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Original Article

Association between C-reactive protein levels and physical fitness in 7 to 9 year old children at poor elementary schools in Surakarta, Indonesia

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Abstract

Background Data regarding inflammatory factors in children are not so well developed as in adults. Higher levels of physical fitness may be helpful in modifying the low-grade inflammatory state that is indexed by C-reactive protein (CRP) levels.

Objective To evaluate the association of physical fitness with CRP levels in children and to identify the possible related factors.

Methods This cross-sectional study was conducted at poor elementary schools in Surakarta, Indonesia using a group of 217 underweight children aged from 7 to 9 years old. Physical fitness was assessed using a modified Harvard Step Test. CRP levels were measured using a high-sensitivity assay. The association between physical fitness and CRP level was assessed using linear regression analysis. Multivariate analyses were used to adjust covariates, and statistical analyses were performed using SPSS for Windows software version 15.0.

Results Subjects were 48% female and 52% male, and eleven children (5%) had a CRP level > 5 mg/L. Mean fitness level and CRP level did not differ by age and gender. Fitness level was not inversely correlated with CRP (r=0.10, P=0.14). Physical fitness was significantly correlated with BMI (r=0.14; P=0.04), physical activity [OR=3.3 (95% CI 1.7 to 6.4)], and fat intake [OR=0.5 (95% CI 0.2 to 0.9)].

Conclusion These findings indicate that physical fitness is not inversely correlated to CRP levels in children. However, our study reveased an association between high fat intake and low physical fitness as well as a significant association between high physical activity and physical fitness. **[Paediatr Indones. 2009;49:75-81]**.

Keywords: *children, C-reactive protein, physical fitness*

Inflammation plays a role in many disease processes, and its contribution to the pathophysiology of cardiovascular disease has become better appreciated in the last decade. Although these conditions are predominantly diseases in adult, they are thought to be lifelong processes that originate from childhood.[1] The promotion of physical activity in early childhood may be important as the initial step in developing lifelong habits that can help prevent future chronic illness.[2]

The presence of early-stage atherosclerosis has been documented extensively in children and young adults,[3] but data regarding inflammatory factors in children are not well reported as in adults.[4] There is evidence that inflammatory factors participating in the early stages of atherogenesis, include impairment of endothelial function[5] and the formation of fatty streaks and plaques,[6-8] as well as in thrombotic events

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that trigger myocardial infarction and some strokes.[9] Two specific mechanisms involving (CRP) that have been described related to monocyte activation[6,10] and to the role of CRP in promoting synthesis of adhesion molecules.[11] These adhesion molecules recruit leukocytes to the endothelial surface and amplify the inflammatory process in the vascular endothelium.

CRP is a good choice for monitoring inflammation as concentrations can be measured easily, accurately, and relatively inexpensively. CRP, an acute-phase reactant, is produced in the liver and belongs to the pentraxin family of proteins is a very sensitive marker of inflammation, and its concentration can increase rapidly in response to a wide range of stimuli. In adults, CRP levels have added to the predictive ability of risk factors for cardiovascular disease.[1,12,13]

Studies in children have shown that fibrinogen level is positively correlated with obesity[14,15] and inversely correlated with physical activity[16] and physical fitness.[17] Physical activity and physical fitness levels are inversely correlated with fibrinogen[18,19] and with CRP levels in adults.[20] One study of CRP in children found an inverse relation with physical activity. Other study reported that exercise training did not lower serum CRP levels despite a significant improvement in cardiorespiratory fitness of the subjects, in contrast to those of several large epidemiologic studies.[21] To our knowledge, there is no published study on the relationship of physical fitness with CRP level in children.

Methods

We studied 217 underweight subjects (112 males and 105 females) aged 7-9 years old, volunteers from ten poor elementary schools in Surakarta, Indonesia. Elementary schools were selected based on economic indicators i.e. parental income and the fees charged by the school. Subjects complied with all of the following inclusion criteria; being underweight (WFA 5-10th percentile CDC), 7-9 years of age (2nd – 3rd class of elementary school), and not suffering from chronic illness including renal disease, congenital heart defects, thyroid disease, diarrhea and/or abnormal organ enlargement at the time of recruitment. Written informed consent was acquired from all subjects and their parents after thorough explanation of data collection procedures. The Research Ethics Committee of the Moewardi Hospital, Surakarta, Indonesia approved the investigation.

The weight, height, and mid upper arm circumference (MUAC) of the subjects were measured as follows. Weight was measured to nearest 0.1 kg with an electronic scale (SECA Corporation, Colombia, MD) and height was measured to the nearest 0.1 cm with a height scale (Microtoire). MUAC was measured to the nearest 1 mm using a non- stretchable plastic measuring tape. All measurements were recorded in duplicate, and the mean value was used for analysis. Z-scores for weight and height (weight-for-age, height-for-age, and weight-for-height) were calculated using EPI-Info software.

We collected venous blood sample using trace element-free syringes. CRP was measured using an immunoturbidimetric assay for the in vitro quantification of CRP in human serum using Roche automated clinical chemistry analyzers. In this assay, anti-CRP antibodies coupled to latex microparticles react with antigen in the sample to form an antigen/antibody complex. Following agglutination, the turbidity of the sample was measured. CRP levels were considered elevated at > 5 mg/L.

A survey to record foods eaten over a three day period was conducted to investigate dietary nutrition intake. Subjects were asked to fill out a record sheet about all food and drink taken for three consecutive days. The 24-hour recall method has been used in children, and reported nutrition intake with this technique compared with a three-day food records survey. NutriSurvey for Windows (Copyright © 2003 Dr. J. Erhadt, Hohenheim University) was used to calculate intake energy and nutrient content per day.

In this study, healthy was defined as not having any chronic medical condition under the treatment of a pediatrician. Recent illness was defined as an affirmative response to the questions "Has your child been ill in the past 14 days?", or "Has your child received medication for illness in the past week?". If the parent did not answer either question in the affirmative but CRP levels were elevated > 5 mg/L, then the child was included in the recently ill group.[22] As noted above, any child with a febrile illness on the day of study enrollment was excluded.

Physical fitness was measured by testing five components as follows: muscle strength, muscle endurance, flexibility, body composition, and cardiorespiratory endurance.[24] Physical fitness was assessed with the Harvard Step Test modified to measure submaximal performance in children. This involved each subject stepping up and down on a step with height 30 cm, width 42 cm, and depth 38 cm. The stepping was repeated 30 times per minute for 5 minutes while wearing a backpack containing bags of sugar equal to 20% of the subject's body weight. The heart rate of each subject was measured at rest, and at 1, 2, 3 and 4 minutes following the exercise. Heart rates of subjects who were physically fit returned to normal more rapidly than those who were less fit. A physical fitness score was calculated as follows: fitness score = duration of test x 100 + sum of heart rates per minute taken at 1, 2 and 3 minutes after test completion.[23] Exercise participation was assessed using the Physical Activity Interview for Children questionnaire, with several modifications. We asked subjects to recall the typical amount of time spent on various activities and team sports (outside of gym class in school), including the types of sports and other activities undertaken. Activities were also grouped by intensity. Activities in the moderate category included: bicycling (on a trail), dancing, gymnastics, soccer, softball/baseball, swimming (recreational), tennis, and walking. Activities grouped in the strenuous category included: aerobics, basketball, bicycling (in the street), running for exercise, swimming laps, and volleyball. From each subject's responses, we computed the hours of physical activity undertaken (outside of gym class) per week.[24,25]

Bivariate associations were analyzed using the independent samples t-test. The association of physical fitness with CRP level was assessed using linear regression analysis. Multivariate analyses were used to adjust for covariates including age, gender, body mass index, dietary intake, morbidity, and physical activity. The level of statistical significance was $P<0.05$. Statistical analyses were performed with SPSS software (SPSS for Windows, version 15.0).

Results

A total of 217 underweight children (48% female and 52% male) whose ages ranged from 7 to 9 years participated in our study. The subject characteristics are presented in **Tables 1** and **2**.

The distributions of CRP concentration in relation to sex, age, and body mass index (BMI) are presented in **Table 3**. CRP concentrations ranged from 0.02 to 27.9 mg/L. The distribution of CRP is skewed. About 21.7 % of participants had CRP concentration < 0.1 mg/L. Eleven children (5.1%)

Table 1. Basic characteristics of subjects

Characteristic	n	% of total participants (217)
Age		
7-8 years	107	49
8-9 years	110	51
Sex		
Male	112	52
Female	105	48
Body Mass Index (P50 = 13.9 kg/m2)		
< P50	115	53
Dietary Intake (< 75% RDA)		
Calorific intake	210	97
Protein intake	167	77
Fat intake	163	75
Illness Status		
Sick in past 14 d	39	18
CRP level of > 5 mg/L	11	5
Physical Activity		
Poor activity level	106	49
Good activity level	111	51

Table 2. Physical Fitness Score, Body Mass Index (BMI), and CRP concentrations of subjects

Characteristic	Male (112)	Female (105)	Total (217)
Physical Fitness Score			
Median (min-max)	6647 (1976 - 30416)	7224 (2120 - 30396)	6938 (1976 - 30416)
Mean (SD)	8681.34 (SD 6310.44)	8669.26(SD 5319.43)	8675.49 (SD 5838.50)
BMI (kg/m2)	14 (12.2 – 16.7) 14 + 0.8	13.8 (11.9 – 16.1) 13.8 + 0.8	13.9 (11.9 – 16.7) 13.9 + 0.8
CRP (mg/L)	0.3 (0.02 – 27.87) 1.2 + 3.9	0.4 (0.02 – 17.71) 1.3 + 3.4	0.4 (0.02 – 27.87) 1.3 + 2.8

Table 3. Percentiles of CRP concentration (mg/L) among subjects

	n	Mean	Percentiles of CRP concentration									
			10	20	30	40	50	60	70	80	90	100
Total	217	1.3	0.02	0.1	0.2	0.3	0.4	0.4	0.6	1.0	2.6	27.9
Sex												
Male	112	1.2	0.02	0.1	0.1	0.2	0.3	0.4	0.5	0.7	2.2	27.9
Female	105	1.3	0.02	0.1	0.2	0.3	0.4	0.5	0.7	1.5	3.3	17.7
Age, years												
7 – 8	107	1.3	0.02	0.1	0.1	0.2	0.3	0.4	0.6	1.3	3.9	17.7
8 – 9	110	1.2	0.03	0.1	0.2	0.3	0.4	0.4	0.6	0.9	2.3	27.9
BMI												
<P50	115	1.3	0.02	0.1	0.1	0.2	0.3	0.4	0.5	0.9	2.4	27.9
>P50	102	1.2	0.02	0.1	0.2	0.3	0.4	0.4	0.7	1.3	3.1	17.7

Table 4. Relationships between physical fitness and CRP, age, and BMI in study subjects

	Physical Fitness	
	r	P
Age	0.07	0.29
Body mass index (BMI)	0.14	0.04
CRP	0.10	0.14

Table 5. Relationship between physical fitness and sex, morbidity, and dietary intake

	Physical Fitness		
	Odd Ratio (OR)	P	95% CI
Sex (female)	1.0	0.97	0.5 to1.8
Physical activity	3.3	<0.001	1.7 to 6.4
Morbidity	0.9	0.77	0.4 to 2.0
Dietary intake			
Caloric intake	2.0	0.52	0.2 to 17.2
Fat intake	0.5	0.02	0.2 to 0.9
Protein intake	0.6	0.31	0.3 to 1.3

Table 6. Multivariate analyses of physical activity and fat intake with physical fitness

	Physical Fitness		
	Odd Ratio (OR)	P	95% CI
Physical Activity	3.2	<0.0001	1.7 to 6.3
Fat Intake	0.5	0.03	0.2 to 0.9

had CRP level > 5 mg/L. CRP levels did not differ by sex, age, and BMI. Mean of CRP concentrations were similar between male and female. We performed an independent samples t test with CRP concentration as the test variable and calculated grouping variable for male and female.

Next, we examined the association of physical fitness with CRP levels using linear regression analysis with physical fitness as the dependent variable; CRP levels and potential confounders as the independent variables. **Tables 4** and **Table 5** show the relationship between physical fitness and CRP levels, age, sex, BMI, physical activity, morbidity, and dietary intake. Linear regression analysis indicated that physical fitness was not correlated with age, BMI, and CRP.

Logistic regression analysis indicated that physical activity was strongly correlated with high physical fitness, did not significantly correlate to caloric and protein intake but showed a significant negative correlation to fat intake (**Table 5**). In a multivariate model, both physical activity (OR=3.2, P<0.0001, 95% CI 1.7 to 6.3) and fat intake (OR=0.5, P=0.03; 95% CI 0.2 to 0.9) were still significantly associated with physical fitness (**Table 6**).

Discussion

General population studies have reported an inverse association between serum CRP levels and self-reported physical activity or physical fitness. These studies suggested that regular physical exercise might lower CRP levels by an anti-inflammatory action.[4,26,27] However, another study assessing the effects of six months' regular exercise training on serum CRP levels in a healthy elderly population showed that on average, although there was an 18% improvement in cardio respiratory fitness in the exercise group, there was no associated change in serum CRP levels. These results were similar for men and women.[21] In our study, we report no inverse association between serum CRP levels and physical fitness in children. There are several possible explanations for this difference. The association between exercise and inflammatory markers observed in other epidemiologic studies may not be causal. The cumulative effects of exercise may influence serum CRP levels over the course of many years, but not by shorter-term changes in exercise levels. A limitation of the current study is individual variability in serum CRP levels. This variability reduces the statistical power of the study and, therefore, a small effect of improved physical fitness on CRP levels cannot be excluded.

The more underweight an individual is, the greater the likelihood of nutrient deficiency and physical problems.[28,29] Moreover, the less the children have BMI level among underweight children, the less the children have physical fitness. High physical fitness is significantly associated with higher BMI among underweight children. Lower BMI can be caused by insufficient calorie and nutrient intake.Weight loss by hypocalorific diets or surgical intervention can reduced CRP levels.[39,40]

Physical activity is a key component of energy balance and is promoted in children as a lifelong positive health behavior, providing a major outlet for daily caloric usage.[2] Our findings suggest a strong association between physical fitness and physical activity among underweight children. Physical activity has to be encouraged among children largely based on the assumption that the behavior will become part of the person's life and carry over to the adult year, where it will help lower the risk of health problems.[2,24,25]

The Third National Health and Nutrition Examination Survey declared that the circulating CRP level is correlated to BMI after adjustment for age, sex, race, or ethnicity among children aged 6–18 yr.[38]

Confirming previous studies, we found that high fat intake is significantly associated with low physical fitness.. Circulating plasma CRP level is elevated in obese subjects, and it is also directly correlated with the amount of body fat, as assessed anthropometrically by BMI and visceral obesity. [36,37]

There are a number of limitations of this study. First, given the cross-sectional design, we cannot overlook the inherent possibility that constitutional and genetic factors may have influenced our findings. Second, we relied on a single baseline blood sample and therefore cannot account for changes in plasma CRP levels that may occur over time. In addition, variability in CRP concentrations can be seen within two weeks of acute inflammatory or infectious episodes.

In conclusion, our study fails to show inverse correlation between physical fitness and CRP levels in underweight children. Significant correlations have been observed between physical fitness with physical activity, and fat intake. The findings of this study suggest that physical fitness in children can be raised by promoting physical activity as part of childhood daily habitual at the family and community levels in addition to the activity conducted in the schools.

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