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Iwona Bil-Lula[1, A, C, D], Sylwia Stąpor[2, B], Anna Krzywonos-Zawadzka[1, B], Mieczysław Woźniak[1, 3, E, F]

Is There any Link Between Visceral Obesity and Adenovirus Infections in the Polish Population?*

[1] Department of Clinical Chemistry, Wroclaw Medical University, Poland
[2] Laboratory of Haematological and Transplant Diagnostics, University Hospital No 1, Wroclaw, Poland
[3] Department of Pharmacology, University of Saskatchewan, Saskatoon, Canada

A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of article; **G** – other

Abstract

Background. Obesity is a chronic disease of multiple etiologies. Alongside the traditionally recognized causes of obesity, such as genetic inheritance and behaviour/environmental factors, in recent years adenoviral infections have been considered as a possible cause of obesity. Although numerous studies involving animals confirmed a strong relation between adenoviral infection and increased predisposition to obesity, an association of AdVs with human obesity has not been established conclusively.
Objectives. The main aim of this study was to establish an association between seroprevalence of adenoviruses and obesity in the Polish population.
Material and Methods. Eighty-six subjects (both obese and non-obese) participated in this study. The presence and the concentration of typically non-specific antibodies to human adenoviruses in serum were determined using ELISA immunoassay. A serum lipid-profile was evaluated using commercial tests.
Results. A total of 89.5% of subjects were positive for AdV-IgG (n = 77); 10.5% (n = 9) were negative. In non-obese or lean AdV-IgG positive subjects, the parameters as: body weight (63.5 vs. 57.0, p = 0.02), WHR (0.77 vs. 0.73, p = 0.02) and waist circumference (74.5 vs. 69.0, p = 0.01) were significantly higher as AdV-IgG negative individuals.
Conclusions. We showed that there is an association between the presence of type unspecific anti-AdV antibodies in the serum and elevated body weight, BMI, WHR and waist circumference in lean and non-obese subjects from the Polish population (**Adv Clin Exp Med 2014, 23, 3, 415–422**).

Key words: adenoviruses, body mass index, waist-hip ratio, antibodies, obesity due to infection.

Obesity is recognized as a serious chronic disease which may have an adverse influence on human health, leading to reduced life expectancy and decreased health due to high risk for cardiovascular diseases and diabetes, orthopaedic problems and mental disorders [1]. The permanently growing number of obese people in all countries, irrespective of the economic status, confirms that this process is alarming. Among the leading contributing factors, such as genetic inheritance, behavior and environmental causes, in recent years viral infections have been considered as a possible cause of obesity. There are some reports suggesting a significant role of adenoviruses in the development of obesity [2–9]. Adenoviruses are a large family of DNA viruses including at least 54 antigenic types of human adenoviruses. They are ubiquitous in the environment, very easily transmitted via respiratory, droplet, venereal and fecal–oral routes [9]; hence, they have a worldwide distribution. Adenoviruses are common among all age groups, with a higher frequency in children below the age of five years [10, 11]. More than half of them have been recognized as causing human illness. In a series of papers over the last ten years, the group of Dhurandhar (USA) demonstrated that AdV36 is

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causally and correlatively associated with increased adiposity and altered metabolic profile in experimentally infected chickens, mice and non-human primates [9]. They indicated that AdV36 has potent pro-adipogenic effects. Currently, particular attention is paid to human adenoviruses: AdV5, AdV9, AdV31, AdV36, AdV37 and avian adenovirus SMAM-1 which might produce a syndrome of visceral obesity [3, 5, 7, 8, 12–15]. Although numerous studies involving animals confirmed a strong relation between adenoviral infection and increased predisposition to excessive accumulation of body fat in the abdominal viscera, there are only few reports on the role of these viruses in the development of obesity in humans and their role has not been established conclusively. Currently, the association between adenovirus infection and obesity has been confirmed in pediatric and adult subjects from Korea [2, 4, 16] adults from Italy [17] and USA [6, 18], but not in studies on Dutch and Belgium groups [19, 20]. For this reason we decided to extend the comparative virological studies on the Polish population in view of the worldwide distribution of adenoviruses and rising problem of obesity also in Poland. Therefore, the main aim of this study was to establish an association between seroprevalence of adenoviruses and obesity in the Polish population and evaluation if the presence of anti-adenovirus antibodies class IgG (against group-specific determinants on the hexon component) in a serum is associated with lipid disorders, increased body fat and weight gain.

Material and Methods

Study Groups and Clinical Materials

Eighty six patients participated in this study. Obese (50%) were recruited by the Clinic of General Surgery and Surgical Oncology, University Hospital in Wroclaw and non-obese volunteers were collected by the Department of Clinical Chemistry, Wroclaw Medical University in Poland. Written informed consent was obtained for a collection of blood samples. The study was approved by the Ethics Boards of the Wroclaw Medical University (no. 115/2011). Study subjects were informed in details about the purpose and principles of this study. Routine measurements of height, weight, and waist circumference were taken by a nurse in triplicate in order to obtain reliable results. Essential data of medical history was also collected. All serum/plasma samples were frozen in aliquots at –80°C until testing.

Classification of Obese Subjects

Obesity was determined by body mass index (BMI) and the waist-to-hip ratio (WHR). Subjects with BMI ≥ 30 kg/m^2 were classified as obese and < 30 kg/m^2 as non-obese (WHO, 2007) [1]. BMI ≥ 25 kg/m^2 was considered as overweight and < 25 kg/m^2 as thinness. Since this does not distinguish between weight associated with excess of muscle or fat, waist circumference was also evaluated. In accordance with the recommendations of the International Federation of Diabetes (2005) [21], women and men were classified as patients with visceral adiposity based on a waist circumference ≥ 80 (WHR > 0.8) and ≥ 94 cm (WHR > 1.0) respectively.

Determination of Serum Anti-AdV Antibodies

The quantitative analyzes of type-nonspecific antibodies to human adenoviruses were performed by enzyme immunoassay (GenWay Biotech, Inc., San Diego, CA; cat. no. 40-375-380004) according to the manufacturer's instruction. Briefly, serum IgG antibodies bound the adenovirus antigen (type-nonspecific) immobilized on the 96 well plates. The complex was detected by anti-human-IgG peroxidase conjugate and colorimetric measurement was carried out. The values below the cut-off standard ± 20% (10 ± 2 IU/mL) (human serum diluted with PBS, contains a low concentration of IgG antibodies against adenovirus) were considered as negative. If the value of the sample were higher than the cut-off standard ± 20%, it was considered as a positive result.

Measurement of Serum Lipids

Serum samples were analyzed for cholesterol, triglycerides, high-density lipoproteins (HDL--Chol) and low-density lipoproteins (LDL-Chol) using commercial tests from BioMaxima (Lublin, Poland, cat. no 1-023-0200, 1-053-0200, 1-029--0200, 1-056-0060, respectively). Lipids concentrations were assessed according to the manufacturer`s instructions. Briefly, measurements of total serum cholesterol (TChol) were performed by cholesterol esterase and cholesterol oxidase phenol aminoantipyrine enzymatic assay with spectrophotometric detection. The assessment of triglicerydes was based on glycerol-3-phosphate oxidase phenol aminoantipyrine enzymatic method. HDL-Chol was estimated in supernatant obtained from the precipitation other lipid factions with phosphotungstic acid, by means of enzymatic method used for TChol. Measurements

of LDL-Chol were performed by enzymatic assay for TChol, after blocking chylomicrons, very low-density lipoproteins (VLDL-Chol) and HDL-Chol. Each sample was analyzed in duplicate.

Measurement of Leptin and CRP Concentrations

Leptin and C-reactive protein (CRP) concentrations were assayed in plasma obtained from fasting blood samples collected in the morning. Concentrations of leptin/CRP were determined by using Human Leptin ELISA and Human CRP Elisa Kits (RayBio, USA; cat. no. ELH-Leptin-001 and ELH-CRP-001, respectively) according to the manufacturer's instructions. Each plasma sample was analyzed in duplicate.

Statistical Analysis

Statistical analysis was performed using Statistica v.8.0 (StatSoft, Krakow, Poland). The Chi square test or Fisher's exact test were used for a multi-variant analysis. The means of the variables were compared using Test *T*, Mann-Whitney or Wald-Wolfowitz test in AdV-IgG positive verse verse AdV-IgG negative subjects. The correlations of continuous variables were analyzed by means of the Spearman correlation test. We also determined whether antibodies status was associated with the severity of obesity by means of correspondence analysis. P value of $< .05$ was considered to be significant.

Results

The prevalence of adenovirus IgG in the whole study group (obese and non-obese, n = 86) was 89.5%. The prevalence of AdV-IgG in obese subjects was similar to that in non-obese subjects, $p > 0.05$. In the whole cohort, males were much more vulnerable to AdV infection than females, $p = 0.03$. The median weight of AdV-IgG positive subjects was similar to the median weight of AdV-IgG negative subjects (Table 1). Taking into account AdV-IgG positivity, other anthropometric indicators also did not differ. Median BMI, WHR and waist circumference in subjects AdV-IgG positive were similar to that found in seronegative individuals, $p > 0.05$. The analysis of the whole cohort has also revealed no difference in serum lipids levels between AdV-IgG positive and AdV-IgG negative participants (Table 1). Although the serum leptin level and CRP

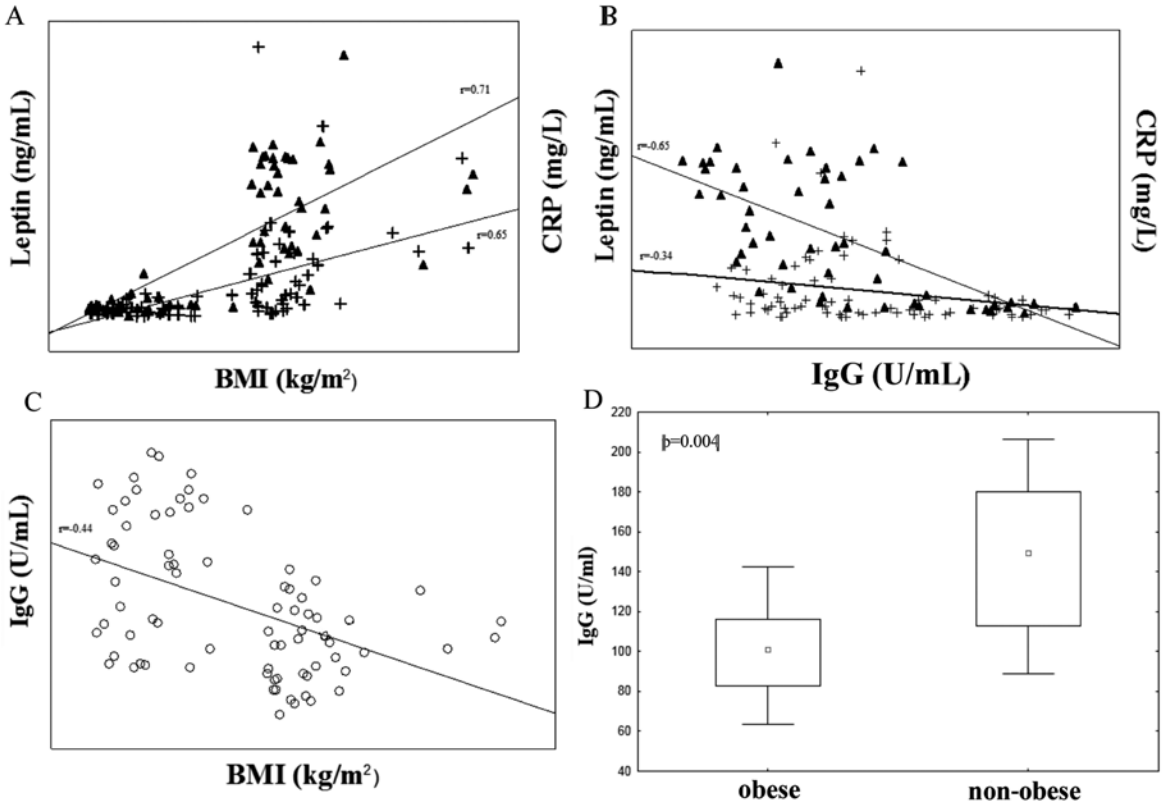

Fig. 1. The positive correlation of BMI and CRP/leptin level in serum (A) and the negative correlation of IgG and CRP/leptin level in serum (B) in the whole study group (obese and non-obese, n = 86, $p < 0.05$); the negative correlation between level of plasma IgG and BMI in both obese and non-obese subjects, $p < 0.05$ (C); median concentration of serum IgG in obese vs non-obese, $p = 0.0000$

Table 1. Characteristic of AdV-IgG positive/negative subjects divided into obese and non-obese participants

	All participants, n = 86			Obese, n = 43			Non-obese, n = 43		
Characteristic	**IgG positive**	**IgG negative**	**p-value**	**IgG positive**	**IgG negative**	**p-value**	**IgG positive**	**IgG negative**	**p-value**
No of subjects, (%)	77 (89.5)	9 (10.5)		39 (90.7)	4 (9.3)		41 (95.3)	2 (4.7)	
Gender, no. (%)									
Male	27 (100)	0 (0)	0.03*	16 (100)	0 (0)	0.04*	11 (100)	0 (0)	0.16
Female	50 (84.7)	9 (15.3)		23 (85.2)	4 (14.8)		27 (84.4)	5 (15.6)	
Weight, median (range), kg	78.0 (48.0–153.7)	78.2 (57.0–90.6)	0.78	94.0 (68.4–153.8)	84.8 (72.5–90.6)	0.15	63.5 (48.0–86.0)	57.0 (49.0–64.0)	0.02*
BMI, median (range) kg/m^2	27.4 (18.1–46.3)	31.1 (18.8–35.8)	0.66	32.5 (30.0–46.3)	32.4 (30.9–35.8)	0.85	21.7 (18.1–28.7)	19.6 (18.8–20.4)	0.07†
WHR, median (range)	0.87 (0.7–1.1)	0.84 (0.7–0.9)	0.23	0.94 (0.7–1.1)	0.86 (0.8–0.9)	0.003*	0.77 (0.7–1.0)	0.73 (0.6–0.7)	0.02*
Waist circumference, median (range), cm	91.2 (62.0–134.0)	81.0 (62.0–103.0)	0.10	104.4 (80.0–134.0)	97.2 (92.0–103.0)	0.09	74.5 (62.0–95.0)	69.0 (62.0–71.0)	0.01*
Total cholesterol, mean ± s.d., mg/dL	184.9 (96.6–301.4)	193.5 (120.2–253.6	0.65	206.0 (145.2–301.6)	214.4 (189.9–253.6)	0.62	164.1 (96.6–229.9)	160.8 (120.2–191.9)	0.81
Triglicerydes, median (range), mg/dL	100.4 (35.8–524.9	105.8 (56.8–182.0)	0.69	119.8 (55.5–524.9)	105.8 (85.5–166.7)	0.47	53.6 (40.2–182.0)	71.3 (35.7–124.1)	0.67
HDL, median (range), mg/dL	52.3 (32.8–179.4)	58.2 (46.0–90.9)	0.47	45.1 (32.8–179.4)	57.1 (46.0–90.8)	0.10	60.6 (33.6–85.2)	65.0 (52.7–74.0)	0.37
LDL, mean ± s.d., mg/dL	133.1 (45.4–212.1)	121.9 (65.9–167.8)	0.49	145.1 (87.9–212.1)	140.6 (112.3–167.8)	0.74	123.4 (45.4–205.5)	84.4 (65.9–102.9)	0.15
Leptin, median (range), ng/mL	7.7 (1.1–165.3)	19.8 (3.9–55.5)	0.18	22.4 (2.8–165.3)	36.8 (19.6–55.5)	0.27	4.1 (1.1–14.8)	4.7 (3.9–5.3)	0.9
CRP, median (range), mg/L	5.9 (0.5–22.1)	7.2 (1.3–12.6)	0.84	10.4 (2.6–22.1)	10.2 (7,5–12.1)	0.90	1.2 (0.5–3.9)	1.3 (1.3–1.3)	0.79

IgG – immunoglobulins klas G; BMI – body mass index; WHR – waist-hip ratio; HDL – high density cholesterol; LDL – low density cholesterol; * – $p < 0.05$; † – close to statistical significance; SD – standard deviation.

Table 2. Characteristic of AdV-IgG positive/negative subjects divided into obese/overweight and lean participants

	Obese/Overweight participants (n = 47)			Lean participants (n = 39)		
Characteristic	**IgG positive**	**IgG negative**	**p-value**	**IgG positive**	**IgG negative**	**p-value**
No of subjects, (%)	43 (91.5)	4 (8.5)		34 (87.2)	5 (12.8)	
Gender, no. (%)						
Male	18.0 (38.3)	0 (0)	0.09	9 (23.1)	0 (0)	0.18
Female	25 (53.2)	4 (8.5)		25 (64.1)	5 (12.8)	
Weight, median (range), kg	90.8 (66.0–153.7)	84.7 (72.5–90.6)	0.27	61.0 (48.0–86.0)	57.0 (49.0–64.0)	0.04*
BMI, median (range) kg/m^2	32.2 (25.6–46.3)	32.4 (30.9–35.8)	0.64	21.4 (18.1–24.8)	19.8 (18.2–21.6)	0.05*
WHR, median (range)	0.92 (0.7–1.1)	0.86 (0.8–0.9)	0.006*	0.77 (0.7–1.0)	0.73 (0.6–0.7)	0.03*
Waist circumference, median (range), cm	104.0 (80.0–134.0)	97.0 (92.0–103.0)	0.24	73.5 (62.0–95.0)	69.0 (62.0–71.0)	0.02*
Total cholesterol, mean ± s.d., mg/dL	204.1 (145.2–301.4)	214.4 (189.9–253.6)	0.53	162.2 (96.5–229.9)	160.8 (120.2–191.9)	0.92
Triglicerydes, median (range), mg/dL	119.7 (56.5–524.9	105.8 (85.5–166.7)	0.59	68.9 (35.8–224.1)	59.7 (40.2–182.0)	0.95
HDL, median (range), mg/dL	47.8 (32.8–179.4)	57.1 (46.0–90.9)	0.14	60.8 (33.6–85.2)	65.0 (52.7–74.0)	0.39
LDL, mean ± s.d., mg/dL	145.0 (87.9–212.1)	140.6 (112.3–167.8)	0.92	119.4 (45.4–205.5)	104.1 (65.9–144.6)	0.31
Leptin, median (range), ng/mL	16.9 (1.3–165.3)	36.8 (16.6–55.5)	0.19	4.6 (1.1–14.8)	3.5 (2.5–5.3)	0.49
CRP, median (range), mg/L	9.6 (1.2–22.1)	10.2 (7.5–12.6)	0.68	1.1 (0.5–3.9)	1.3 (1.1–1.8)	0.04*

IgG – immunoglobulins klas G; BMI – body mass index; WHR – waist-hip ratio; HDL – high density cholesterol; LDL – low density; * – $p < 0.05$; † – close to statistical significance; SD – standard deviation.

level in obese subjects were significantly higher ($p = 0.000$) than in non-obese subjects, the leptin and CRP levels in the plasma samples of AdV-IgG positive were similar to plasma levels of leptin and CRP in AdV-IgG negative subjects, $p > 0.05$. The correlation coefficient confirmed a positive association for parameters: CRP/BMI, $r = 0.71$ ($p < 0.05$) and leptin/BMI, $r = 0.65$, but reverse correlation for parameters: CRP/IgG, $r = -0.65$ ($p < 0.05$), leptin/ /IgG, $r = -0.34$ (Fig. 1 A, B) and IgG/BMI, $r = -0.44$ ($p < 0.05$) (Fig. 1C), respectively.

A similar analysis was done separately in the group of obese (n = 43) and non-obese subjects (n = 43) (Table 1). In the group of obese subjects, we observed a higher prevalence of antibodies in males in comparison to females, $p > 0.05$. Interestingly, we noticed significantly higher WHR in obese AdV-IgG positive in comparison to obese AdV-IgG negative, $p = 0.003$. The same association was observed in non-obese AdV-IgG positive verse non-obese AdV-IgG negative, $p = 0.02$. AdV-IgG positive non-obese subjects had also a greater median of waist circumference than IdV-IgG negative subjects, $p = 0.01$. Moreover, non-obese seropositive subjects were also significantly heavier than their seronegative counterparts, $p = 0.02$. The median BMI of non-obese AdV-IgG positive adults was greater than was seronegativity and this association was close to statistical significance, $p = 0.07$. Increasing the sample size would clarify the significance of this difference. We also evaluated the serum level of AdV-IgG antibodies and we noticed much higher IgG levels in non-obese than in obese participants: median 148.2 U/mL (89.0–206.5) vs. 101.3 U/mL (63.3–142.6), $p = 0.0004$ (Fig. 1D) and in lean subjects in comparison to obese/overweight: median, 149.6 U/mL (89.0–206.6) vs. 101.3 U/mL (63.4–181.5), $p = 0.0003$, respectively.

We analyzed whether the presence of AdV-IgG antibodies in the serum is associated with changes in serum lipid profile. We noticed that AdV infection was not accompanied by changes of total cholesterol, triglicerydes, HDL-Chol and LDL-Chol in serum both in the whole study group (obese and non-obese together) and separately in obese and non-obese groups, $p > 0.05$ (Table 1).

In the third analysis we had taken into consideration if a combined group of subjects who are obese or overweight (BMI $\geq$ 25 kg/m^2) is associated with the presence of AdV-IgG antibodies. The prevalence of AdV-IgG antibodies in obese/overweight subjects was similar to lean counterparts and WHR in both analyzed groups was higher in AdV-IgG positive subjects than in AdV-IgG negative subjects, $p = 0.006$ and $p = 0.03$, respectively (Table 2). In the group of lean participants, AdV-IgG positive individuals also revealed higher median weight, BMI and waist circumference than did AdV-IgG negative counterparts, $p < 0.05$. The median CRP in the plasma of lean AdV-IgG negative was higher in comparison to AdV-IgG positives, $p = 0.04$.

Discussion

Adenovirus infections were linked to obesity in animal models and in humans. Experimental studies involving chickens, mice, sheep, goat, dogs, rats and hamsters have shown that AdV infection may lead to greater spontaneous differentiation of preadipocytes into mature fat cells, reduced leptin secretion, higher lipid accumulation in adipocytes combined with low levels of serum cholesterol and triglycerides [3, 18, 22, 23]. Nevertheless, a causative role of adenoviral infections in obesity is a relatively novel conception and data reported so far is still controversial and distinct. On this basis the main aim of this study was to evaluate the prevalence of AdV infections in the cohort recruited from the Polish population and to assess the association of adenoviruses and obesity.

Data of this study indicated that the prevalence of type-nonspecific anti-AdV antibodies, both in obese and non-obese subjects was more than 90%. This high seroprevalence is consistent with previous studies reporting worldwide distribution of adenoviruses due to virus circulation in the environment [24, 25]. We did not confirm an association between the presence of AdV-IgG antibodies in the serum and obesity in studied adults. The prevalence of AdV-IgG antibodies was similar both in obese and non-obese groups, but men were more frequently affected by adenoviruses in the whole group and in the group of obese subjects. Lack of evidence for the association of human adenoviruses and obesity in this cohort may be a result of testing type-nonspecific antibodies to human adenoviruses. Taking into account that the incidence of adenovirus infections peaks in infants and children between the age of 6 months and 5 years and more than 90% of the human population was affected by adenoviral infections, it is obvious that not all types of human adenoviruses are associated with the development of obesity. This was also confirmed by some previous reports that indicated several AdV types (AdV36, AdV37, AdV5) associated with the pathological accumulation of body fat, but there are also reports excluding adenoviruses from the group or etiological factors of obesity, like AdV2 [22].

Although we demonstrated insignificant differences in anthropometric indicators of obesity and in lipid profile between AdV-IgG positive and AdV-IgG negative obese and non-obese participants (considered together), we have observed several important associations that are different in the group of subjects with BMI $\geq$ 30 kg/m^2 and subjects with BMI < 30 kg/m^2. WHR of AdV-IgG positive obese/non-obese was significantly higher than of AdV-IgG negative counterparts, indicating visceral adiposity. This is consistent with previous reports on animals or human studies, which have confirmed that adenoviral infection increases the pathological accumulation of adipose tissue particularly around the viscera [7, 22, 26]. The presence of AdV-IgG antibodies in the serum was associated with elevated BMI and body weight in the group of lean subjects. AdV-IgG positives were over 6.5 kg heavier than their seronegative counterparts. This observation was similar to results obtained by Atkinson et al. (2010) who examined obese children infected with AdV36 [2]. This suggests that greater body weight, higher BMI, WHR and waist circumference in non-obese and lean AdV-IgG positive subjects may by the result of stronger immunological response to adenoviruses in comparison to obese and overweight subjects (Fig. 1 C, D).

A similar association was observed in the group of obese/overweight (BMI $\geq$ 25 kg/m^2) and lean (BMI < 25 kg/m^2) subjects. WHRs of AdV-IgG positive patients both from obese/overweight and lean groups, and BMIs, body weights and waist circumference of AdV-IgG positive lean subjects were significantly greater in comparison to their AdV-IgG negative counterparts. The above observations confirm that there is an association between AdV seropositivity and increased accumulation of body fat, especially in visceral area. A lack of the association in the combine group of obese/non-obese may be a consequence of significant influence of obese patients, who also did not demonstrate the association with AdV-seropositivity. Lack of the associations in obese group may be the result of

metabolic changes and disturbances accompanying obesity, due to genetic and behaviour/environmental causes, which camouflage the influence of adenoviral infection. We are aware that adenoviral infections may be only one of many other, stronger and unambiguous etiological factors, which directly influence the lipid metabolism and may be dominant in development of obesity in comparison to adenoviral infection. We also consider that adenovirus infection may play the role of a risk (not causative) factor for obesity and perhaps AdVs increase adiposity only in the presence of other risk factors. Nevertheless, the associations of anthropometric measurements and AdV-IgG seropositivity in lean and non-obese participants provide strong evidence of the relationship between adenoviruses and greater visceral fat in humans.

Previous studies presented controversial reports with regards to changes in serum lipids due to AdV infection [13, 14, 19, 22, 23, 27–29]. This may suggest that there are some different mechanisms underlying lipid disturbances in different species. Adipogenic and lipidemic effects may by mediated via separate pathways and animal, or *in vitro* models, may not be appropriate to forecast lipid changes in humans. In this study we noticed that the presence of AdV infection was not associated with changes in serum lipids levels. Our results are contrary to the findings of Atkinson et al., who reported that levels of TG and TChol were significantly lower in AdV36-positive individuals than in AdV36 antibodies negative individuals [22]. These contrary observations may be the consequence of type-unspecific antibodies detection in our study.

Hypoleptinemia was reported in studies involving animals and *in vitro* studies as main pathomechanism of infectobesity. The experiment reported by Vangipuram et al. showed that adenoviral infection leads to a suppression of expression and secretion of leptin in adipose tissue; the pathogenesis of "infectobesity" [8]. In our study, the level of serum leptin of AdV-IgG subjects was similar to those of AdV-IgG negative, probably as a function of BMI and a greater amount of fat tissue. The data showed no difference in the serum leptin concentration in AdV-IgG positive obese vs. AdV-IgG negative obese and in AdV-IgG positive non-obese vs. AdV-IgG negative, confirming that leptin levels are elevated due to much greater fat deposits, not due to AdV infection.

In our study, we did not confirm that the increased accumulation of visceral fat was the result of chronic low-grade inflammation due to adenoviral infection in adipose tissue. We noticed that the increased level of CRP was the function of BMI and the amount of body fat, not AdV infection. We observed a decreased level of serum CRP in AdV--IgG positive in lean participants. This confirms that the inflammation associated with obesity is not related to adenoviral infection but AdV infection might be associated with decreased secretion of CRP in adipocytes or liver, but this needs further investigation.

The authors showed that there is an association between the presence of type unspecific anti-AdV antibodies in the serum and increased body weight, BMI, WHR and waist circumference but only in the group of lean and non-obese subjects from the Polish population, not in obese or overweight subjects. We are aware that indirectly linking an episode of a particular infection to obesity developed later in life, without simultaneous considering of other causative or risk factors, is risky. Therefore, the intention was to point out the possible association between immune response to adenoviral infection and changes in lipid metabolism leading to greater body weight, BMI, WHR and visceral distribution of fat. But interestingly, we noticed that the concentration of IgG in the serum of non-obese subjects was higher than that of obese subjects, suggesting that higher level of IgG to AdVs may protect subjects against obesity or overweight. Therefore, further studies on the role of less effective immune response to AdV infections in obese/ /overweight subjects are needed. We are also aware that further, more insightful studies are necessary to clearly define the association between adenoviral infection and obesity, including other risk factors. Therefore, our further study will focus on a quantitative evaluation of adenoviral infection (qRT-PCR), on the metabolic changes due to adenovirus replication and immune response to infection and multivariate analysis of risk factors (including AdV infections) for the development of obesity. In our opinion, this data should alert clinicians to the possibility of infectobesity and promote further research to explain the underlying mechanism of increased fat accumulation and to develop new prevention and treatment strategies in the future.

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Address for correspondence:

Iwona Bil-Lula
Department of Clinical Chemistry
Wroclaw Medical University
Borowska 211
50-556 Wrocław
Poland
Tel.: 00 48 71 78 40 621
E-mail: iwona.bil-lula@umed.wroc.pl

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