Nutrition, Metabolism and Cardiovascular Diseases xxx (xxxx) xxx

Contents lists available at ScienceDirect

Nutrition, Metabolism and Cardiovascular Diseases

journal homepage: www.elsevier.com/locate/nmcd

Plasma adiponectin levels are associated with habitual dietary polyphenol intake in individuals at high cardiometabolic risk: a cross-sectional study

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ARTICLE INFO

Handling Editor: Dr. A. Siani

Keywords:
Adiponectin
Dietary fiber
Dietary polyphenols
Cardiometabolic risk

ABSTRACT

Background and aim: Adiponectin, the most abundant adipokine secreted by adipose tissue, plays a key role in glucose and lipid metabolism while exhibiting anti-inflammatory properties. Its expression is influenced by age, sex, physical activity, and diet. While adherence to healthy dietary patterns like the Mediterranean and DASH diets has been linked to higher adiponectin levels, the specific impact of individual dietary components remains uncertain. In this cross-sectional study we investigated the relationship between plasma adiponectin levels, metabolic parameters, and habitual dietary composition in individuals at high cardiometabolic risk.

Methods and results: Seventy-five overweight/obese participants from the Etherpaths European Project, with increased waist circumference and one additional metabolic syndrome component, were included in this cross-sectional study. Dietary intake was assessed using a 7-day food record, and plasma adiponectin levels were measured via ELISA. Correlations were analyzed at baseline, before any dietary intervention. Mean plasma adiponectin concentration was 10.2 ± 2.5 μg/mL. Adiponectin levels correlated inversely with diastolic blood pressure ($r = -0.288$, $p = 0.015$) and directly with HDL cholesterol ($r = 0.268$, $p = 0.020$). A significant positive association was observed with dietary fiber ($r = 0.259$, $p = 0.028$) and total polyphenol intake ($r = 0.319$, $p = 0.006$). Among polyphenols, phenolic acids ($r = 0.308$, $p = 0.009$), flavones ($r = 0.270$, $p = 0.023$), and tyrosols ($r = 0.279$, $p = 0.018$) showed the strongest associations. Adiponectin was significantly correlated with fruit and vegetable intake ($r = 0.266$, $p = 0.021$), but not with other food groups.

Conclusion: A higher habitual intake of polyphenol-rich plant-based foods is associated with increased plasma adiponectin levels, which in turn correlate with a more favorable metabolic profile in individuals at high cardiometabolic risk.

1. Introduction

Adiponectin is the most abundant adipokine synthesized and secreted by adipose tissue. Its serum concentration ranges between 3 and 30 mg/mL accounting for up to 0.05 % of total serum protein [1]. It plays a crucial role in glucose and lipid metabolism and exerts significant anti-inflammatory effects, contributing to protection against obesity-related diseases [1]. Human studies have shown that circulating adiponectin levels are reduced in obese individuals [2] and are inversely associated with metabolic syndrome, insulin resistance, type 2 diabetes (T2D), and cardiovascular disease, highlighting its critical role in metabolic health [3–6].

Several factors influence adiponectin expression, including age, sex, ethnicity, physical activity, and diet [7,8]. The Mediterranean Diet, characterized by a high intake of fruits, vegetables, fiber, unsaturated fats, whole grains, and unrefined carbohydrates, along with moderate consumption of dairy and fish and low intake of saturated fats and simple sugars, has been consistently associated with increased

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https://doi.org/10.1016/j.numecd.2025.104164
Received 14 March 2025; Received in revised form 19 May 2025; Accepted 21 May 2025
Available online 25 May 2025

adiponectin levels [9–11]. Similarly, the Dietary Approaches to Stop Hypertension (DASH) diet, which emphasizes vegetables, fruits, nuts, legumes, whole grains, and low-fat dairy while limiting processed red meat, sugary drinks, and high-sodium foods, has shown comparable effects on adiponectin levels [12]. Both dietary patterns are rich in bioactive compounds with anti-inflammatory properties, such as omega-3 fatty acids and polyphenols, which are believed to contribute to these effects. However, the specific role of individual dietary components in modulating adiponectin levels remains controversial.

Higher cereal fiber intake, for instance, has been associated with increased adiponectin levels in both healthy women [9] and individuals with T2D [13]. Supporting this, a randomized controlled trial in people with T2D showed a significant postprandial—but not fasting—increase in adiponectin after an 8-week intervention with a high-fiber, low-glycemic-index diet compared to a diet rich in monounsaturated fatty acids (MUFA) [14]. Conversely, in individuals with metabolic syndrome, a 12-week intervention with a whole-grain cereal-based diet did not significantly affect fasting or postprandial adiponectin levels compared to a refined cereal-based diet [15]. Polyphenols, plant-derived bioactive compounds with potent anti-inflammatory properties [16], may also influence adiponectin concentrations. Human studies investigating the effects of polyphenol supplementation [17] or the intake of polyphenol-rich foods such as coffee, green tea, black raspberry, and grapes have generally reported positive associations with plasma adiponectin levels [18,19]. Nevertheless, the overall relationship between dietary composition and adiponectin expression remains unclear [20].

Therefore, this cross-sectional study aimed to evaluate the association between plasma adiponectin levels, metabolic parameters, and habitual diet composition in individuals at high cardiometabolic risk under real-life conditions.

2. Methods

2.1. Participants and study design

In this cross-sectional study, we analyzed baseline data from the European Etherpaths (FP7-KBBE-222639) Project, a randomized controlled clinical trial investigating the effects of diets naturally rich in polyphenols and/or long-chain omega-3 fatty acids in individuals at high cardiovascular risk. The study was conducted in accordance with the Declaration of Helsinki, approved by the Ethics Committee of Federico II University (Naples, Italy), and registered at ClinicalTrials.gov (NCT01154478). All participants provided written informed consent.

Details on the study protocol, inclusion, and exclusion criteria have been published elsewhere [21]. For the present analysis, we included 75 individuals (both sexes, aged 35–70 years) with a body mass index (BMI) of 27–35 kg/m^2 and an increased waist circumference (WC) (men >102 cm; women >88 cm). In addition to a high BMI and WC, participants were required to have at least one other component of metabolic syndrome, as defined by the National Cholesterol Education Program (NCEP)/Adult Treatment Program (ATP) III criteria [22]. Baseline data collected before the intervention were used for this analysis (Supplementary Fig. 1).

2.2. Anthropometric measurements and dietary assessment

Body weight, height, and WC were measured following standardized procedures [23]. Blood pressure was taken in duplicate after 15 min of rest with an automatic sphygmomanometer. If blood pressure measurements differed by more than 5 mmHg, a third measurement was taken. The blood pressure measurements were then averaged. Dietary habits were assessed using a 7-day food record completed by participants prior to the intervention. An expert dietitian collected and reviewed the food records during the run-in visit. Daily intake of energy, macronutrients, and micronutrients was calculated and compared with the dietary recommendations for adults set by the LARN-V guidelines [24].

Food records were analyzed using Metadieta software, incorporating the food database of the Italian National Institute for Food and Nutrition [25]. The polyphenol content of the various food items was primarily estimated using the USDA database [26]. When certain foods were not available in the USDA database, data from the Phenol-Explorer database [27] were used as a complementary source. This was the case of extra virgin olive oil (EVO) and Arabica coffee blends—two food items commonly consumed in Southern Italy— and wholegrain cereals, which were not included in the USDA tables. This approach allowed for a more comprehensive and accurate assessment of total dietary polyphenol intake.

Food intake was categorized into five food groups based on the classification provided by the Italian Dietary Guidelines [28]: 1. Meat, fish, eggs and legumes, 2. Dairy products (milk, cheese, yogurt), 3. Cereals and derivatives (bread, pasta, rice, etc.), 4. Animal fats and oils, 5. Fruits and vegetables. Each food group was formed by aggregating the consumption of its characteristic food items.

2.3. Laboratory methods

Plasma concentrations of cholesterol, triglycerides, and glucose were measured using enzymatic methods (ABX Diagnostics) on an ABX Pentra 400 analyzer (HORIBA Medical). HDLs were isolated via the phosphotungstic acid/magnesium chloride precipitation method, while LDL cholesterol was calculated using the Friedewald formula. Insulin resistance was estimated using the homeostatic model assessment of insulin resistance (HOMA-IR) formula:

HOMA-IR=Fasting glucose (mg/dL) × Fasting insulin (μU/mL)/405. Fasting plasma total adiponectin concentrations were measured using an enzyme-linked immunosorbent assay (ELISA) utilizing a polyclonal antibody, in house produced, versus a human adiponectin sequence region (H2N-ETTTQGPGVLLPLPKG-COOH), as previously described [29]. A calibration curve was established, and quantification was performed using human recombinant adiponectin as a standard (Biovendor R&D, USA). Each plasma sample was diluted 1:5000 and assayed three times in duplicate.

2.4. Statistical analysis

Data are presented as mean ± SD, unless otherwise specified. The Shapiro–Wilk test was used to assess the normality of variable distributions. Variables that did not follow a normal distribution were log-transformed prior to analysis. Differences in anthropometric and metabolic parameters and in daily composition of the habitual diet between men and women were assessed using an unpaired *t*-test.

Associations between fasting plasma adiponectin concentrations and metabolic parameters, nutrients, and food groups were analyzed using Spearman's rank correlation. Partial correlation analyses were performed to adjust for gender. Stepwise linear regression analysis was conducted to identify the nutrient most strongly associated with circulating adiponectin levels.

A p-value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 28.0 (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Metabolic parameters of study participants

The clinical characteristics of the study cohort are summarized in Table 1, comprising 75 participants (33 men and 42 women). As expected, both men and women exhibited elevated waist circumference and low HDL cholesterol levels. Stratification by sex revealed significant differences, with systolic blood pressure, diastolic blood pressure,

Table 1
General characteristics of the study participants in the whole population and according to sex.

	Whole population	Men (n = 33)	Women (n = 42)
Age (years)	54 ± 9	53 ± 9	55 ± 8
Body mass index (kg/m^2)	32 ± 3	31 ± 3	32 ± 4
Waist circumference (cm)	104 ± 8	109 ± 7	100 ± 7
Systolic blood pressure (mm Hg)	121 ± 12	125 ± 13	119 ± 10*
Diastolic blood pressure (mm Hg)	75 ± 8	78 ± 8	72 ± 8*
Plasma triglycerides (mg/dL)	127 ± 63	144 ± 69	115 ± 57
Plasma total cholesterol (mg/dL)	193 ± 31	185 ± 34	200 ± 27
Plasma HDL cholesterol (mg/dL)	42 ± 11	35 ± 8	48 ± 10
Plasma LDL cholesterol (mg/dL)	115 ± 27	111 ± 29	118 ± 25
Plasma glucose (mg/dL)	103 ± 12	105 ± 14	102 ± 11
Plasma insulin (μU/mL)	18 ± 7	20 ± 7	16 ± 7*
Homa-IR	4.6 ± 2.0	5.2 ± 2.1	4.2 ± 1.8*
Plasma Adiponectin (μg/ml)	10.2 ± 2.5	9.9 ± 2.5	10.5 ± 2.5

Data are Mean ± SD. *p < 0.05 *vs.* Men, unpaired *t*-test. HDL, high density lipoprotein; LDL, low density lipoprotein; HOMA-IR, homeostatic model assessment of insulin resistance.

plasma total cholesterol, plasma insulin, and HOMA-IR being lower in women compared to men. However, adiponectin levels did not differ between sexes.

3.2. Correlations between adiponectin and metabolic parameters

Fasting plasma adiponectin levels were negatively associated with diastolic blood pressure (r = −0.288, p = 0.015) and positively associated with HDL cholesterol (r = 0.268, p = 0.020) (Fig. 1). These associations remained significant after adjusting for gender. No other significant correlations were observed between fasting adiponectin concentration and metabolic parameters.

3.3. Correlations among adiponectin, dietary components and food groups

Table 2 summarizes the composition of the participants' habitual diet. The mean daily intake of energy, macronutrients, and micronutrients was consistent with the LARN dietary recommendations for both men and women. As expected, men had a higher energy intake than women, as well as higher absolute intakes (in grams) of carbohydrates and cholesterol. However, these differences were not evident when nutrient intakes were expressed as a percentage of total energy (TE) intake. No significant differences were observed between sexes in total polyphenol intake or across different polyphenol classes or subclasses (Table 2).

Table 2
Daily composition of the habitual diet of the study participants (n = 75).

	Wole population	Men (n = 33)	Women (n = 42)
Total energy (kcal)	1811 ± 497	1971 ± 484	1700 ± 479*
Total fat (g)	66.7 ± 23.8	71.7 ± 24.1	63.1 ± 23.1
(% of energy)	32.8 ± 4.8	32.4 ± 5	33.0 ± 4.7
SFA (g)	20.4 ± 8.3	22.5 ± 8.5	19.0 ± 7.8
(% of energy)	10 0.0 ± 2.2	10.1 ± 2.2	9.8 ± 2.2
MUFA (g)	29.8 ± 10.8	31.6 ± 11.2	28.5 ± 10.5
(% of energy)	14.7 ± 2.8	14.3 ± 3.2	15.0 ± 2.5
n-6 PUFA (% of energy)	3.1 ± 0.7	3.0 ± 0.6	3.1 ± 0.7
n-3 PUFA (% of energy)	0.13 ± 0.20	0.50 ± 0.10	0.50 ± 0.10
EPA (% of energy)	0.06 ± 0.05	0.10 ± 0.08	0.10 ± 0.10
DHA (% of energy)	0.07 ± 0.07	0.10 ± 0.10	0.10 ± 0.10
Cholesterol (mg)	242 ± 83	270 ± 99	222 ± 65*
Total CHO (g)	240 ± 67	263 ± 68	224 ± 63*
(% of energy)	50 ± 5	50 ± 5	49 ± 4
Fiber (g)	20 ± 6	21 ± 6	19 ± 6
Vitamin C (mg)	124 ± 70	115 ± 54	129 ± 78
Vitamin E (mg)	9.2 ± 3.1	9.2 ± 3.3	9.1 ± 3.0
Polyphenols (mg)	635 ± 429	628 ± 291	634 ± 507
Phenolic acids (mg)	535 ± 317	536 ± 335	537 ± 295
Flavones (mg)	1.9 ± 1.5	2.0 ± 1.4	1.8 ± 1.5
Flavonols (mg)	20.2 ± 22.0	21.8 ± 30.6	18.3 ± 12.3
Flavanols (mg)	22.3 ± 23.0	20.0 ± 15.0	24.0 ± 27.0
Flavanones (mg)	24.2 ± 27.0	24.2 ± 26.8	24.3 ± 28.0
Anthocyanidins (mg)	16.7 ± 11.0	16.0 ± 12.0	16.5 ± 11.0
Tyrosols (mg)	13.3 ± 7.3	13.2 ± 7.5	13.5 ± 7.2

Data are Mean ± SD. SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; CHO, carbohydrate. *p < 0.05 vs. women (*t*-Test).

Among dietary components, plasma adiponectin levels correlated positively with fiber intake (r = 0.259, p = 0.028) and polyphenol intake (r = 0.319, p = 0.006) (Fig. 2). In a stepwise linear regression analysis, with plasma adiponectin as the dependent variable and nutrient intake as independent variables, polyphenol intake emerged as the only significant predictor of adiponectin levels (β = 0.307, p = 0.009).

Further analysis revealed strong associations between adiponectin and specific polyphenol classes and subclasses, including phenolic acids (r = 0.308, p = 0.009), flavones (r = 0.270, p = 0.023), and tyrosols (r = 0.279, p = 0.018) (Fig. 3). No significant correlations were observed for the other polyphenol classes/subclasses (Supplementary Table 1). Among food groups, fruit and vegetable intake was positively associated with adiponectin levels (r = 0.266, p = 0.021), while no significant correlations were observed with other food groups (Fig. 4). Additionally, a positive and significant correlation was found between adiponectin levels and coffee consumption (r = 0.249, p = 0.031) (Fig. 5).

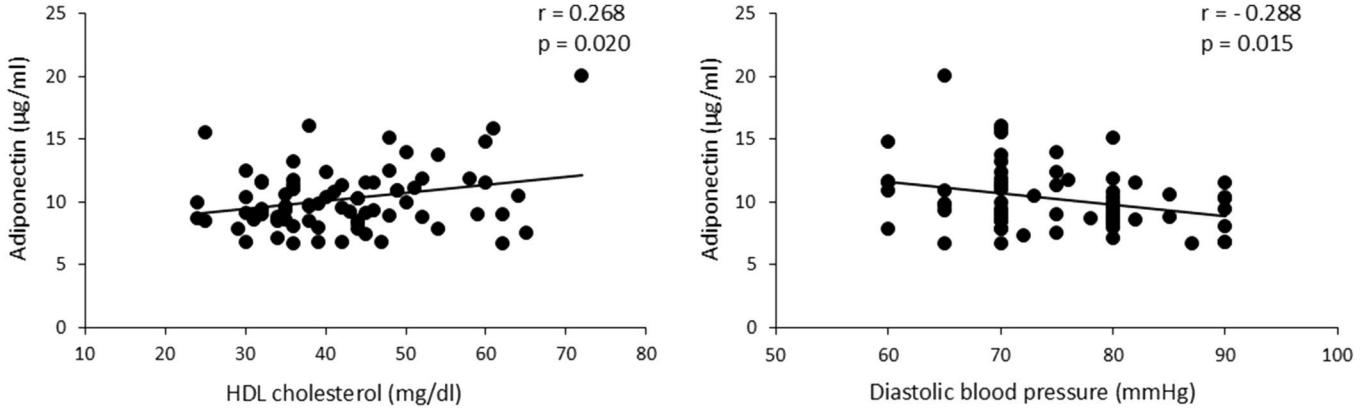

Fig. 1. Correlation analysis between fasting plasma adiponectin levels and HDL-cholesterol and diastolic blood pressure in the whole population (n = 75).

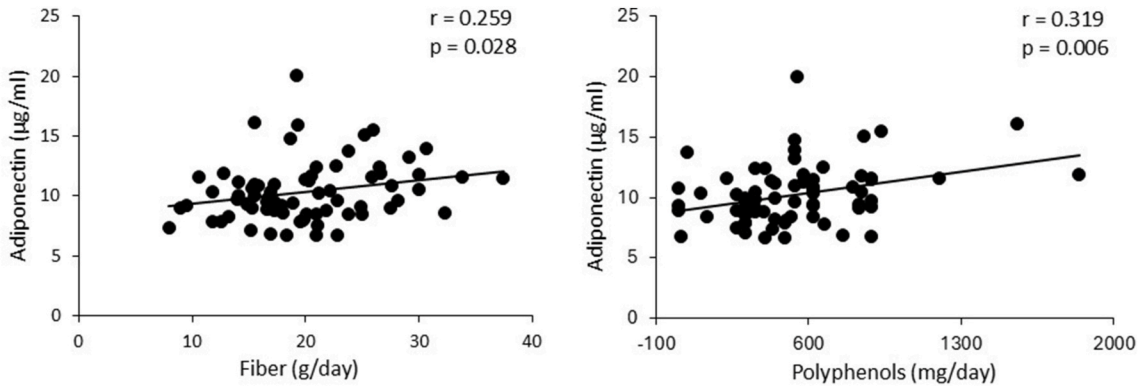

Fig. 2. Correlation analysis between fasting plasma adiponectin levels and dietary intake of fiber and polyphenols in the whole population (n = 75).

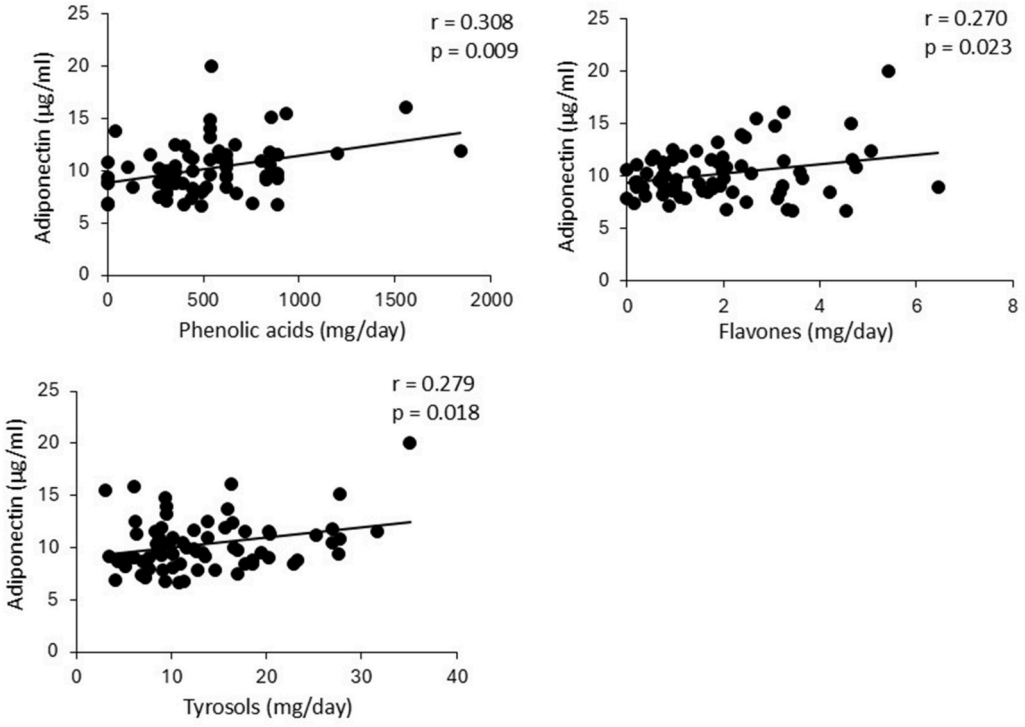

Fig. 3. Correlation analysis between fasting plasma adiponectin levels and dietary intake of phenolic acids, flavones, and tyrosols in the whole population (n = 75).

4. Discussion

This cross-sectional study demonstrates that in individuals at high cardiovascular risk, fasting adiponectin levels were inversely correlated with blood pressure and positively associated with HDL cholesterol levels, fiber and polyphenol intake, particularly from fruits and vegetables.

According to linear regression analysis, polyphenol intake emerged as the main determinant of adiponectin levels. Polyphenols are known for their antioxidant and anti-inflammatory properties, which could enhance metabolic function beyond the direct effects of fiber.

These results are further supported by the direct associations between adiponectin and specific polyphenol classes and subclasses, including phenolic acids, flavones and tyrosols. The mean estimated daily polyphenol intake in our study population (635 mg/day) is consistent with Italian dietary patterns, as also reported by Godos et al. in the Mediterranean healthy Eating, Aging and Lifestyle (MEAL) study, where the mean daily polyphenol intake was approximately 660 mg/day [30].

Several observational and intervention studies have linked polyphenol supplementation in the form of green tea extracts to increased adiponectin levels [31,32]; indeed, both Hsu et al. and Chen et al. demonstrated that a high-dose green tea extract (Epigallocatechin gallate, EGCG) in a 12-week program, induce an elevation in adiponectin levels [31,32]. Additionally, two studies have reported that consuming more than three cups of coffee per day is associated with higher adiponectin levels [33,34]. These find-ings align with our study, as our population had a habitual coffee intake exceeding three cups per day.

Although the exact mechanisms by which polyphenols influence adiponectin levels remain unclear, several potential pathways have been suggested: 1. Enhancement of insulin signaling, leading to increased adiponectin secretion [35,36]; 2. Anti-adipogenic and lipogenic effects, modulating the secretion of leptin and adiponectin [37,38]; 3. Reduction of oxidative stress, which may positively regulate adiponectin expression [39]; 4. Modulation of gut microbiota, which could play a role in adiponectin regulation [40].

A direct relationship between adiponectin and fiber intake was also

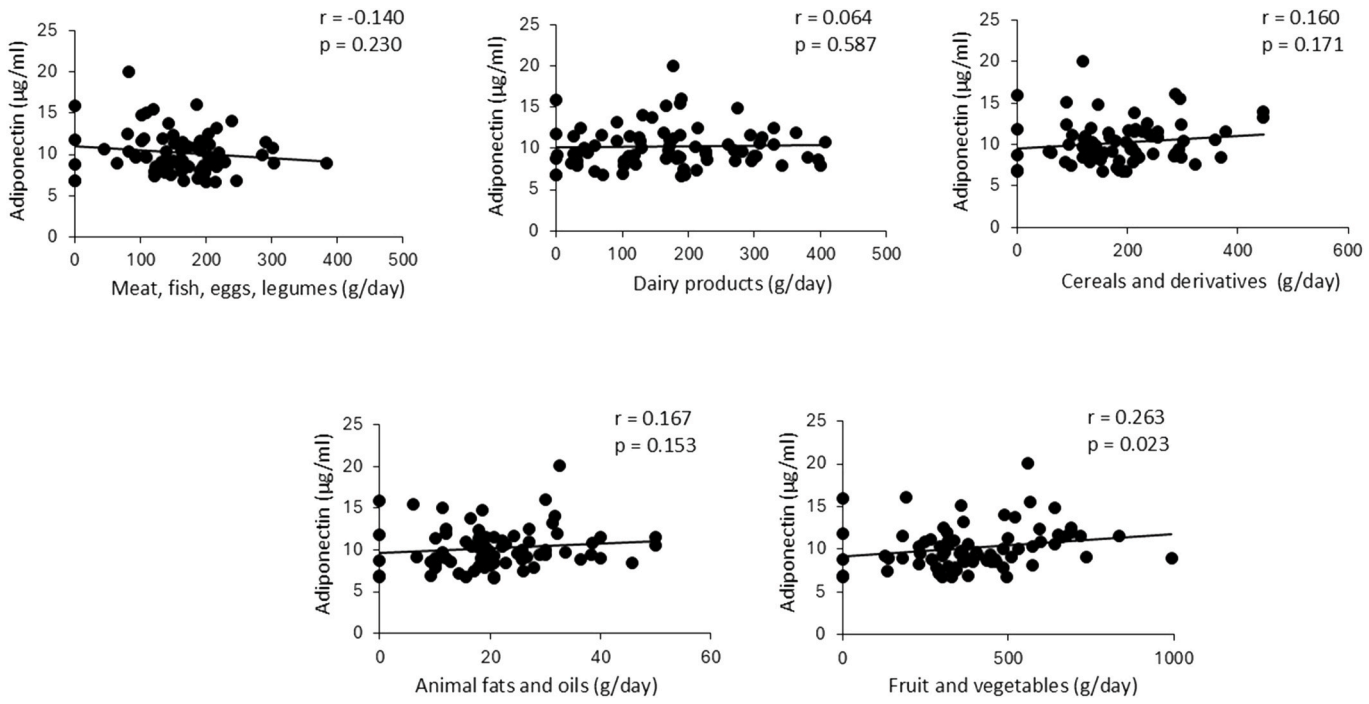

Fig. 4. Correlation analysis between fasting plasma adiponectin levels and daily intake of five food groups in the habitual diet of the study participants in the whole population (n = 75).

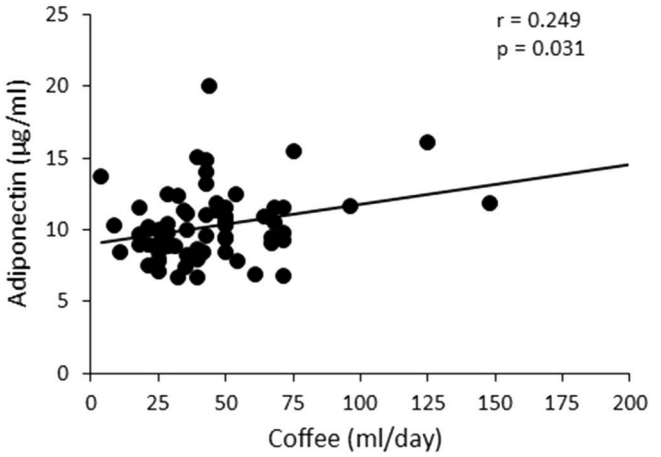

Fig. 5. Correlation analysis between fasting plasma adiponectin levels and daily intake of coffee in the whole population (n = 75).

observed, supporting previous studies that have linked fiber consumption to higher adiponectin levels in healthy individuals [9] and those with type 2 diabetes [11,13]. The positive association between adiponectin, polyphenols, and fiber intake is further reinforced by the correlation with fruit and vegetable consumption, aligning with prior research showing that Mediterranean and plant-based diets increase circulating adiponectin levels [18,41–43]. Median plasma adiponectin concentrations is reported 23 % higher in women who most closely follow a Mediterranean-type diet than in low adherers [10].

Regarding the metabolic effects of adiponectin regulation in response to dietary patterns, several data suggest that it might be associated to improvement of cardiovascular health. Indeed, adiponectin was positively associated with HDL cholesterol and inversely correlated with diastolic blood pressure. The relationship between HDL cholesterol and adiponectin has been well-documented in individuals with [44–46] and without [47] diabetes. Adiponectin increases HDL cholesterol levels via two primary mechanisms: stimulating hepatic ApoA-I production, the main apolipoprotein of HDL, and enhancing ATP-binding cassette transporter A1 (ABCA1) activity, which promotes HDL assembly through reverse cholesterol transport [48,49]. Adiponectin has also been suggested to reduce hepatic lipase (HL) activity, leading to the formation of larger HDL2 particles, which are less readily cleared from circulation [49].

The inverse relationship between adiponectin and blood pressure is supported by several studies [50,51], suggesting that adiponectin may lower blood pressure through central and vascular mechanisms [52]. Possible mechanisms include: *a.* reducing renal sympathetic nerve activity, *b.* enhancing nitric oxide production in endothelial cells, and *c.* Suppressing TNF-α activity, which may prevent atherosclerotic progression and smooth muscle cell migration [51,52].

To the best of our knowledge, this is the first cross-sectional study to link individual polyphenol classes to adiponectin levels in individuals at high metabolic risk. However, our study has some limitations: firstly, the cross-sectional design prevents the assessment of changes in knowledge or awareness over time and limits causal inferences; secondly the small sample size may limit the generalizability of our findings; lastly, longer nutritional intervention program might induce different result in adiponectin levels as well as in other metabolic and cardiovascular parameters.

5. Conclusion

This study highlights a significant association between fiber and polyphenol intake with adiponectin levels in individuals at high metabolic risk. These findings further support the metabolic benefits of polyphenol-rich foods, such as coffee, fruits, and vegetables. Additionally, the direct correlation between adiponectin and HDL cholesterol levels, along with its inverse relationship with diastolic blood pressure, confirms the role of adiponectin as a biomarker of metabolic health.

Our findings emphasize the importance of plant-based diets, including the Mediterranean diet, in promoting higher adiponectin levels and better metabolic health.

Informed consent statement

Informed consent was obtained from all subjects involved in the study.

Author contributions

Conceptualization, G.A.; A.R; A.D.; L.B. and G.C; methodology, R.T; D.S. M.V.; E.N.; M.M.; P·C.; formal analysis, R.T.; D.S. G.C.; investigation, R.T.; M.V.; L.B.; G.C.; resources, G.A.; A.D.; data curation, L.B.; G. C.; R.T.; writing—original draft preparation, R.T.; D.S.; G.C.; writing—review and editing, G.C.; G.A.; supervision, G.A.; L.B.; A.R.; project administration, A.R.; G.A.; funding acquisition, A.R. All authors have read and agreed to the published version of the manuscript.

Institutional review board statement

The study was conducted according to the guidelines of the Declaration of Helsinki, and all procedures involving human subjects were approved by "Federico II" University Ethics Committee. The study was registered at www.clinicaltrials.gov (identifier NCT01154478).

Data availability statement

Additional data are available from the corresponding author on reasonable request.

Trial registration number

ClinicalTrials.gov(NCT01154478).

Funding

The research leading to these results received funding from the European Community's Seventh Framework Programme FP7/2009–2012 under grant agreement FP7-KBBE-222639, Etherpaths Project.

Declaration of competing interest

The authors declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2025.104164.

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