Original Article

The Relationship between a Mediterranean Diet and Circulating Adiponectin Levels is Influenced by Cigarette Smoking

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Aim: Adherence to a Mediterranean diet has been shown to lower the risk of developing several chronic diseases. The ability to augment circulating adiponectin levels is proposed as an underlying mechanism mediating the beneficial effects of this diet. We aimed to examine whether the positive relationship between the Mediterranean diet and adiponectin is altered by cigarette smoking, taking potential confounders into consideration.
Methods: Plasma adiponectin levels were enzymatically measured in 45 never smokers, 61 smokers and 34 ex-smokers who adhered to a Mediterranean style diet and in 41 never smokers who did not adhere to the diet.
Results: Plasma adiponectin levels increased significantly in nonsmoking diet adherents compared to nonsmoking non-diet adherents. Among the diet adherents adiponectin decreased significantly in both moderate and heavy smokers compared to never smokers and significantly increased in quitters compared to smokers. Multiple regression analysis, controlling for age, obesity, Mediterranean diet and insulin resistance revealed an independent inverse association of smoking with adiponectin. Adiponectin levels remained significant and similar in subjects stratified according to age ($</>50$ years), BMI ($</>25$ kg/m^2) and HOMA-IR ($</>1.6$).
Conclusions: Despite its positive effects on adiponectin, the Mediterranean diet failed to negate the adiponectin-lowering effect of cigarette smoking, demonstrating the profound and independent capacity of cigarette smoke to negatively influence human health.

Introduction

Adiponectin is an adipose tissue-derived protein with insulin sensitizing, antiatherogenic and anti-inflammatory properties. Adiponectin has been consistently identified to play a crucial role in the development of metabolic syndrome, type 2 diabetes mellitus (T2DM), and cardiovascular diseases (CVD)[1].

Cigarette smoking remains the leading preventable cause of death in developed and developing countries alike as despite increased public awareness of its detrimental effects, the number of active smokers remains significantly high[2]. It has been unambiguously proven that cigarette smoking is a strong risk factor for several chronic diseases, including cardiovascular diseases, diabetes, cancers, and respiratory disorders[3]. Recent reports have indicated the negative modulation of adiponectin by cigarette smoke[4]. Smokers are reported to have lower circulating adiponectin, while its levels tend to increase in quitters following smoking abstinence, suggesting a possible mechanistic link between cigarette smoking and the increased risk of developing chronic diseases[5-12]. Addi-

tionally, the inverse association of smoking with adiponectin levels is independent of several confounding risk factors, including age, obesity and insulin resistance[7-10].

Epidemiological studies have shown that people consuming a Mediterranean diet tend to have a lower risk of developing cardiovascular diseases, diabetes, and cancer[13]. At the molecular level, the beneficial effects of consuming Mediterranean diet components are believed to be mediated at least in part by their positive modulation of adiponectin[14-16]; however, it is unclear whether the linear relationship between a Mediterranean diet and adiponectin is sustained under the influence of the adiponectin-lowering effects of cigarette smoking and whether this relationship is independent of potential confounders in subjects adhering long term to a Mediterranean-style diet.

Aim

The aim of the present study was to test if the linear relationship between a Mediterranean diet and adiponectin levels is affected by the inverse relationship of smoking with adiponectin and whether this effect of smoking is independent of confounders. Towards this end, we measured plasma adiponectin levels and examined their association with the Mediterranean-style diet in smokers and quitters, taking potential confounders into consideration.

Materials and Methods

Subjects

This study was conducted in accordance with the guidelines set by the Ethics Committee, College of Science, King Saud University. Forty-one apparently healthy nonsmoking, non-Mediterranean diet adherents, 45 nonsmoking Mediterranean diet adherents, 32 moderate smoking Mediterranean diet adherents, 29 heavy smoking Mediterranean diet adherents and 34 quitters adhering to a Mediterranean diet were recruited from the RIYADH COHORT, a nationwide screening program for biomarkers. All the participating subjects were Saudi citizens, hailing from different regions of the country and well representing the target population. Subjects were randomly recruited to avoid selection bias. Since smoking is not prevalent among women in the country, the study comprises only male smokers. Informed consent was obtained from all the participating subjects. A structured questionnaire collecting information on socio-demographic characteristics and present and past medical conditions was completed. Information was obtained on the Mediterra-

nean diet and smoking history, comprising the duration of cigarette smoking, the number of cigarettes smoked per day and any discontinuity or a major change in smoking behavior. Subjects who had been adhering to a Mediterranean diet for at least five years, smoking for at least two years and had quit smoking for a minimum of one year at the time of recruitment to the study were considered as Mediterranean diet adherents, smokers and quitters, respectively. Smoking status of the subjects was confirmed by assessing the plasma cotinine levels. Smokers were further divided into moderate (n=32, 10-20 cigarettes/day) and heavy (n=29, >20 cigarettes/day) smokers.

Dietary Assessment

Dietary data were obtained using a semi-quantitative food frequency questionnaire, aiming to retrieve information about the consumption frequency of the specified amount (unit/portion) of each food[17]. Using the data from the questionnaire, diet scores were calculated for the Mediterranean diet components, including fruit, vegetables, legumes, cereals, fish, nuts, whole grains and the ratio of polyunsaturated to saturated fat[18]. A value of 0 or 1 was assigned to each of the components using sex-specific medians as cutoffs. A value of 0 was assigned to subjects consuming a food component below the median, while a value of 1 was assigned to subjects consuming a food component at or above the median. For components deviating from the Mediterranean diet, including red meat and dairy products, a value of 1 was assigned for below median consumption and 0 for above median consumption. A value of 0 was assigned to a lower polyunsaturated to saturated fat ratio and 1 for a higher ratio, measured against the median cutoff. A Mediterranean diet score was generated for each subject by adding the scores of evaluated food components. A higher score indicated closer adherence to the Mediterranean diet.

Anthropometrics and Clinical Parameters

Height and weight were recorded to the nearest 0.5 cm and 0.1 kg, respectively. Waist circumference (WC) and hip circumference (HC) were measured using a standardized tape measure and were recorded to the nearest 0.1 cm. Body mass index (BMI) was calculated by the formula: weight (kg)/height (m)^2. Systolic and diastolic blood pressures were measured using an automated oscillometric device with the cuff fitted on the upper arm after allowing the subjects to rest for 30 min. An appropriate cuff size was used for obese individuals. The average blood pressure of two readings taken at an interval of 30 min was accepted.

Table 1. Anthropometric, clinical and biochemical characteristics of Mediterranean diet-adhering never smokers, smokers and ex-smokers

Variables	NS-MDA	MS-MDA	HS-MDA	ES-MDA	p-value
N	45	32	29	34	
Age	43.0 ± 6.1	45.2 ± 9.2	48.5 ± 10.1*	54.1 ± 11.0*, **, ***	< 0.001
BMI (kg/m²)	27.2 ± 3.6	24.0 ± 3.1*	23.2 ± 2.5*	25.9 ± 3.1*, **	< 0.001
WC (cm)	99.2 ± 14.4	93.1 ± 12.7*	91.3 ± 11.3*	96.1 ± 10.1	< 0.05
Glucose (mmol/L)	6.2 ± 1.5	6.0 ± 1.2	5.9 ± 1.4	6.4 ± 1.6	0.51
SBP (mmHg)	118.2 ± 10.1	125.4 ± 12.1*	128.4 ± 13.2*	121.10 ± 12.7***	< 0.001
DBP (mmHg)	78.1 ± 6.5	81.2 ± 6.8	84.5 ± 7.2*	80.2 ± 6.9***	< 0.001
HDL-C(mmol/L)	1.2 ± 0.32	0.75 ± 0.20*	0.69 ± 0.18*	0.82 ± 0.23*, ***	< 0.001
LDL-C (mmol/L)	3.3 ± 1.0	4.2 ± 1.3*	4.4 ± 1.2*	3.8 ± 1.1**, ***	< 0.001
TG (mmol/L)	1.5 ± 0.78	2.0 ± 0.93*	2.2 ± 1.0*	2.1 ± 0.91*	< 0.05
Insulin	5.7 ± 0.74	8.9 ± 1.2*	8.3 ± 1.1*	7.2 ± 1.0*, **	< 0.001
HOMA-IR	1.8 ± 0.56	2.2 ± 0.62	2.5 ± 0.78*	2.1 ± 0.69***	< 0.001

NS-MDA: never smokers-Mediterranean diet adherents; MS-MDA: moderate smokers-MDA (10-20 cigarettes/day); HS-MDA: heavy smokers-MDA (over 20 cigarettes/day); ES-MDA: ex-smokers-MDA (2 years post-abstinence); BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL-C: HDL-cholesterol; LDL-C: LDL-cholesterol; TG: triglycerides; HOMA-IR: homeostasis model assessment-insulin resistance. *significantly different from NS-MDA; **significantly different from MS-MDA; ***significantly different from HS-MDA. All subjects had adhered to the Mediterranean diet for a minimum of 5 years.

Biochemical Measurements

Fasting blood samples were collected and the plasma was separated by Ficoll-Paque PLUS (GE Healthcare Bioscience AB, Uppsala, Sweden) gradient centrifugation and stored at −80℃ until analyzed. Glucose, total cholesterol and triglycerides were measured using standard enzymatic methods and a fully automated analyzer (Konelab Instruments, Espoo, Finland). HDL-cholesterol levels were determined by phosphotungstic acid/magnesium chloride precipitation (Konelab Instruments, Espoo, Finland). LDL-cholesterol was calculated using the Friedewald equation. Since the Friedewald formula is valid for triglyceride values < 400 mg/dL, we excluded subjects with triglyceride levels ≥ 400 mg/dL to accurately calculate the LDL-cholesterol.

Adiponectin and Insulin Assessment

Plasma adiponectin and insulin levels were quantified using multiplex assay kits that utilize fluorescent microbead technology, allowing simultaneous quantification of several target proteins within a single plasma sample of 50-100 μL. These include pre-mixed and fully customized panels that utilize the Luminex xMAP Technology platform (Luminex Corp., Austin, TX, USA). Insulin resistance was assessed by homeostasis model assessment-insulin resistance (HOMA-IR) calculated using the formula: insulin (μU/mL) × glucose (mmol/L)/22.5 [19].

Statistical Analysis

Statistical analyses were carried out using SPSS version 16.0. (SPSS, Inc., Chicago IL, USA). All variables were checked for normality. Non-Gaussian variables were appropriately log or square root transformed for normality. Data are shown as the mean ± standard deviation. Analysis of variance (ANOVA) was performed across the four groups followed by Bonferroni post-hoc analysis. Pearson's partial correlation was performed, controlling for age. Multiple linear regressions were performed to screen the effects of potential confounders on estimates of adiponectin. Analysis of co-variance (ANCOVA) was carried out across the fixed factors of smoking status, controlling for potential confounding factors. Significance was set at $p < 0.05$.

Results

The anthropometric, clinical and biochemical characteristics of non-smokers, smokers and quitters adhering to a Mediterranean diet are presented in **Table 1**. Quitters were older than moderate, heavy and non-smokers, while heavy smokers were significantly older than non-smokers. No significant age difference was noted between moderate and heavy smokers or between moderate and non-smokers. Non-smokers were heavier than moderate and heavy smokers as well as quitters, while quitters were heavier than heavy smokers. These data confirm the weight-modulating

A

B
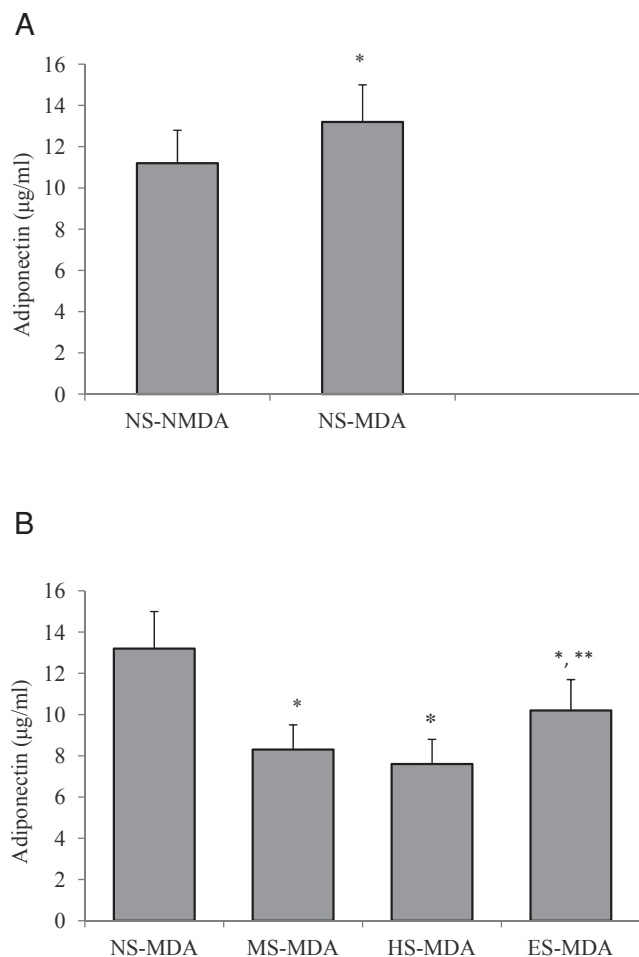
Fig. 1. Adiponectin levels in non-adherent and Mediterranean deit adherent never smokers, smokers and quitters.

A. Plasma adiponectin levels were measured enzymatically in never smokers ($n=45$) of Mediterranean diet adherent (NS-MDA) and never smokers ($n=45$) of non-Mediterranean diet adherent normal healthy subjects (NS-NMDA). Adiponectin levels were significantly higher in NS-MDA than NS-NMDA (13.2 ± 1.8 vs. 11.2 ± 1.6 μg/mL respectively). *Significantly different ($p=0.01$) from NS-NMDA. B. Plasma adiponectin levels were measured similarly in never smokers ($n=45$) of Mediterranean diet adherents (NS-MDA), moderate smokers ($n=32$) of Mediterranean diet adherents (MS-MDA), heavy smokers ($n=29$) of Mediterranean diet adherents (HS-MDA) and in ex-smokers (34) of Mediterranean diet adherents (ES-MDA). Compared to NS-MDA adiponectin levels were significantly lower in MS-MDA (13.2 ± 1.8 vs. 8.3 ± 1.2 μg/mL, respectively) and in HS-MDA (13.2 ± 1.8 vs. 7.6 ± 1.2 μg/mL, respectively). ES-MDA had significantly elevated adiponectin concentrations compared to MS-MDA (10.2 ± 1.5 vs. 8.3 ± 1.2 μg/mL, respectively) and HS-MDA (10.2 ± 1.5 vs. 7.6 ± 1.2 μg/mL, respectively). *Significantly different ($p=0.01$) from NS-MDA. **Significantly different ($p=0.01$) from NS-MDA, MS-MDA and HS-MDA.

effects of cigarette smoking. Heavy smokers were more insulin resistant than non-smokers and quitters

Adiponectin levels in the studied subjects are pre-

Table 2. Age adjusted Pearson's correlation between adiponectin and the variables in NS-MDA ($n=45$), MS-MDA ($n=32$), HS-MDA ($n=29$) and ES-MDA ($n=34$)

Variables	r	p-value
BMI (kg/m^2)	−0.28	0.006
Waist circumference (cm)	−0.21	0.04
Glucose (mmol/L)	−0.19	0.03
SBP (mmHg)	−0.22	0.01
DBP (mmHg)	−0.18	0.04
HDL-cholesterol (mmol/L)	0.25	0.01
LDL-cholesterol (mmol/L)	−0.16	0.07
Triglyceride (mmol/L)	−0.18	0.04
HOMA-IR	−0.23	0.009
Smoking status (No/Yes)	−0.17	0.04

NS-MDA: never smokers-Mediterranean diet adherents; MS-MDA: moderate smokers-MDA (10-20 cigarettes/day); HS-MDA: heavy smokers-MDA (over 20 cigarettes/day); ES-MDA: ex-smokers-MDA (2 years post-abstinence); BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; HOMA-IR: homeostasis model assessment-insulin resistance; r: correlation coefficient. All subjects had adhered to a Mediterranean diet for a minimum of 5 years.

sented in **Fig. 1**. The intra-assay correlation co-efficiency (CV %) and the inter-assay CV % were found to be 5.6 and 12.8, respectively, for adiponectin. Compared to nonsmoking non-Mediterranean diet adherents, adiponectin levels were significantly high in nonsmoking diet adherents. Compared to nonsmoking Mediterranean diet adherents, adiponectin levels significantly decreased in both Mediterranean diet-adherent moderate and heavy smokers. Adiponectin levels in quitters were significantly high compared to both moderate and heavy smokers and significantly low compared to nonsmoking diet adherents.

Age-adjusted partial correlation of adiponectin with the measured variables in Mediterranean diet-adherent subjects ($n=140$) are presented in **Table 2**. Adiponectin levels were negatively correlated with smoking, BMI, WC, glucose, triglycerides, and systolic and diastolic blood pressures, while positively correlated with HDL-cholesterol.

Several studies have previously reported the modulating effects of age, BMI, smoking, a Mediterranean diet, systolic and diastolic blood pressures, triglycerides, HDL- and LDL-cholesterols and HOMA-IR on adiponectin levels[7, 9, 10, 15, 20-24]. Accordingly, we selected these confounders to assess their influence on adiponectin. Consistently, the multiple regression model including these potential confounders revealed age, smoking, BMI, a Mediterranean diet and HOMA-IR as independent predictors of adiponectin, and the

Table 3. Multiple linear regression analysis of adiponectin in NS-NMDA ($n=41$), NS-MDA ($n=45$), MS-MDA ($n=32$), HS-MDA ($n=29$) and ES-MDA ($n=34$)

Variables	Model 1 $β$ (p-value)	Model 2 $β$ (p-value)	Model 3 $β$ (p-value)	Model 4 $β$ (p-value)
Age	0.26 (<0.001)	0.24 (0.001)	0.23 (0.002)	0.22 (0.005)
BMI (kg/m^2)	-0.23 (0.001)	-0.21 (0.003)	-0.20 (0.007)	-0.19 (0.02)
SBP (mmHg)	-0.11 (0.14)	-0.09 (0.22)	-0.10 (0.18)	-0.07 (0.35)
DBP (mmHg)	-0.09 (0.22)	-0.07 (0.35)	-0.08 (0.28)	-0.05 (0.50)
Triglycerides (mmol/L)	-0.12 (0.10)	-0.10 (0.18)	-0.09 (0.22)	-0.12 (0.10)
HDL-cholesterol (mmol/L)	0.15 (0.04)	0.14 (0.07)	0.15 (0.06)	0.14 (0.07)
LDL-cholesterol (mmol/L)	-0.09 (0.18)	-0.08 (0.28)	-0.09 (0.22)	-0.06 (0.42)
HOMA-IR	-0.17 (0.009)	-0.16 (0.03)	-0.17 (0.02)	-0.18 (0.01)
Smoking status (NS/ES/MS/HS)	$-$	-0.12 (0.04)	$-$	-0.15 (0.04)
Mediterranean Diet	$-$	$-$	0.14 (0.06)	0.17 (0.02)

NS-NMDA: Never smokers-non-Mediterranean diet adherents; NS-MDA: never smokers-Mediterranean diet adherents; MS-MDA: moderate smokers-MDA (10-20 cigarettes/day); HS-MDA: heavy smokers-MDA (over 20 cigarettes/day); ES-MDA: ex-smokers-MDA (2 years post-abstinence); BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; HOMA-IR: homeostasis model assessment-insulin resistance; $β$: standard coefficient. All subjects had adhered to a Mediterranean diet for a minimum of 5 years.

association between smoking and its negative adiponectin-modulating effect remained significant even after adjusting for these interfering factors (**Table 3**).

To understand the relationship between adiponectin and the smoking status in Mediterranean diet adherents, while accounting for insulin resistance status, age and BMI, subjects were further stratified according to age ($>$ or <50 years), BMI ($>$ or <25 kg/m^2) and HOMA-IR ($>$ or <1.6). Compared to nonsmoking Mediterranean diet adherents, adiponectin levels were significantly and similarly decreased in smoking diet-adherent subjects irrespective of age, BMI and HOMA-IR (**Table 4**).

Discussion

In this study we examined whether the inverse association between cigarette smoking and adiponectin was sustained in subjects adhering long term to a Mediterranean diet and whether this relationship was independent of confounders. Although, in the present study, a Mediterranean diet significantly elevated adiponectin as opposed to a non-Mediterranean diet among non-smokers, cigarette smoking effectively negated the diet-induced effect on adiponectin.

A number of studies have previously reported the adiponectin-lowering effects of cigarette smoking in both men and women with or without preexisting morbidities[5-12]. Of importance, cigarette smoking has also been shown to reduce peripheral blood mononuclear cell adiponectin levels[25]. Further, a dose-dependent positive response on adiponectin levels is seen with smoking intensity[6, 8-10, 26]. Refining the inverse association further, studies have found that the relationship between smoking and adiponectin remained significant even after controlling for multiple confounding factors, including insulin resistance, age, obesity, and alcohol consumption[7-10, 27]. Collectively, this experimental evidence strengthens the inverse relationship between smoking and circulating adiponectin levels. Similarly, smoking cessation has been shown to restore adiponectin levels, albeit transiently, in quitters, further substantiating the negative modulation of adiponectin by cigarette smoking[11, 12].

Previous studies have found increased adiponectin levels in people adhering to a Mediterranean-style diet, with or without clinical complications[14-16]. Consistent with these reports, among non-smokers we found a significant increase in adiponectin levels in subjects adhering to a Mediterranean diet compared to non-adherent subjects, underscoring the ability of this diet to positively modulate adiponectin levels in apparently healthy subjects. However, the status of the linear relationship between a Mediterranean diet and adiponectin under the influence of cigarette smoking has not been comprehensively examined. In the present study, among diet adherents, we found a significant decrease in adiponectin in both moderate and heavy smokers compared to non-smokers. In fact, adiponectin in diet-adhering smokers was down-modulated to the extent that its levels were significantly lower than those found in non-smoking non-adherents, indicating the profound negative modulating effects of cigarette smoking on adiponectin while

Table 4. Mean log adiponectin levels§ (95% CI) in the studied subjects categorized according to age, BMI and HOMA-IR

	NS-MDA (*n*=45)	ES-MDA (*n*=34)	MS-MDA (*n*=32)	HS-MDA (*n*=29)	*p* value
Age (years)					
< 50	2.4 (2.1-2.6)	1.93 (1.7-2.1)	1.92 (1.7-2.0)	1.92 (1.7-2.1)	< 0.05
≥ 50	2.6 (2.4-2.7)	2.8 (2.6-2.9)	2.2 (2.0-, 2.3)	2.0 (1.8-2.1)	0.01
BMI (Kg/m²)					
< 25	2.6 (2.4-2.7)	2.4 (2.2-2.5)	2.1 (1.9-2.2)	1.9 (1.8-2.0)	< 0.05
≥ 25	2.4 (2.2-2.5)	2.3 (2.1-2.4)	2.0 (1.8-2.1)	1.9 (1.8-1.9)	< 0.001
HOMA-IR					
< 1.6	2.7 (2.5-2.8)	2.5 (2.3-2.5)	2.3 (2.1-2.4)	2.1 (1.9-2.2)	< 0.05
≥ 1.6	2.5 (2.3-2.6)	2.2 (2.0, 2.3)	2.0 (1.8-2.1)	1.9 (1.8-2.0)	< 0.05

NS-MDA: never smokers-Mediterranean diet adherents; MS-MDA: moderate smokers-MDA (10-20 cigarettes/day); HS-MDA: heavy smokers-MDA (over 20 cigarettes/day); ES-MDA: ex-smokers-MDA (2 years post-abstinence); BMI: body mass index; HOMA-IR: homeostasis model assessment-insulin resistance. §-adjusted for age, BMI, HOMA-IR, SBP, DBP, triglycerides, LDL- and HDL-cholesterol. All subjects had adhered to a Mediterranean diet for a minimum of 5 years.

competing with the positive modulating effects of a Mediterranean diet. Providing further evidence, adiponectin levels were found to be significantly restored in diet-adhering quitters as compared to the levels in diet-adhering smokers, pointing to the withdrawal of the inhibitory effects of cigarette smoking. Adiponectin levels in moderate smokers decreased to the same extent as in heavy smokers, indicating that even moderate smoking can potentially bring about an adverse change. Moreover, the relationship of smoking with adiponectin remained significant even after controlling for age, HOMA-IR, a Mediterranean diet and BMI. Taken together, these data underscore that the linear relationship of the Mediterranean diet with adiponectin is altered in smokers and that cigarette smoking significantly influenced the diet's positive effect on adiponectin. To our knowledge, a lone relevant study has found that adiponectin levels remain significant in apparently healthy Mediterranean diet adherents unadjusted for smoking status[15]. The likely explanation for the inconsistency of this study with ours with respect to the significance between diet and increased adiponectin is the marked difference in the inclusion criteria of smokers with respect to the number of cigarettes smoked. The previous study set the criteria to include subjects who smoked a minimum of one cigarette a day, which likely exerted lower adiponectin-reducing effects than in ours, in which even moderate smokers smoked a minimum of 10 cigarettes a day.

Previous studies have shown that the change in adiponectin levels in smokers is a result of cigarette smoking and is independent of age, obesity, insulin resistance or alcohol consumption[7, 9]. To verify these observations in subjects adhering to a Mediterranean-style diet, we further stratified the data according to age, BMI and HOMA-IR. Compared to never smokers, the effect of smoking on adiponectin was found to be similar in subjects irrespective of age, obesity and insulin resistance states. These data support that the adiponectin-modulating effects of cigarette smoking are independent of potential confounders, at least those included in this study, viz. age, BMI and HOMA-IR.

Several studies have proposed mechanisms that possibly mediate the adiponectin-lowering effects of cigarette smoking. Oxidative stress generated by smoking can attenuate adiponectin expression and secretion via phosphatidylinositol 3-kinase inhibition in adipocytes[6]. Nicotine, the major constituent of cigarette smoke, can initiate lipolysis by adipose tissue-localized activation of nicotinic cholinergic receptors[6, 28]. Additionally, by augmenting post-ganglionic sympathetic nerves, nicotine may suppress adiponectin gene expression[29]. Alternatively, increased inflammatory cytokines often seen in smokers may suppress the adiponectin expression[30].

Limitations of this study include the small sample size, which can influence the observed associations and can lead to misinterpretation of the findings. Setting the recruiting criteria to include only strict Mediterranean diet adherents limited our efforts to study a larger population. Due to the cross-sectional nature of this study, the observations of the study need to be followed up in a prospective setup to make a causal inference. Additionally, the demographics and men-only study also limited the generalization of results. Alcohol consumption has previously been reported to significantly reduce adiponectin levels[27]. Since alcohol consumption is not prevalent among the Saudi population, the effect of alcohol as a confounding factor could not be ascertained in the study.

Conclusion

In conclusion, we found that despite its well-proven overall beneficial effects and, in particular, the positive modulating effects on adiponectin, the Mediterranean diet failed to limit the adiponectin-lowering effects of cigarette smoke. Moreover, these effects were independent of potential confounders. To our knowledge, this is the first study to comprehensively examine the inverse relationship between cigarette smoking and adiponectin in subjects adhering to a long-term Mediterranean diet.

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Conflict of Interest

None.

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