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Original Article

Correlation between obesity with atopy and family history of atopy in children

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Abstract

Background The prevalence of childhood obesity and atopy has increased in recent decades. Research on links between obesity and atopy has shown varied results. Few previous studies have reported on the significance of family history of atopic disease in children.

Objective To determine correlation between obesity with atopy and family history of atopic disease in children.

Methods This cross-sectional study was conducted from April to September 2010 in the Pediatric Allergy-Immunology subdivision, Hasan Sadikin Hospital. Children aged 6−11 years were divided into four groups of 40 each: obese subjects with and without family history of atopic disease, and normal weight subjects with and without family history of atopic disease. Skin prick test was performed to determine which subjects had atopy. Chi-square test was used to analyze mutual independence, and partial Chi-square test was used to analyze correlation of obesity to atopy and family history of atopic disease in children. Environmental factors, type of childbirth, and pregnancy history were also analyzed as risk factors for atopy.

Results Of 80 obese children with and without family history of atopic disease, 40 (100%) and 38 (95%), respectively, were atopic. Of 80 normal weight children with and without family history of atopic disease, 39 (98%) and 9 (23%), respectively, were atopic. Thus atopy was observed in 126 subjects, while the remaining 34 subjects were non-atopic. Partial test showed a correlation between obesity with atopy and family history of atopic disease ($P < 0.001$). There were no significant differences in risk factors for atopy by group.

Conclusion Obesity correlates with atopy and family history of atopic disease in children. **[Paediatr Indones. 2011;51:227-33]**.

Keywords*: atopy, family history of atopic disease, obesity*

Obesity has become global epidemic. The prevalence of obesity in children aged 6−11 years increased from 4% in the 1970s to 15.3% in 2000.[1,2] Some diseases associated with obesity include type 2 diabetes mellitus, cardiovascular disease, infection, hypertension, sleep apnea, dyslipidemia, depression, asthma, and atopy.[1,3,4] Leptin in obesity has a role in the development of atopy.[3,5,6] Visness *et al*.[7] in the United States reported a significant correlation between obesity and atopy. However, a Hong Kong study by Tin *et al*.[8] showed that obesity was not a risk factor for atopy in children.

Obesity in Indonesia is different from that in the United States, but similar to that of Hong Kong, in that obesity is more common in urban areas of higher socioeconomic class. This urban environment encourages exposure to allergens, such as cockroaches, dust, and mites. Exposure to these allergens may cause greater susceptibility to atopy. Therefore, urban environments in Indonesia increase the risk of both atopy and obesity. Controversies remain on the correlation between obesity and atopy in children. So

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we aimed to determine if obesity correlated with atopy and family history of atopic disease in children.

Methods

We performed a cross-sectional study from April to September 2010 on subjects from 8 private elementary schools in Bandung, Indonesia.

Subjects were children aged 6−11 years with normal weight or obese, according to WHO 2007 guidelines. Based on the formula for determining sample size from family planning operations research,[2,10,11] we calculated the minimum number of subjects needed to be 154. There were 160 children randomly selected and divided into 4 groups. Group 1 comprised of obese children with a family history of atopic disease. Group 2 comprised of normal weight children with a family history of atopic disease. Group 3 comprised of obese children without a family history of atopic disease. Group 4 comprised of normal weight children without a family history of atopic disease. We performed skin prick tests on all subjects. We excluded subjects with drug reactions that disrupted the skin prick test, diffuse dermatological conditions, and dermatographism.

Atopy was defined by positive skin prick test to one of the allergens and formation of an induration with diameter ≥ 3 mm.[9] There were 12 allergens tested, *Blomia tropicalis, Dermatophagoides pteronyssinus, Dermatophagoides farinae, Alternaria alternate, Aspergillus mix,* cocoa, shrimp, soybean, cockroaches, cat dander, egg white, and egg yolk. Obesity was defined as Z-score BMI greater than 3 SD. Normal weight was defined as Z-score BMI of 1 to -2 SD by WHO 2007 references. Family history of atopic disease was ascertained by using the *International Study of Asthma and Allergies in Childhood* (ISAAC) validated questionnaire. Maternal pregnancy and childbirth history, as well as home environmental

Table 1. Characteristics of subjects by group

Characteristics	Group			
	1	2	3	4
	(n=40)	(n=40)	(n=40)	(n=40)
Age, years				
Mean (SD)	9.7 (1.1)	9.7 (1.1)	9.4 (1.5)	9.4 (1.3)
Range	7 –11	7 – 11	6 –11	6 –11
Sex				
Male	25 (63%)	25 (63%)	25 (63%)	25 (63%)
Female	15 (37%)	15 (37%)	15 (37%)	15 (37%)
Mother's education				
Primary	0	2 (5%)	0	1 (2%)
Junior high	3 (8%)	2 (5%)	5 (12%)	6 (15%)
Senior high	16 (40%)	20 (50%)	18 (45%)	22 (55%)
University	21 (52%)	16 (40%)	17 (43%)	11 (28%)
Father's education				
Junior high	1 (2%)	2 (5%)	1 (2%)	0
Senior high	11 (28%)	20 (50%)	17 (43%)	29 (73%)
University	28 (70%)	18 (45%)	22 (55%)	11 (27%)
Family monthly income*				
Low < Rp1,160,000	2 (5%)	6 (15%)	5 (12%)	7 (17%)
Middle Rp1,160,000-2,885,000	12 (30%)	14 (35%)	12 (30%)	18 (46%)
High > Rp2,885,000	26 (65%)	20 (50%)	23 (58%)	15 (37%)

Note: *Source of income: Regional socioeconomic surveilance in West Java Indonesia, 2007.
Rp: Rupiah (Indonesian currency)
Group 1: Obese children with family history of atopic disease.
Group 2: Normal weight children with family history of atopic Disease.
Group 3: Obese children without family history of atopic disease.
Group 4: Normal weight children without family history of atopic disease.

factors were recorded as possible risk factors for atopy. This study was approved by the Ethics Committee of the Medical Faculty, University of Padjajaran, Hasan Sadikin Hospital.

Table 2. Maternal pregnancy and childbirth history by group

	Group				P
	1	2	3	4	
	(n=40)	(n=40)	(n=40)	(n=40)	
Pregnancy, weeks					
< 37	0	0	0	1 (2%)	
37-42	40 (100%)	40 (100%)	40 (100%)	39 (98%)	0.25
Childbirth					
Spontaneous	34 (85%)	34 (85%)	28 (70%)	36 (92%)	
Vacuum	0	0	4 (10%)	1 (2%)	0.4
Forceps	0	1 (2%)	1 (2%)	1 (2%)	
Caesarian birth	6 (15%)	5 (13%)	7 (18%)	2 (4%)	
Birth weight, gm					
< 2,500	0	2 (5%)	1 (2%)	3 (7%)	0.16
≥ 2,500	40 (100%)	38 (95%)	39 (98%)	37 (93%)	

Note: P= Fisher's exact test

Table 3. Environmental factors by group

Environmental Factor	Group				P
	1	2	3	4	
	(n=40)	(n=40)	(n=40)	(n=40)	
Pet in the first year of life					
Yes	11 (27%)	6 (22%)	5 (13%)	5 (13%)	
No	29 (73%)	31 (78%)	35 (87%)	35 (87%)	0.28
Carpet in the first year of life					
Yes	11 (27%)	6 (15%)	6 (15%)	15 (37%)	
No	29 (73%)	34 (85%)	34 (85%	25 (63%)	0.5
Child's bedding					
Cotton	1 (2%)	2 (5%)	2 (5%)	4 (10%)	
Spring bed	39 (98%)	37 (95%)	36 (92%)	38 (90%)	**0.34
Carpet	0	0	1 (3%)	0	
Cigarette exposure					
Yes	20 (50%)	29 (73%)	25 (63%)	19 (73%)	
No	20 (50%)	11 (27%)	15 (37%)	21 (53%)	0.08
Mother smoking during pregnancy					
Yes	1 (2%)	2 (5%)	0	2 (5%)	
No	39 (98%)	38 (95%)	40 (100%)	38 (95%)	**0.36
Breastfeeding					
Mean (SD)	17 (9)	19 (9)	20 (7)	19 (8)	*0.37
Range (months)	(2–36)	(0–26)	(2–24)	(0–24)	
Immunizations					
Complete	40 (100%)	40 (100%)	39 (98%)	40 (100%)	**0.7
Incomplete	0	0	1(2%)	0	
Σ Sibling					
≤ 3	40 (100%)	37 (93%)	39 (98%)	38 (95%)	
>3	0	3 (7%)	(2%)	2 (5%)	**0.46
Antibiotics in the first year of life					
Yes	21 (52.5%)	26 (65%)	24 (60%)	16 (40%)	
No	19 (47.5%)	14 (35%)	16 (40%)	24 (60%)	0.12

Note: P=Chi-square test *P = Kruskal-Wallis test **P= Fisher's exact test

To test the significance of numerical data for more than 2 groups, we used one-way ANOVA on data of normal distribution and the Kruskal-Wallis test for data of non-normal distribution. Chi-square test was used to test the significance of categorical data and Fisher's exact test was used when cell expectation was less than 5. Chi-square test for mutual independence and partial Chi-square test were used to analyze for correlation of obesity to atopy and family history of atopic disease in children. Significance was determined by $P < 0.05$. *Statistical Program for Social Sciences* (SPSS) software version 17 was used in the overall data analysis.

Table 3 shows that there were no significant differences between groups for possible risk factors for atopy, including pet and carpet exposure in the first year of life, cigarette smoke exposure, or use of antibiotics in the first year of life. The Kruskal-Wallis test was used to analyze duration of breastfeeding, and Fisher's exact test was used to eveluate child's bedding material, maternal smoking, immunizations, and number of siblings. Overall, there were no significant differences between groups for all these variables.

Table 4 shows the correlation between obesity, atopy and family history of atopic disease by groups. In the test for partial independence **(Table 5),** obesity was shown to not be independent from atopy and family history of atopic disease. Therefore, obesity correlated with atopy and family history of atopic disease.

Table 4. Correlation between obesity, atopy, and family history of atopic disease by group

	Atopic		Non-atopic		Total	P
	Positive family history of atopic disease	Negative family history of atopic disease	Positive family history of atopic disease	Negative family history of atopic disease		
	N	n	N	n		
Normal weight	39	9	1	31	80	<0.001
Obese	40	38	0	2	80	
Total	79	47	1	33	160	

Note: Test for mutual independence P<0.001

Table 5. Correlation of atopy with obesity and family history of atopic disease by group

	Obese		Normal weight		Total	P
	Positive family history of atopic disease	Negative family history of atopic disease	Positive family history of atopic disease	Negative family history of atopic disease		
	N	n	N	n		
Atopic	40	38	39	9	126	<0.001
Non- atopic	0	2	1	31	34	
Total	40	40	40	40	160	

Note: Test for partial independence p<0.001

Results

We had 160 subjects from 8 private elementary schools in our study. Normal weight and obese children with and without family history of atopic disease were divided into 4 groups, of 40 children each. Subjects' age, gender, and their parents' education and income levels are shown in **Table 1**. Maternal childbirth and pregnancy history, as well as exposure to environmental factors are shown in **Tables 2** and **3**. There were no significant differences between the groups in terms of gestational age at birth, mode of delivery, and birth weight.

Discussion

Our study showed a correlation of obesity, atopy and family history of atopic disease and a correlation between obesity to atopy and family history of atopic

disease. Previous studies by Visness *et al*.[7] in the United States and Tin *et al*.[8] in Hong Kong showed different results.[7,8] Visness *et al*.[7] had a larger sample size and showed a correlation between obesity and atopy, as well as an analysis of risk factors for atopy. In contrast, Tin *et al*.[8] showed no correlation between obesity and atopy in children, but a limitation in their study was the lack of environmental data related to atopy. For our purposes, we divided subjects into four groups based on family history of atopic disease, while the 2 previous studies did not. Family history of atopic disease has been shown to contribute to the development of atopy.[12] Genetic factors for atopy have been difficult to identify, but genetic polymorphisms in the IgE receptor β chain (Fc RI-β) located on chromosome 11q12-13, as well as the human leukocyte antigen (HLA) class II may be involved. It is thought that specific IgE production is associated with HLA class II, and genetic polymorphisms of cytokine IL-4 may cause the formation of specific IgE.[13]

It is possible that obesity is predisposing factor for atopy or there is a common factor that predisposes children to both obesity and atopy. Leptin resistance in the leptin receptor of obese people maybe one such factor. The cause of leptin resistance in obesity is not clear, but hypotheses include defective receptors, receptor polymorphisms, imbalance of free leptin and bound leptin, or leptin signaling disruption. Leptin resistance leads to suppression of TH1 cytokine production, but increased secretion of TH2 cytokines, such as IL-4, IL-5, and IL-13. IL-4 secretion may cause B lymphocytes to produce specific IgE, a marker for atopy.[14-16]

It has been observed that obesity in Indonesia is more prevalent among wealthier people. The correlation between obesity and atopy may be related to hygiene. Children from low socioeconomic backgrounds tend to have a higher risk of infections, leading to a lower risk for atopy. In contrast, obese children in Indonesia who come from higher socioeconomic backgrounds tend to have a lower risk of infections, leading to a higher risk for atopy.[12,17]

We also found a correlation between atopy with obesity and family history of atopic disease. Koning *et al*.[18] reported that the risk of developing atopy was 20−40% if one parent had atopic disease. This risk increased to 60−80% if both parents had atopic disease. Similarly, we found a correlation of atopy and family history of atopic disease. In addition, leptin resistance or genetic pleiotropy may explain the correlation of obesity with atopy. Genetic pleiotropy occurs when a gene or set of genes influences two or more traits. Hallstrand *et al*. reported covariation between asthma and obesity to be predominantly caused by a shared genetic risk factor for both conditions.[19]

Out of 80 normal weight children, we found 39 atopic children with a family history of atopic disease. As previously stated, atopic disease in one or both parents increases the risk of atopy in children. In addition, if siblings had atopy, the risk of developing atopy was 20−30%. However, if neither parent had atopic disease, the risk of developing atopy was 10%.[18] One explanation for our high degree of family history of atopy in normal weight, atopic children may be that exposure to environmental allergens was higher in our subjects. Exposure to allergens such as dust mites, cockroaches, and pollutants has been shown to be an important environmental factor for development of atopy, so the risk for atopy in this group was higher than previously reported.

There was only one child with a family history of atopic disease of the 80 normal weight children who did not develop atopy. This child was a firstborn, term infant product of spontaneous vaginal birth. He had two siblings, was breastfed 24 months, and had no exposure to animals and carpet in the first year of life. The mother did not smoke during pregnancy nor was there exposure to tobacco smoke. He had complete immunizations and received no antibiotics in the first year of life.

Of 40 obese subjects without family history of atopic disease, there were 38 (95%) with atopy. Similarly, previous studies have shown a correlation between obesity and atopy.[7,16,20]

A limitation of our study was that family history of atopic disease was only confirmed by ISAAC questionnaire. Skin prick test to determine atopy should be performed on parents and siblings to confirm atopy in family members in future studies.

Maternal pregnancy and childbirth history, including infant gestational age, mode of delivery, and birth weight may influence the incidence of atopy. Premature pregnancy and low birth weight (<2,500 grams) had been previously shown to decrease the risk of atopy, while caesarian section was reported

to increase the incidence of atopy.[21] Environmental factors also may affect the incidence of atopy. However, we observed no differences in incidence of atopy among the groups due to environmental factors. Exposure to allergens such as dust mites from carpet or bedding and pets in the first year of life increases the risk of atopy, as the human immune system in the first year of life is relatively immature. The birth to 24 month period has been considered to be a 'window period' for increased risk of allergic sensitization and atopic disease.[22,23] All environmental factors in our study were collected using the ISAAC questionnaire. Since no difference was found between the 4 groups, environmental factors were deemed to not affect our results.

Overall, we found a correlation of obesity, atopy, and family history of atopic disease in children. Obesity was correlated with atopy and family history of atopic disease. In addition, atopy correlated with obesity and family history of atopic disease. Knowing these correlations may be a first step in developing prevention programs for the risk of atopy in children.

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