J. Microbiol. Biotechnol. (2015), 25(12), 2169–2172
http://dx.doi.org/10.4014/jmb.1509.09003

jmb

Tracking Study About Adenovirus 36 Infection: Increase of Adiposity

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Received: September 2, 2015
Revised: September 18, 2015
Accepted: September 25, 2015

First published online
October 2, 2015

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pISSN 1017-7825, eISSN 1738-8872

This study investigated the cross-sectional and longitudinal association between adenovirus 36 (Ad36) and obesity in 79 Korean adolescent boys over 1 year. We analyzed the changes in body composition and metabolic risk factors according to the presence of Ad36 antibodies. Ad36 antibodies in serum were detected using the constant virus-decreasing serum method. We found that the fat percentage and fasting insulin in the Ad36-seropositive group were greater than the Ad36-seronegative group. These results suggest that Ad36 infection is associated with an increase of adiposity, and the experience of Ad36 infection may affect the future fat gain of adolescents.

Keywords: Adenovirus 36, body composition, metabolic risk factor, adiposity

Obesity is a risk factor that leads to chronic diseases such as cardiovascular disease, type 2 diabetes, and cancer [9, 11]. Despite the many strategies available for obesity prevention, the prevalence of obesity is increasing in most parts of the world [17]. Thus, obesity is one of the most pressing global health issues.

Recently, infectious agents such as gut microbiota and some viruses have been identified as obesity-inducing agents. Na and Nam [16]. found that Ad36 infection is associated with an increase of human body weight or an increase of reproductive fat pad in mice. In particular, the human adenovirus 36 (Ad36) has been shown to be the only adipogenic virus that is associated with the human obese state [1, 2, 5, 14, 15]. Epidemiological studies have shown that the prevalence of Ad36 infection in obese and nonobese individuals in Korea is 28% and 13%, respectively [14]. Furthermore, it has been documented that the Ad36 antibody status is related to the obese state [3, 18]. However, these previous studies only examined the temporal association between Ad36 infection and adiposity. Therefore, the present study aimed at identifying a longitudinal association between adenovirus infection and adiposity over 1 year among Korean adolescent boys.

Seventy-nine Korean boys aged 14 years old were recruited and they were followed for 1 year from 2012 to 2013. All boys participated both in 2012 and 2013. To investigate the change (Δ) of body composition and metabolic risk factors in serum over 1 year according to the presence of Ad36 antibodies, we categorized the study participants into two groups as follow; Past Ad36 infection (+) and Past Ad36 infection (-). Informed written consents were obtained from their parents or guardians before participation of the adolescent boys in this study. The study protocol was approved by the Institutional Review Board of Ewha Womans University (ECT 11-11-06).

Body weight and height were measured using an automatic height-weight scale, wearing only underwear and no shoes. Body mass index (BMI) was calculated as the weight (kg) divided by the height squared (m^2). Waist circumference was measured using the line at the point of the middle waist, between the lowest margin of the 12^{th} rib and the middle part of the iliac crest, at minimal respiration. Fat mass (kg), fat percentage (%), and fat-free mass (kg) were measured using bioelectrical impedance analysis (InBody 720; Biospace Co., Ltd., Seoul, Korea) [4]. After a 12 h overnight fast, blood samples were obtained from the antecubital vein of each participant by venipuncture and were immediately centrifuged, aliquoted, and frozen at –80°C until analysis. Total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglyceride, and fasting glucose levels in the plasma were measured by enzymatic methods using a Hitachi 7600-110 automated chemistry analyzer (Hitachi, Tokyo, Japan) [7]. Low-density lipoprotein cholesterol (LDL-C) levels were calculated using the following formula: LDL-C = total cholesterol – HDL-C – (triglyceride / 5). Fasting insulin level was measured *via* electroluminescence immunoassay (Roche, Indianapolis, IN, USA) [19].

Ad36 antibodies in serum samples were detected using the constant virus-decreasing serum method as described previously [1]. Serum samples that did not induce a cytopathic effect in dilutions of 1:8 or more were taken as being positive for the presence of neutralizing antibodies against Ad36 and as evidence of erstwhile Ad36 infection [1, 14].

We analyzed the data collected from cross-sectional (observation at one specific point) and longitudinal (follow-up observation over time) studies [13]. All analyses were performed using GraphPad Prism software (ver. 5.01; GraphPad, La Jolla, CA, USA). Data are expressed as the mean ± SEM. The differences in body composition and metabolic risk factors according to the presence of serum Ad36 antibodies between 2012 and 2013 were evaluated using a Wilcoxon rank sum test. Statistical significance was set at $p < 0.05$.

Body composition and metabolic risk factors according to the presence of Ad36 antibody are shown in Table 1. The prevalence of Ad36 antibody was 21.5% and 13.9% in 2012 and 2013, respectively. In a cross-sectional analysis, the fat percentage ($p = 0.02$) and fasting insulin level ($p = 0.01$) were significantly higher in the Ad36-seropositive group compared with the Ad36-seronegative group in 2013

Table 1. Body composition and metabolic risk factors according to the presence of the Ad36 antibody.

	2012 Ad36-seronegative(-) (*n* = 62)		2012 Ad36-seropositive(+) (*n* = 17)			2013 Ad36-seronegative(-) (*n* = 68)		2013 Ad36-seropositive(+) (*n* = 11)		
	Mean	SEM	Mean	SEM	*P*-value	Mean	SEM	Mean	SEM	*P*-value
Demographics										
Gender / Age	14.43	0.06	14.28	0.15	0.18	15.42	0.06	15.28	0.18	0.28
Body composition										
Height, cm	165.55	0.83	165.07	1.09	0.59	169.63	0.63	170.07	1.22	0.40
Body weight, kg	58.40	1.34	58.22	1.65	0.78	60.81	1.17	67.10	3.70	1.00
BMI, kg/m^2	21.28	0.45	21.37	0.59	1.00	21.12	0.38	23.27	1.42	0.28
Waist circumference, cm	75.10	1.22	76.35	2.00	0.81	74.45	2.94	81.05	1.01	0.40
Fat mass, kg	11.29	0.80	11.77	1.28	0.74	11.00	0.71	15.52	2.73	0.26
Fat percentage, %	18.31	0.99	19.58	1.68	0.57	17.15	0.83	21.77	2.75	0.02*
Fat-free mass, kg	47.12	0.75	46.45	0.77	0.34	50.03	0.61	51.35	1.28	0.70
Metabolic risk factor										
Total cholesterol, mg/dl	160.82	4.48	144.29	4.14	0.33	152.94	3.04	160.18	14.33	0.64
HDL-C, mg/dl	53.73	1.43	51.53	2.24	0.49	60.40	1.48	58.73	4.78	0.90
LDL-C, mg/dl	91.21	3.48	83.35	6.05	0.26	88.09	2.25	88.55	11.93	0.57
Triglyceride, mg/dl	73.48	11.07	71.41	6.72	0.74	98.40	10.37	103.91	9.07	0.64
Fasting insulin, mU/l	9.26	2.17	11.92	0.82	0.24	13.87	3.68	21.39	0.94	0.01*
Fasting glucose, mg/dl	99.06	0.82	96.65	2.10	0.18	95.90	0.86	97.91	1.81	0.14

Significant differences are indicated by *$p < 0.05$ (Ad36-seropositive *vs*. Ad36-seronegative).

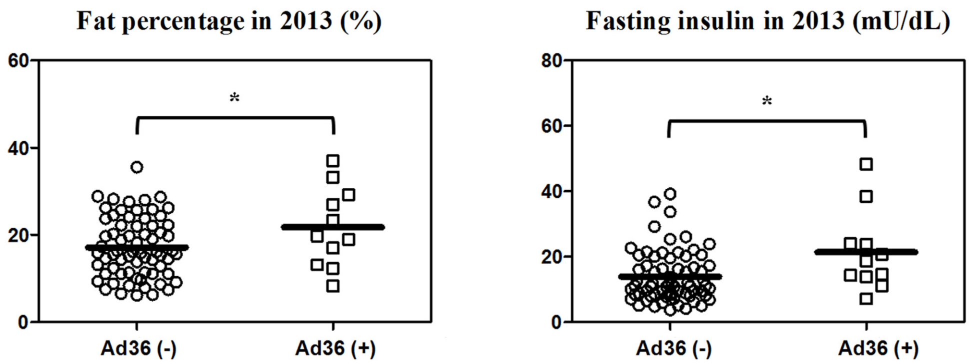

Fig. 1. Cross-sectional analysis of fat percentage (%) and fasting insulin (mU/dl) in 2013.
Antibody prevalence against Ad36 represented by Ad36 (-) or Ad36 (+). $*p < 0.05$.

(Table 1 and Fig. 1). However, body weight, BMI, waist circumference, fat mass, and lipid and glucose levels did not differ between the two groups.

Moreover, we observed the changes (Δ) in body composition and metabolic parameters for 1 year between 2012 and 2013 (Fig. 2). The ΔBody weight, ΔBMI, ΔFat mass, and ΔFat percentage seemed to be higher in Past Ad36 infection (+) group than the Past Ad36 infection (-) group, even though the changes did not reach statistical significance.

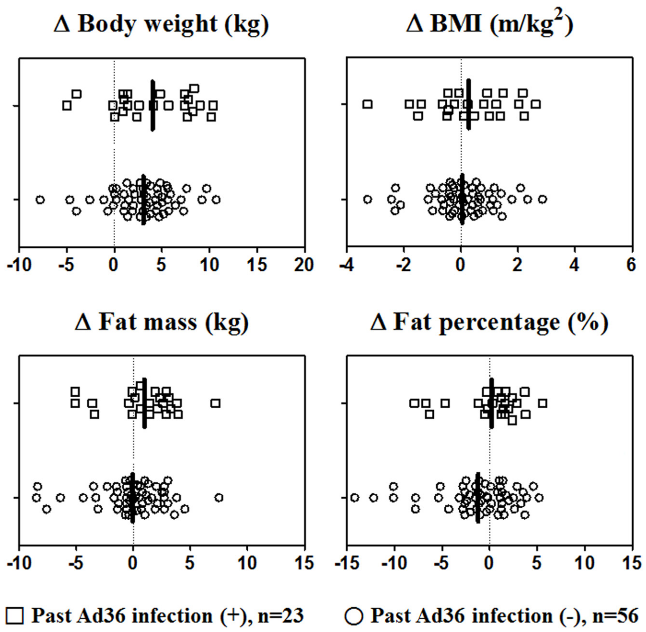

Fig. 2. Distribution of ΔBody weight, ΔBMI, ΔFat mass, and ΔFat percentage according to the experience of the Ad36 infection in both 2012 and 2013; Past Ad36 infection (+) and Past Ad36 infection (-).

This study found that the percentage of body fat was significantly greater in the Ad36-seropositive group than in the Ad36-seronegative group in a cross-sectional analysis. This result suggests that Ad36 infection is associated with greater adiposity. Similarly, Atkinson *et al.* [2] documented that Ad36 infection was correlated with increased body weight in Americans. Lin *et al.* [12] also showed that past Ad36 infection was associated with long-term changes in adiposity among Mexican Americans. The suggested mechanism for this effect is Ad36-mediated glucose uptake *via* Ras-PI3K-Akt axis-dependent Glut4 translocation [6]. In our study, changes in body composition, such as body fat mass and BMI, over 1 year seemed to increase with past Ad36 infection, albeit without statistical significance. The lack of association between the experience of Ad36 infection and changes in adiposity over 1 year in this study may be related to the natural body changes, such as pubertal growth and sexual maturity, during adolescence. Hormones may also change to promote growth and development during adolescence. The pubertal growth spurt begins between the ages of 10 and 15 years in boys [8], which is the age period of Korean adolescent boys.

As expected, insulin levels increased in the presence of Ad36 seropositivity because greater adiposity is associated with an insulin dysfunction [10]. However, other lipid levels did not change according to Ad36 infection in Korean adolescent boys, although body fat increased in the presence of Ad36 infection. These data are consistent with our previous report [14]. In fact, some studies reported a reduction in lipid levels in the presence of Ad36 infection. Atkinson *et al*. [2] showed that Ad36 induces an obese state while paradoxically reducing the serum levels of triglycerides and cholesterol in Caucasian adults. Differences in the race or age of subjects among studies may be responsible for the inconsistent results obtained.

This study had a limitation. We did not measure other potential risk factors, such as maturational status or hormonal changes, which might have affected adiposity levels in adolescent boys. Nonetheless, to the best of our knowledge, this was the first longitudinal study to identify a longitudinal association between Ad36 infection and body fat mass in Asian adolescents.

In conclusion, Ad36 seropositivity was associated with an increase of body fat in Korean adolescent boys. This study suggests that the experience of Ad36 infection may affect the future fat gain of adolescent boys. In the future, a larger-scale study over a longer period should be conducted to evaluate the longitudinal association between Ad36 infection and adiposity/metabolic risk factors during puberty.

Acknowledgments

This work was supported by the Basic Science Research Program of the National Research Foundation of Korea (2012R1A1A2039819 and 2015M3A9B5030116), and the Korean Health Technology R&D Project, Ministry of Health & Welfare (HI13C0826). We thank Dr. Ha-Na Na for excellent guidance in the serum-neutralizing assay.

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