# Study of serum adiponectin level as an atherosclerotic index in the elderly and its relationship to carotid intima–media thickness

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**Background**
It is well known that aging is associated with several hormonal alterations. However, the consequence of aging on the endocrine function of adipose tissue is not fully elucidated. Adiponectin is a new anti-inflammatory protein secreted exclusively by adipocytes and plays a protective role against insulin resistance and atherosclerosis.
**Aim of the work**
The aim of the work was to assess serum adiponectin as a biomarker for atherosclerosis and its relation to the carotid intima–media thickness (CIMT) as a clinical surrogate marker of atherosclerosis in elderly patients.
**Patients and methods**
The study was conducted on 80 participants aged 20–85 years who were subdivided into four groups. The first group was the control group (GI), which included 20 healthy young volunteers aged 20–40 years. The other three groups each included 20 elderly participants aged above 65 years who were classified according to arterial blood pressure and serum blood glucose levels into elderly healthy (GII), elderly hypertensives (GIII), and elderly diabetics (GIV).
**Results**
The mean adiponectin level (control, 12.48±3.95; GII, 9±3.25; GIII, 8.49±2.40; and GIV, 7.16±3.23) was significantly lower in individuals with high CIMT than in those with low CIMT (GI, 0.64±0.05; GII, 0.75±0.06; GIII, 0.72±0.08; GIV, 1.03±0.15). Adiponectin level was negatively correlated with age, BMI, systolic blood pressure, diastolic blood pressure, triglyceride, low-density lipoprotein cholesterol, and blood glucose, and positively correlated with high-density lipoprotein cholesterol.
**Conclusion**
Adiponectin was significantly negatively correlated with CIMT independently of age, sex, and all metabolic risk factors. The present study found that serum adiponectin level in humans is lower in elderly individuals and in patients with diabetes mellitus and essential hypertension than in healthy participants, and is negatively affected by the duration of these diseases.

**Keywords:**
adiponectin, atherosclerosis, carotid intima–media thickness

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## Background

Atherosclerosis and the subsequent cardiovascular complications, such as myocardial infarction, stroke, and ischemic heart disease, are a major cause of death. The risk factors of atherosclerosis are well known, including hypertension, diabetes, serum total and low-density lipoprotein (LDL) cholesterol, and smoking. Increasing evidence indicates that aging is also an important risk factor for atherosclerosis and persists as an independent contributor when all other known factors are controlled [1].

The first structural change that can be detected in atherosclerosis is an increase in carotid intima–media thickness (CIMT) [1].

There is growing evidence that adipose tissue *per se* is a large endocrine organ secreting several biologically active substances with systemic action [2,3], such as leptin, adiponectin, plasminogen activator inhibitor-1, angiotensin II, tumor necrosis factor-α, and resistin [2,3].

Adiponectin is a kind of circulating adipokine that inhibits the proatherogenic process. The exact mechanism is yet to be elucidated but may include

enhancing endothelial nitric oxide synthase activity, inhibiting inflammatory changes that lead to increased expression of endothelial adhesion molecules and suppression of macrophage activation required for development of foam cells [4].

These pathophysiologic actions of adiponectin have led many authors to suggest that it may play a protective role against atherosclerosis and cardiovascular risk [5]. The expression of adiponectin is inversely correlated with obesity, insulin resistance [6], and development of early atherosclerosis [7]. Because adiponectin exerts protective effects on the cardiovascular system, it could also be highlighted as a therapeutic target molecule for preventing atherosclerosis and atherosclerotic events [8].

Therefore, the aim of the present study was to assess serum adiponectin as a biomarker for atherosclerosis and its relation to the CIMT as a clinical surrogate marker of atherosclerosis in elderly individuals.

## Patients and methods

This cross-sectional descriptive study was carried out in September 2015 at the Internal Medicine Unit of Karmouz Health Insurance Hospital, Alexandria, Egypt. Informed consent was taken from all participants. The study was conducted on 80 participants aged 20–85 years who were subdivided into four groups. The first group was the control group (GI), which included 20 healthy young volunteers aged 20–40 years of normal body weight and BMI as well as arterial blood pressure measurement. The other three groups each included 20 elderly individuals aged above 65 years who were classified according to arterial blood pressure and serum blood glucose levels into elderly healthy (GII), elderly hypertensives (GIII), and elderly diabetics (GIV). All participants in the present study underwent the following: history taking, full clinical examination, routine laboratory investigations, and evaluation of glomerular filtration rate (GFR), which was calculated as endogenous creatinine clearance according to the formula by Cockroft and Gault: GFR=[140–age (years)]×body mass (kg)×1 (for males) or 0.85 (for females)/72×serum creatinine concentration (mg/dl). Plasma adiponectin concentration was estimated with an enzyme-linked immunosorbent assay from blood samples drawn in the morning after overnight fasting, and B-mode ultrasound examination of the common carotid arteries was performed for estimation of CIMT.

Data entry and statistical analysis were performed using SPSS 18.0 (SPSS Inc., Chicago, Illinois, USA). The distributions of quantitative variables were tested for normality using the Kolmogorov–Smirnov test, which revealed that the data were normally distributed. Correlation between quantitative variables was determined using Pearson's correlation test. Com- parison of quantitative variables between two groups of cases was made using the independent sample *t*-test. Comparison of quantitative variables between three or more groups of cases was made using one-way analysis of variance. The Kruskal–Wallis test was used when the sample size per group was small. Statistical significance was set at *P* value less than 0.05.

## Results

The mean age was 66.40±1.88 in group II, 68.10±4.40 in group III, 68.40±2.46 in group IV, and 33.25±5.05 years in controls.

Female patients were fewer than male patients: 10% in group II, 20% in group III, and 30% in group IV. Among controls the proportion of female participants was 30%.

Serum adiponectin concentration tended to be lower (statistically significant) only in elderly individuals aged more than 65years when compared with the control group (7.77 and 10.93, respectively). Plasma adiponectin concentration was lower in the diabetic group than in healthy elderly or hypertensive elderly (median 6.72, 7.77, and 754, respectively).

Comparison among the four groups in this study was also performed for weight, BMI, systolic blood pressure, diastolic blood pressure, glucose concentration, HbA1c, disease duration, cholesterol, triglyceride, high-density lipoprotein (HDL), LDL, and CIMT (Table 1). The mean CIMT was 0.75± 0.06, 0.72±0.08, and 1.03±0.15 in group II, group III, and group IV, respectively, whereas in the control group it was 0.64±0.05. We have observed significantly lower blood adiponectin level values with higher CIMT in elderly participants of both sexes when compared with individuals younger than 40 years of age ($P<0.001$) (Table 1). The mean BMI was 29.30±7.25 in group II, 30.30±5.33 in group III, 28.67±6.54 in group IV, and 25.40±2.75 in controls.

There was significant negative correlation between adiponectin level and age in all studied groups (*P* values: group I, 0.503; group II, 0.011*; group III, 0.035*; group IV, 0.002*).

There was significant negative correlation between adiponectin and cholesterol, LDL cholesterol,

**Table 1 Comparison of the four groups on the basis of different parameters**

| | Control (GI) (*n*=20) | Nonhypertensive nondiabetic (GII) (*n*=20) | Hypertensive (GIII) (*n*=20 | Diabetic (GIV) (*n*=20) | Test of significance | *P* |
|---|---|---|---|---|---|---|
| Sex [*n* (%)] | | | | | | |
| Male | 14 (70.0) | 18 (90.0) | 16 (80.0) | 14 (70.0) | $\chi^2$=3.222 | 0.365 |
| Female | 6 (30.0) | 2 (10.0) | 4 (20.0) | 6 (30.0) | | |
| Age (years) | 33.25±5.05 | 66.40±1.88 | 68.10±4.40 | 68.40±2.46 | *F*=435.96* | <0.001* |
| Smoking [*n* (%)] | 9 (45.0) | 5 (25.0) | 13 (65.0) | 12 (60.0) | $\chi^2$=7.696 | 0.058 |
| Systolic | 122.50±12.82 | 119.0±12.10 | 130.0±12.98 | 124.0±10.46 | 2.862* | 0.042* |
| Diastolic | 79.50±6.86 | 75.50±10.50 | 83.50±8.75 | 78.0±7.68 | 3.067* | 0.033* |
| FBG (mg/dl) | 89.30±10.61 | 88.30±17.89 | 95.65±26.17 | 151.65±59.13 | 16.084* | <0.001* |
| HbA1c % | 4.89±0.24 | 5.27±0.76 | 5.46±0.50 | 7.53±1.50 | 35.945* | <0.001* |
| BMI (kg/m$^2$) | 25.40±2.75 | 29.30±7.25 | 30.30±5.33 | 28.67±6.54 | *F*=2.648 | 0.055 |
| Cholesterol (mg/dl) | 146.85±31.72 | 178.25±52.60 | 197.30±47.38 | 194.0±54.25 | *F*=4.743* | 0.004* |
| HDL-C (mg/dl) | 49.0±9.80 | 47.75±12.30 | 39.15±10.97 | 42.55±10.83 | *F*=3.473* | 0.020* |
| LDL-C (mg/dl) | 116.08±8.57 | 110.80±49.71 | 141.74±32.13 | 120.64±40.01 | *F*=2.841* | 0.043* |
| Triglycerides (mg/dl) | 103.70±25.91 | 126.25±54.65 | 144±90.19 | 148.60±70.97 | $^{KW}\chi^2$=6.329 | 0.097 |
| CIMT (mm) | 0.64±0.05 | 0.75±0.06 | 0.72±0.08 | 1.03±0.15 | 64.040* | <0.001* |
| Adiponectin (mg/l) | 12.48±3.95 | 9±3.25 | 8.49±2.40 | 7.16±3.23 | 23.739* | <0.001* |

CIMT, carotid intima–media thickness; *F*, *F*-test (analysis of variance); FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; KW, Kruskal–Wallis test; LDL-C, low-density lipoprotein cholesterol. *Statistically significant at $P \leq 0.05$.

hypertension, and diabetes mellitus, and a positive correlation with HDL cholesterol (*P* values: group I, 0.001*; group II, 0.001*; group III, 0.016*; group IV, 0.035*).

The correlation was significantly negative between adiponectin and CIMT in the control group and in group II, group III, and group IV (*P* values: 0.010*, 0.030*, 0.029*, and 0.004*, respectively).

There was no significant difference in adiponectin level between the two sexes in any of the groups (Table 2).

The adiponectin level in controlled hypertensive patients was higher than that in uncontrolled patients but there was no significant difference between them (median 8.22, 7.20) (*P*=0.244) (Table 3).

Adiponectin level in diabetic patients under oral hypoglycemic drugs was higher than the level in patients on insulin therapy (median 7.25, 4.95) (*P*=0.161) and this correlation was statistically not significant (Table 3).

There was a negative correlation between adiponectin level and duration of diabetes with no statistically significant difference between controlled and uncontrolled patients on oral hypoglycemic drugs (*P*=0.961, 0.087, respectively). In uncontrolled insulin-dependent patients the *P* value was 0.222 (Table 4).

The duration of hypertension was significantly negatively correlated with adiponectin level in controlled hypertensive patients ($P<0.001$*) (Table 5).

## Discussion

In the present study, we have found significant negative correlation between serum adiponectin concentration and age. In addition serum adiponectin level was found to be unaffected by sex in all studied groups. Controversial data exist in the literature. Vilarrasa *et al.* [9] referred to a decline in levels with age. In contrast, Adanczak *et al.* [10] reported that in healthy participants its level increases with age. Yamamoto *et al.* [11] failed to find a correlation.

In the present study, serum adiponectin levels were significantly lower in hypertensive patients (GIII) when compared with normotensive patients (GII and GIV).

The previous data are in accordance with the study by Iwashima *et al.* [12]. In contrast, Mallamaci *et al.* [13] reported in their study elevated levels of adiponectin in hypertensive men, as 60% of the patients included in their work were under antihypertensive drug therapy, which may cause divergent results. In the current study, we have found that adiponectin level in controlled hypertensive patients was higher than its level in uncontrolled patients but with no significant

**Table 2 Correlation between adiponectin and different parameters in each group**

| | Adiponectin | | | |
|---|---|---|---|---|
| | Control (*n*=20) | Nonhypertensive nondiabetic (*n*=20) | Hypertensive (*n*=20) | Diabetic (*n*=20) |
| Age | | | | |
| *r* | –0.159 | –0.555* | –0.0.473* | –0.650* |
| *P* | 0.503 | 0.011* | 0.035* | 0.002* |
| BMI | | | | |
| *r* | –0.437 | –0.451* | –0.657* | –0.485* |
| *P* | 0.054 | 0.046* | 0.002* | 0.030* |
| SBP | | | | |
| *r* | –0.284 | –0.653* | –0.618* | –0.317 |
| *P* | 0.255 | 0.002* | 0.004* | 0.174 |
| DBP | | | | |
| *r* | –0.078 | –0.605* | –0.576* | –0.371 |
| *P* | 0.743 | 0.005* | 0.008* | 0.107 |
| FBG | | | | |
| *r* | –0.042 | –0.481* | –0.027 | –0.609* |
| *P* | 0.860 | 0.032* | 0.911 | 0.004* |
| Cholesterol | | | | |
| *r* | –0.160 | –0.547* | –0.523* | –0.652* |
| *P* | 0.501 | 0.013* | 0.018* | 0.002* |
| TG | | | | |
| *r* | 0.100 | –0.460* | –0.517* | –0.621* |
| *P* | 0.673 | 0.041* | 0.020* | 0.003* |
| HDL | | | | |
| *r* | 0.663* | 0.681* | 0.532* | 0.473* |
| *P* | 0.001* | 0.001* | 0.016* | 0.035* |
| LDL | | | | |
| *r* | 0.015 | –0.479* | –0.528* | –0.473* |
| *P* | 0.951 | 0.033* | 0.017* | 0.035* |
| CIMT | | | | |
| *r* | –0.563* | –0.486* | –0.489* | –0.608* |
| *P* | 0.010* | 0.030* | 0.029* | 0.004* |

CIMT, carotid–intima media thickness; DBP, diastolic blood pressure; FBG, fasting blood glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; *r*, Pearson's coefficient; SBP, systolic blood pressure; TG, triglycerides. *Statistically significant at $P \leq 0.05$.

**Table 3 Relation between adiponectin and hypertension and diabetes therapy (*n*=20)**

| Adiponectin | Hypertension | | Diabetes therapy | |
|---|---|---|---|---|
| | Controlled (*n*=17) | Uncontrolled (*n*=3) | Oral hypoglycemic (*n*=14) | Insulin dependent (*n*=6) |
| | 8.22 (6.28–14.29) | 7.20 (6.40–7.30) | 7.25 (4.30–12.90) | 4.95 (2.20–16.50) |
| *P* | 0.244 | | 0.161 | |

*P*, *P* value for Mann–Whitney test.

**Table 4 Correlation between adiponectin and diabetes duration**

| | Adiponectin | | | |
|---|---|---|---|---|
| | Oral hypoglycemic (*n*=14) | | Insulin dependent (*n*=6) | |
| | Controlled (*n*=4) | Uncontrolled (*n*=10) | Controlled (*n*=1) | Uncontrolled (*n*=5) |
| Diabetes duration | | | | |
| *r* | 0.039 | –0.567 | – | –0.664 |
| *P* | 0.961 | 0.087 | – | 0.222 |

*r*, Pearson coefficient.

difference. We also found that there was significant negative correlation between adiponectin level and duration of hypertension in controlled hypertensive patients.

In the present study, we found that older type 2 diabetes mellitus patients presented with significantly lower adiponectin levels when compared with the controlled group, which was in

**Table 5 Correlation between adiponectin and hypertension duration**

| | Adiponectin | |
|---|---|---|
| | Controlled ($n$=17) | Uncontrolled ($n$=3) |
| Hypertension duration | | |
| $r$ | −0.816* | −0.912 |
| $P$ | <0.001* | 0.269 |

$r$, Pearson coefficient. *Statistically significant at $P \leq 0.05$.

concordance with the results of Mantzoros *et al.* [14].

Adiponectin level in diabetic patients on oral hypoglycemic drugs was higher than its level in diabetic patients on insulin therapy but with no significant difference between them. The adiponectin level in controlled diabetic patients who are on oral hypoglycemic drugs or on insulin therapy is higher than that in uncontrolled patients but with no significant difference between them.

The present results are consistent with previous reports of an inverse association between adiponectin and atherosclerosis in the elderly population [15,16]. We found that the correlation between adiponectin and CIMT was stronger among diabetic patients (Table 2). Our findings concur with those of Taniwaki *et al.* [17].

On the basis of correlation analysis we have confirmed that, in healthy individuals, serum adiponectin concentration inversely depends on BMI, systolic blood pressure, diastolic blood pressure, triglyceride, LDL cholesterol, and glucose, and correlated positively with HDL cholesterol. Adiponectin was significantly negatively correlated with CIMT independently of age, sex, and all metabolic risk factors.

## Conclusion

Elderly men over 65 years of age are characterized by a significantly lower serum adiponectin level than are younger ones, but there was no difference between its levels in the two sexes. Adiponectin level is significantly negatively correlated with CIMT.

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**Conflicts of interest**
There are no conflicts of interest.

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