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Seropositivity of human Adenovirus -36 and lymphocyte count in relation with Iraqi Obese patients

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ABSTRACT

Background: The complications associated with obesity firstly duo to systemic inflammation that develops within adipose tissue. Adenovirus 36 (Adv36) has been suggested to be an obesity associated virus that regulates the metabolism of adipose tissue. Therefore, this study is aimed to investigate whether there is an association between Adv36 seropositivity and obesity, and whether it correlates with body mass index (BMI) or lymphocyte count.

Methods: Eighty-one subjects were included in the study: 62 with obesity and 19 healthy normal weight controls. Serum antibodies specific for Adv36 were detected by enzyme-linked immunosorbent assay (ELISA). The clinical data collected comprised age, lymphocyte ،body mass index (BMI), and lipid profile. Statistical comparisons were made for Adv36 seropositivity among obese and control groups and the relationships between Adv36 status and BMI, WBC, lymphocyte or lipid indices were analyzed.

Results: In both groups, results showed the overall Ad-36 seroprevalence was negative in non-obese and obese participant. Which revealed no association between Adv36 seropositivity and obesity. Furthermore, no significant correlations were found between Adv36 negative and triglycerides, HDL C, LDL C, BMI, or total cholesterol.

Conclusions: In this cohort, Adv36 was not significantly linked to obesity; these null results may reflect limitations such as small sample size, limited power, or population-specific factors (e.g. environmental, genetic, viral exposure heterogeneity) .

While previous studies suggest a possible role of Adv36 in "infect obesity," our data do not support a connecting or strong association in this population. Larger, studies are suggested to better clarify the relationship between Adv36 infection and obesity development.

KEYWORDS: Obesity, Human adenovirus-36, white blood cells, body mass index, lipid profile.

1. Introduction

Obesity is a multifactorial condition driven by neuronal, endocrine, genetic and environmental factors. Nevertheless, infectious agents due to its global rapid spread have been implicated in pathophysiology of obesity [1, 2]. The complications associated with obesity firstly duo to systemic inflammation that develops within adipose tissue. In reality this chronic inflammation is caused by a subset of macrophages which play an essential role in the pathophysiological processes of obesity [3]. Based on person's body mass index (BMI) threshold values, adult overweight and obesity are defined [4]. Three human viruses include: adenovirus-37(Adv37), adenovirus-36(Adv36), adenovirus-5(Adv5) and have been linked to obesity, according to studies [5, 6, 2] It has been shown that Adv36 infection, both natural and artificial, causes obesity in a variety of animal species by promoting preadipocyte differentiation and proliferation as well as lipid buildup in mature adipocytes [7]. Individuals with evidence of a previous, natural Adv36 infection are exhibit elevated body weight than those with no evidence of infection, according to the majority of later studies on Adv36 and obesity in humans [8]. While there is considerable variation in the data about the relationship between Adv36 and obesity in adults, the results in children consistently link Adv36 infection to obesity. Adv36-associated obesity, in contrast to most obese patients, has been linked to decreased blood lipid levels in both adult humans and animals [8, 9]. Additionally, Adv36 has been shown to enhance glucose absorption

in skeletal muscle and adipose tissue, decrease hepatic glucose release, and improve glycemic control in experimental model, as well, a similar effect has been observed in human skeletal muscle cells independent of insulin signaling [10,11,12].

Additionally, in around 1500 slim, obese, and overweight otherwise healthy adults and children of various ethnic backgrounds residing in the United States, Adv36 was linked to improved insulin sensitivity [13]. Dhurandhar *etal* coined the term "infectobesity" in 2001 to suggest that there may be an infectious component to the etiology of obesity [14]. In the United States, Atkinson *et al.* (2005) reported a substantial (relative risk = 2.7, $P < 0.001$) correlation between obesity and the presence of Adv36 neutralizing antibodies in human serum [13]. Another research examines individual adipose tissue and reported that some had Adv36 DNA because of a natural infection [11]. As far as we are aware, there is a dearth of Ad-36 data on people outside of the US, such as Korean children, as reported by Atkinson *et al.* (2005) [13] thus, we investigated this potential correlation in the Iraqi population statistics.

2. Subjects and methods

2.1 Participants

The obese and non-obese volunteers were taken randomly (BMI of ≥25 kg/m^2 was defined as overweight, and a BMI of ≥30 kg/ m^2 was defined as obesity) [17] .The relevant clinical examination, and detail history were taken from participants, as well all the routine investigations were done.

Eighty-one participants with age (18-83) years, Gender (male, female) who were presented at The National Center of Hematology/ Mustansiriyah university between September 2024 and February 2025 included in this study. Sixty-two of them diagnosed with obesity and 19 were control group. From all participants a written informed consent was taken.

2.2 Laboratory measurements

The instruction of overnight fasting at least (12-14) hours was advised for all participants. Ten milliliters of venous blood are withdrawn from the obese and control with a disposable syringe. A total of 7ml collected in gel tubes to sperate serum for determination the lipid profile (cholesterol, triglycerides, LDL, HDL, and VLDL) which immediate analyzed using a semi-automated instrument (COBAS MIRA). As well as to determine the antibodies to Adv36 by using a qualitative enzyme-linked immunosorbent assay (ELISA) (Adv36-Ab ELISA Kit, MyBioSource). 3ml of venous blood was collected in EDTA tubes to examine complete blood count (CBC), which is assessed at the same institutional laboratory. Patients with WBC count $\geq 20.0 \times 10^3/\mu L$ were excluded from study due to the possibility of abnormal conditions including infectious disease at the time of examination.

2.3 Clinical and anthropometric measurements

According to WHO classification, the BMI was calculated (weight (kg)/ height (m^2)) as the participants height measured by using height meter, which was mounted on a wall, and weight measured by using a mechanical scale.

2.4 Statistical analysis

Utilizing GraphPad Prism software 7.0, statistical analysis was carried out. The unpaired t-test was used to determine the probability. We utilized the Mann-Whitney test for non-parametric data. For categorical data, the probability was determined using Fisher's exact test.

To determine the correlation between parameters, the Spearman test used for non-parametric data and the Pearson test for the parametric data.

3. Results

Results showed the overall Adv36 seroprevalence was negative in non-obese and obese participant. Which revealed no association between Adv36 seropositivity and obesity?

Table (1) enumerates the biochemical, anthropometric, and demographic features of the control and obese groups. Nineteen controls of normal weight and sixty-two obese people were involved in the study. Age (P= 0.713) and gender (P= 0.5111) distribution between the two groups did not differ statistically significant, suggesting that individuals were appropriately matched and reducing the possibility of confounding effects from these characteristics.

As anticipated, the obese group's mean BMI was significantly greater than the control group's (41.11 ± 0.6456 kg/m²; 20.87 ± 0.4456 kg/m²; respectively; $p<0.0001$) confirming the classification of obesity within the case group.

Significant differences were seen in lipid profiles across several factors. Obese people had significantly higher triglyceride levels (219.8 ± 12.83 mg/dL vs. 128.9 ± 7.08 mg/dL; $p = 0.0002$) and higher median total cholesterol levels (187.5 mg/dL vs. 150 mg/dL; $p = 0.0029$). Similarly, the obese group had significantly higher levels of low-density lipoprotein (LDL) cholesterol and very-low-density lipoprotein (VLDL) ($p = 0.0041$ and $p = 0.0053$, respectively), suggesting a pattern of dyslipidemia frequently linked to obesity. It's interesting to note that the obese group also had greater levels of high-density lipoprotein (HDL) cholesterol (52.5 mg/dL vs. 43 mg/dL; $p = 0.0462$), despite the fact that this discovery goes against the usual findings that HDL tends to decline in obesity. This disparity can be the result of different eating patterns, hereditary variables, or the control group's small sample size.

In comparison to controls (6.219 ± 0.3584 × 10^3/µL; $p < 0.0001$), obese people had significantly higher mean white blood cell (WBC) counts (9.216 ± 0.3128 × 10^3/µL), according to the hematological parameters. In the same way, the obese group had considerably more lymphocytes (3.54 ± 0.1885 × 10^3/µL vs. 2.181 ± 0.2259 × 10^3/µL; $p = 0.000$). These results might point to a low-grade systemic inflammatory state that is frequently seen in obesity, which is a result of immune system activation and a persistent inflammatory response.

In summary, the data show that, in comparison to normal-weight controls, obese patients showed notable changes in inflammatory markers and lipid metabolism. Ad-36 seropositivity did not significantly differ between the two groups, indicating that although metabolic and inflammatory problems are present in obese individuals, they are unlikely to be connected to Ad-36 infection in this population.

Table 1: **Baseline data for study groups**

	Control	Obese	P-value
Number	19	62	-
Gender (male:female)	5:14	11:51	0.5111 ***
Age (years) median (Range)	34 (18-52)	33 (18-83)	0.713 **
BMI (Mean ± SE)	20.87 ± 0.4456	41.11 ± 0.6456	< 0.0001 *
Median cholesterol (range)	150 (117-187)	187.5 (105-282)	0.0029 **
Mean ± SE Triglycerides (mg/dl)	128.9 ± 7.081	219.8 ± 12.83	0.0002 *
Median HDL (range)	43 (26-57)	52.5 (24-85)	0.0462 **
Median LDL (range)	102 (85-140)	152 (30-262)	0.0041 *
Median VLDL (range)	43 (17-60)	65 (11-113)	0.0053 **
Mean ± SE WBC (x 10^3/µL)	6.219 ± 0.3584	9.216 ± 0.3128	< 0.0001 *
Mean ± SE Lymphocyte (x 10^3/µL)	2.181 ± 0.2259	3.54 ± 0.1885	0.0003 *
Statistical analysis was performed using *t-test, ** Mann-Whitney test, * Fisher's exact test.**			

The correlation analysis of the control (normal weight group) examined the relationships among anthropometric, biochemical, and hematological traits. Pearson's correlation coefficients (r values) reflect the strength and direction of correlations between variable as shown in (Table 2).

1. Lipid Profile Relationships.

There was a significant positive correlation between triglycerides and very-low-density lipoprotein (VLDL) ($r = 0.86$, $p \leq 0.0001$). This is a predicted physiological finding as VLDL is responsible for transporting triglycerides through the bloodstream and since its concentration is directly related to triglyceride levels. No other lipid measurements showed significant relationships in the control group. The statistically insignificant and weak relationships between HDL, LDL, and cholesterol suggest that the lipid components were stable and not dependent on one another in non-obese individuals.

2. Age and Hematological Parameters

The relationship between age and WBC count was found to be somewhat positive and statistically significant ($r = 0.52$, $p < 0.05$). This suggests that among control subjects, WBC levels tended to slightly increase with age. Age-related immune system alterations or mild inflammatory processes could be the cause of the connection. Age and lymphocyte count, however, did not significantly correlate ($r = -0.12$), indicating that age had no effect on lymphocyte levels in this cohort.

3. Metabolic markers and BMI

Although there was a modest positive link ($r = 0.29$) with LDL and a moderate positive correlation ($r = 0.41$) with triglycerides, body mass index (BMI) did not approach statistical significance. Even among people of normal weight, this trend suggests a propensity for greater BMI values to be associated with higher levels of LDL and triglycerides, however the correlation was not significant enough to be definitive.

4. White Blood Cell and Lipid Interactions

The majority of biochemical indicators (cholesterol, triglyceride, HDL, LDL, and VLDL) exhibited weak correlations with WBC counts, suggesting that there was no significant association between inflammatory activity and lipid metabolism in the control group.

5. Relationships of Lymphocytes

In healthy-weight subjects, lymphocyte counts showed weak, non-significant relationships with other parameters, indicating that lymphocyte levels were unaffected by anthropometric and lipid measurements.

Regarding the correlation analysis of Obese group shown in (Table 3) are depicted the associations between age, anthropometric measurements, lipid parameters, and hematological markers in the correlation matrix for the obese group. Spearman's correlation coefficients (r values) are used. Numerous noteworthy associations were found, emphasizing different inflammatory and metabolic processes in obese individuals as opposed to the control group.

1. Relationships between lipid profiles:

The components of the lipid profile showed several strong and highly significant positive correlations: Triglycerides had a strong association with both VLDL ($r= 0.93$, $p< 0.0001$) and LDL ($r= 0.75$, $p\leq 0.0001$). High correlation between cholesterol and both LDL ($r = 0.72$, $p\leq 0.0001$) and VLDL ($r= 0.64$, $p< 0.0001$) demonstrated. Moreover, HDL had strong positive correlations with LDL ($r =0.54$, $p\leq 0.0001$), VLDL ($r= 0.66$, $p\leq 0.0001$), and triglycerides ($r= 0.49$, $p< 0.0001$).

According to these results, lipid fractions are more closely linked in obese people than in the control group, pointing to a disruption in lipid metabolism whereby rises in one lipid parameter are probably accompanied by increases in others. Dyslipidemia, which is frequently observed in obesity and metabolic syndrome, is characterized by this clustering of lipid abnormalities.

2. Correlations with Age

Younger obese people tended to have greater LDL and triglyceride levels than older participants, according to a negative correlation between age and LDL ($r = –0.33$, $p \leq 0.01$) and age and triglycerides ($r = –0.31$, $p \leq 0.05$). This could be the result of food and lifestyle variations between age groups or age-related metabolic changes. Age, on the other hand, had a small but significant positive connection with lymphocyte count ($r = 0.26$, $p < 0.05$), suggesting that immune cell activity in obese people increased somewhat with age.

3. Hematological Correlations

A strong positive correlation was observed between WBC and lymphocyte counts ($r = 0.66$, $p \leq 0.0001$), consistent with the expected relationship between total white blood cells and their lymphocyte subset. This reflects heightened immune or inflammatory activity, a common feature in obesity associated with chronic low-grade inflammation. However, WBC counts did not correlate significantly with lipid parameters, suggesting that the inflammatory response in obesity might be independent of serum lipid alterations in this group.

4. BMI Correlations

Within the obese range, BMI was not a good predictor of lipid or immunological changes, as seen by the weak and non-significant correlations it displayed with all biochemical and hematological indicators. This might be because of the obese sample's homogeneity, as most people had high BMIs with little variation.

Table 2: A correlation table (Control group)

Parameters	Age	BMI	Chol	Tri	HDL	LDL	VLDL	WBC	Lymphocyte
Age		-0.18	-0.30	0.17	0.39	0.11	0.16	0.52*	-0.12
BMI	-0.18		-0.12	0.41	-0.24	0.29	0.16	0.16	0.32
Chol	-0.30	-0.12		-0.22	-0.11	-0.11	-0.11	-0.22	-0.02
Tri	0.17	0.41	-0.22		-0.07	0.23	0.86****	0.13	0.08
HDL	0.39	-0.24	-0.11	-0.07		-0.02	0.13	0.24	-0.19
LDL	0.11	0.29	-0.11	0.23	-0.02		0.15	0.16	-0.01
VLDL	0.16	0.16	-0.11	0.86****	0.13	0.15		-0.12	-0.03
WBC	0.52*	0.16	-0.22	0.13	0.24	0.16	-0.12		0.26
Lymphocyte	-0.12	0.32	-0.02	0.08	-0.19	-0.01	-0.03	0.26	

Value represent Spearman correlation coefficient (r).
Correlation strength based on r: ≥0.9-1 very high, 0.7-0.9 high, 0.5-0.7 moderate, 0.3-0.5 low, <0.3 negligible.
Significance levels: * P ≤ 0.05. ** P ≤ 0.01. *** P ≤ 0.001. **** P ≤ 0.0001 (two-tailed).

Table 3: A correlation table (obese group)

Parameters	Age	BMI	Chol	Tri	HDL	LDL	VLDL	WBC	Lymphocyte
Age		0.03	-0.17	-0.31*	0.10	-0.33**	-0.24	0.06	0.26*
BMI	0.03		0.09	0.07	0.07	0.09	0.10	0.003	-0.10
Chol	-0.17	0.09		0.76****	0.24	0.72****	0.64****	-0.10	-0.16
Tri	-0.31*	0.07	0.76****		0.49****	0.75****	0.93****	-0.19	-0.19
HDL	0.10	0.07	0.24	0.49****		0.54****	0.66****	-0.10	-0.07
LDL	-0.33**	0.09	0.72****	0.75****	0.54****		0.73****	-0.03	-0.12
VLDL	-0.24	0.10	0.64****	0.93****	0.66****	0.73****		-0.19	-0.20
WBC	0.06	0.003	-0.10	-0.19	-0.10	-0.03	-0.19		0.66****
Lymphocyte	0.26*	-0.10	-0.16	-0.19	-0.07	-0.12	-0.20	0.66****	

Value represents Spearman correlation coefficient (r).
Correlation strength based on r: ≥0.9-1 very high, 0.7-0.9 high, 0.5-0.7 moderate, 0.3-0.5 low, <0.3 negligible.
Significance levels: * P ≤ 0.05. ** P ≤ 0.01. *** P ≤ 0.001. **** P ≤ 0.0001 (two-tailed).

The Receiver operating characteristic curve (ROC) analysis of WBC showed a very good prediction of control versus patients with 79.03 sensitivity and 73.68 specificity. As shown in (Table 4; Fig 1).While the lymphocyte showed a good prediction of the AUC (0.767) when predicting the control from patients as shown in (Table 5; Fig 2).

Table 4: The receiver operating characteristic curve analysis of WBC level

Comparison groups	AUC	95% CI of AUC	P-value	Optimum Cut off value	SN (%)	SP (%)
Control vs. Patients	0.839	0.75 - 0.93	<0.0001	6.93	79.03	73.68
(AUC) area under the curve, (CI) confidence interval, (SN) sensitivity, (SP) specificity AUC reference: 0.9-1 (excellent), 0.8-0.9 (very good), 0.7-0.8 (good), 0.6-0.7, (satisfactory), 0.5-0.6 (unsatisfactory).						

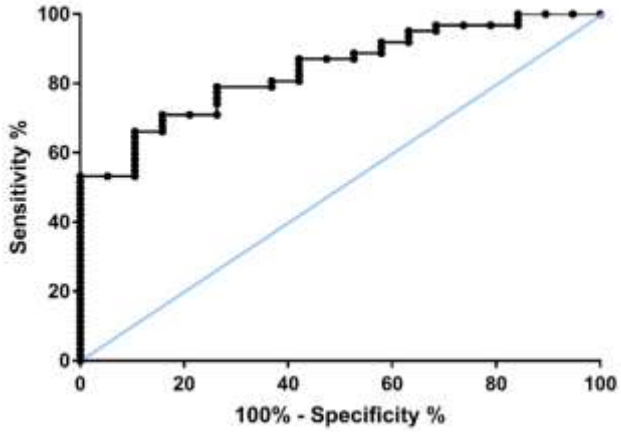

Fig 1 The Receiver operating characteristic curve analysis of WBC

Table 5: The Receiver operating characteristic curve analysis of lymphocyte level

Comparison groups	AUC	95% CI of AUC	P-value	Optimum Cut off value	SN (%)	SP (%)
Control vs. Patients	0.767	0.66 - 0.87	0.0004	2.59	67.74	73.68
(AUC) area under the curve, (CI) confidence interval, (SP) specificity, (SN) sensitivity AUC reference: 0.9-1 (excellent), 0.8-0.9 (very good), 0.7-0.8 (good), 0.6-0.7 (satisfactory), 0.5-0.6 (unsatisfactory).						

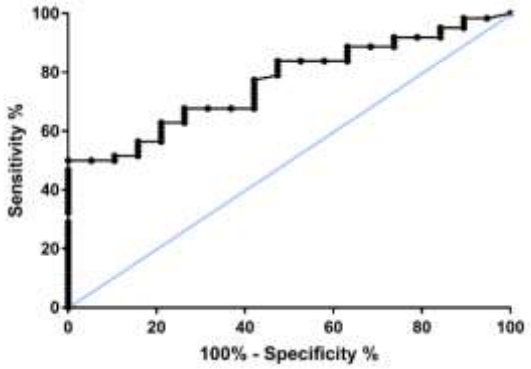

Fig 2 Receiver operating characteristic curve analysis of lymphocyte

4. Discussion

This study of (81) individuals show, a non-significant association was found between Adv36 seropositivity and obesity. Given that the overall Adv36 seroprevalence was negative in both the obese and non-obese groups, which may indicate that adenovirus 36 exposure is not a contributing factor to the development of obesity in this population. These results agree with some earlier research that did not show a connection between Adv36 infection and a rise in body fat [20]. They contrast with data that suggest Adv36 may play a part in promoting adipogenesis and fat accumulation [19, 20,21]

Differences in geographic location, sample size, detection techniques, or demographic variables like age, nutrition, and genetic background could all be responsible for the lack of relationship seen here. The lack of a link may also be explained by the low or nonexistent Adv36 seroprevalence in both groups, which suggests that the cohort under study had little contact to viruses. All things considered, our findings imply that Ad-36 is not likely to be a determinant in obesity in this context that our findings differ from seroprevalences in the US that have been previously reported across different cohorts, wich range from approximately 20%%-36% [18].

A study on Adv36 seropositivity in a Mexican population conclude there is no association between Adv36 and obesity, while it shows that Ad-36 linked to metabolic and inflammatory alteration as well these changes are independent of BMI [22].

Significant variations in several metabolic and hematological markers were noted between the control and obese groups in this investigation. As anticipated, obese people had significantly higher levels of BMI, cholesterol, triglycerides (TG), LDL, VLDL, WBC, and lymphocytes than controls ($p < 0.05$). These results are consistent with the body of research showing that obesity is linked to low-grade systemic inflammation and dyslipidemia [23, 24].

Obese persons raised VLDL and triglyceride levels are indicative of decreased lipid clearance and increased hepatic lipogenesis, which are characteristics of the metabolic syndrome [25]. Obesity-related atherogenic risk is further increased by elevated LDL and total cholesterol levels. Although HDL levels are somewhat greater in the obese group, this could be due to dietary variables or individual variability; nonetheless, HDL's cardio protective effect is often determined by its functionality rather than its concentration [26].

The idea of inflammation brought on by obesity is supported by the rise in WBC and lymphocyte counts in obese people. As an endocrine organ, adipose tissue secretes proinflammatory cytokines, such as TNF-α and IL-6, which cause leukocytosis [27, 28]. Insulin resistance and the advancement of cardiovascular disease are facilitated by chronic inflammation.

5. Conclusion

This study results revealed that the obesity and Adv36 infection are not associated. These findings imply that Adv36 is not likely to be a major contributor to the pathophysiology of obesity in the population under study. To elucidate the possible role of Adv36 in the development of obesity, more research with bigger and more varied cohorts is necessary. Significant increases in BMI, total cholesterol, triglycerides, LDL, VLDL, WBC, and lymphocyte counts, as well as strong correlations among lipid fractions that suggest dysregulated lipid metabolism and elevated inflammatory markers that highlight chronic low-grade inflammation as a hallmark of obesity, are all linked to obesity, according to the study. In order to lower cardiovascular risk, our data highlight the necessity of early screening and intervention aimed at lipid and inflammatory markers in obese people.

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Conflict of Interest: None.
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