normal birth weight children ($P < 0.001$). We observed no correlation between homocysteine level and systolic blood pressure in the small for gestational age group ($r = 0.151$, $P = 0.189$). However, there was a weak correlation between homocysteine level and diastolic blood pressure in the small for gestational age group ($r = 0.237$, $P = 0.049$).

Conclusion Children who were small for gestational age at birth have significantly higher mean homocysteine level than that of normal birth weight children. Higher homocysteine levels are associated with higher diastolic blood pressure in children who were small for gestational age at birth. [Paediatr Indones. 2013;53:254-7].

Keywords: homocysteine, blood pressure, small for gestational age

Coronary heart disease is a heart condition caused by narrowing of coronary arteries, with atherosclerosis as the most common cause. The process of atherosclerosis starts in childhood, though only becoming visible in adults.¹ Elevated plasma homocysteine is one factor recently found to have a direct relationship to blood pressure and hypertension.^{2,3} Homocysteine also plays an important role during pregnancy,⁴ as increased maternal homocysteine may directly influence infant prematurity and birth weight. In addition, fetal malnutrition causes increased blood pressure.^{5,6} A history of small for gestational age is a predictive factor of high blood pressure in early adulthood, due to increased systemic vascular resistance at the descending aorta.⁷

There has been little prospective research on the direct relationship between plasma homocysteine and blood pressure, especially in small for gestational age children. Therefore, the objective of this study was to assess for an association between plasma homocysteine level and blood pressure in children who were born small for gestational age.

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Methods

We conducted an observational study between December 2011 to April 2012 in Manado, North Sulawesi. The study was approved by the Ethics Committee of Sam Ratulangi University Medical School, Prof. Dr. R. D. Kandou Hospital.

Subjects were healthy children who were born 7-8 years prior to the study (year 2004-2005) in Prof. Dr. R. D. Kandou Hospital, resided in Manado, had complete medical records, and were born small for gestational age (or normal weight without any complications for the control group), and whose parents consented to participation. We excluded children who were in puberty, were obese, had renal disease, or who were undergoing treatment with medications that affect blood pressure (e.g., corticosteroids or anti-hypertensive agents). Anthropometric measurements, physical examinations and blood pressure of each child were performed and recorded. Body weight was measured using a platform beam balance scale, while height was measured with a microtoise with the child in a standing position. Blood pressure was measured on the right arm with the subject sitting quietly for 5 minutes, according to the method described by the Working Group on High Blood Pressure in Children and Adolescents 2004.⁸ The onset of the first Korotkoff phase was used to determine systolic blood pressure, and the onset of the fifth Korotkoff phase was used to determine diastolic blood pressure. Blood specimens were taken with aseptic technique. Plasma homocysteine levels were measured and analyzed using *ADVIA Centaur HCY by Bayer Healthcare*.

The correlation between homocysteine level and blood pressure in small for gestational age children was analyzed using regression and simple correlation tests. Independent T-test was applied to determine independent and dependent variable association. The required sample size was calculated to obtain 90% power, and P values of <0.05 were considered to indicate statistical significance. Statistical analysis was performed using SPSS for Windows version 20.0.

Results

During the period of year 2004-2005, 324 low birth weight infants (212 small for gestational age and 112 appropriate for gestational age) and 3,138 normal birth weight infants were identified. Subjects were chosen consecutively from those meeting the inclusion criteria. Therefore, we recruited 100 subjects, consisted of 50 small for gestational age (SGA) children and 50 normal birth weight (NBW) children.

Table 1 shows the subjects' baseline characteristics. In the small for gestational age group, 22 (44%) children were male and 28 (56%) children were female. In the normal birth weight group, 29 (58%) children were male and 21 (42%) children were female. Most subjects were 7 years old with normal anthropometric status.

Table 1. Baseline characteristics of subjects

Characteristics	SGA group n=50	NBW group n=50
Gender, n (%)		
Male	22 (44)	29 (58)
Female	28 (56)	21 (42)
Mean age (SD), years	7 (0.30)	7 (0.30)

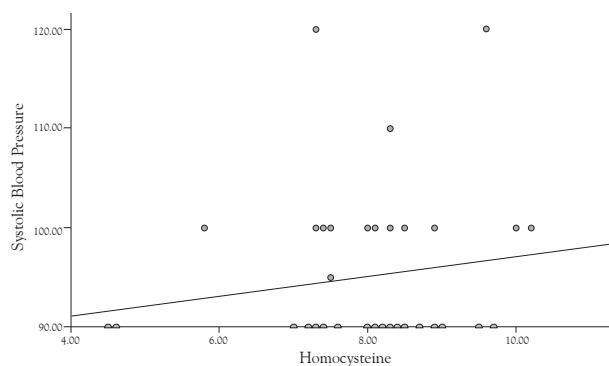


Figure 1. Plasma homocysteine level ($\mu\text{mol/L}$) and systolic blood pressure (mmHg) in children born small for gestational age

Table 2. Homocysteine levels in the small for gestational age (SGA) and normal birth weight (NBW) groups

Plasma homocysteine level	SGA group	95% CI	NBW group	95% CI	t	P value
Mean (SD), $\mu\text{mol/L}$	8.08 (1.094)	7.77 to 8.40	5.28 (0.665)	5.09 to 5.47	15.484	0.001

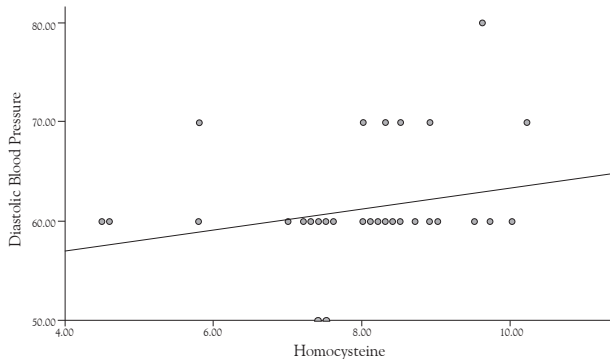


Figure 2. Plasma homocysteine level ($\mu\text{mol/L}$) and diastolic blood pressure (mmHg) in children born small for gestational age

Table 2 shows the mean homocysteine levels in the small for gestational age and normal birth weight groups. Mean homocysteine level was significantly higher in the small for gestational age group than in the normal birth weight group [8.08 (1.094) $\mu\text{mol/L}$ vs. 5.28 (0.665) $\mu\text{mol/L}$, respectively, ($P=0.001$)].

Figures 1 and 2 show the relationship between homocysteine levels and blood pressures in subjects who were small for gestational age at birth. There was no correlation between homocysteine level and systolic blood pressure ($r=0.151$, $P=0.189$), while there was a weak correlation between homocysteine level and diastolic blood pressure in the small for gestational age subjects ($r=0.237$, $P=0.049$).

Discussion

In this study, homocysteine levels in small for gestational age children were higher than in normal birth weight children, similar to results from previous trials.^{9,10,11} Tayama *et al.*, reported that high plasma homocysteine concentration was associated with a later stage of stiffness in the systemic arteries and greater blood pressure response to stress in patients with hypertension.¹² Mori *et al.*¹³ found endothelial dysfunction, decreased vascular compliance and atherosclerosis in children and adults with low birth weights.

We found no correlation between homocysteine level and systolic blood pressure ($r=0.151$, $P=0.189$). However, the weak correlation between homocysteine

level and diastolic blood pressure in children who were small for gestational age at birth was statistically significant ($r=0.237$, $P=0.049$). Franco *et al.*¹⁴ found a positive correlation between homocysteine and vascular function with blood pressure in children aged 8-13 years with low birth weight. Homocysteine is related to the risk of cardiovascular diseases and there may be a correlation between low birth weight and increased risk of vascular diseases in later life, which mediated by the disturbance in the biomarker's pathways (related with insulin resistance, oxidative stress, and inflammatory process).¹⁴

Changes in arterial walls may be due to several mechanisms, including endothelial dysfunction, proliferation of smooth muscle, collagen synthesis, and deterioration in elastic material of the arterial wall, all of which may contribute to stiffening of the walls.¹⁴

A limitation of this study was that the blood pressure measurements were performed only on one occasion. It has been suggested that 24-hour ambulatory measurement of blood pressure is more accurate. Another limitation was that homocysteine measurements were performed only once, hence, further study is needed to monitor the homocysteine levels of subjects.

In conclusion, children who were small for gestational age at birth have higher mean homocysteine concentration than normal birth weight children. Also, higher homocysteine level is associated with higher diastolic blood pressure in children who were small for gestational age at birth.

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