Investigation of the association between pistachio consumption and kidney plus liver function parameters: A Cross-Sectional study using the data from the Rafsanjan Cohort Study (2022)

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Abstract

Aim and objectives: One of the key elements in the emergence of liver and renal disorders is thought to be oxidative stress. Antioxidants are abundant in pistachios. Thus, the purpose of this study was to inspect the relationship between kidney as well as liver function and pistachio intake.
Methodology: As part of the Prospective Epidemiological Research Studies in IrAN (PERSIAN), cross-sectional research was carried out using data from the baseline phase of the Rafsanjan Cohort research (RCS). There were 5597 participants in this research, ages 35 to 70, including 3020 men and 2577 women. A validated food frequency questionnaire (FFQ) of 128 questions was used to gather dietary consumption data. Using a Biotecnica analyzer, the following enzymes were measured: creatinine (Cr), BUN, γ-glutamyl transferase (GGT), aspartate transaminase (AST), alanine transaminase (ALT), and alkaline phosphatase (ALP). The MDRD formula was employed to estimate the glomerular filtration rate (GFR) from serum creatinine. The relationship between pistachio intake and liver plus kidney function markers was examined using multiple logistic regression models.
Results: Participants with higher consumption of pistachio were more likely to be male and had significantly lower mean age as well as higher levels of education and wealth score index (WSI). After adjusting for confounding variables, no significant association was seen between liver function parameters (AST, ALT, GGT, and ALP) or kidney function parameters (BUN, Cr, and GFR) and any quartile of pistachio consumption ($p>0.05$).
Conclusion: The current investigation found that, following correction for confounding factors, there was no statistically significant variation between the various quartiles of pistachio intake and measures related to liver function (AST, ALT, GGT, and ALP) and renal function (BUN, Cr, and GFR).

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1. Introduction

Pistachio Vera L. (pistachio) is one of the plants in the Anacardiaceae family [1], which is usually found in western and central areas of Asia including the Middle East [2-4]. The main world pistachio producers are Iran, Turkey, and the USA [5]. Pistachio has a lower content of energy compared to other nuts [6]. It possesses multiple nutrients including carbohydrates, dietary fibers, proteins [1], high levels of unsaturated fatty acids [6], and various vitamins such as vitamin A, vitamin K, vitamin E, vitamin B1, vitamin B2, vitamin B3, vitamin B6, biotin, and vitamin C [1, 7], certain minerals such as potassium, copper, iron, and magnesium [1, 8]. In addition, pistachio has a high level of compounds with anti-inflammatory properties and antioxidants such as polyphenols, tocopherols, phytochemicals [9, 10], beta-carotene, vitamin E, and coenzyme 10 which can improve overall health [11].

Different investigations have shown favorable effects of pistachio consumption on various clinical statuses such as diabetes [12-14], hypertension [15, 16], hyperlipidemia [17, 18], metabolic syndrome [19], and heart diseases [18, 20]. It was also reported that pistachio has beneficial effects on weight management [21, 22], gut function [1, 10, 23], endothelial function, and vascular stiffness [15, 24-26]. Furthermore, some other experimental studies have demonstrated the regulatory effects of pistachio on the liver function [11, 27]. Hamed et al. have reported the medical benefits of pistachio on the liver function [27]. In contrast, another investigation by Jamshidi et al. reported no significant effect of pistachio on the liver function in rats [28].

Some studies have revealed the nephroprotective effect of pistachio in rats [27, 29-31]. Ehsani et al have mentioned the protective effect of pistachio on kidney function in an experimental study in rats [29]. Also, in another investigation by Hakimizadeh et al., it was found that pistachio had a favorable effect on nephrotoxicity in mice [32].

Although the etiology of some liver and kidney diseases has not yet been correctly determined, oxidative stress is considered one of the important factors in the development of liver and kidney diseases [11, 33, 34]. Pistachio is a rich source of antioxidants such as vitamin E and some anti-inflammatory factors, and as such it may play an important role in liver and kidney activity [11]. Thus, this study was conducted to investigate the association between pistachio consumption and kidney plus liver function.

2. Methods:

Study design and setting

This cross-sectional investigation was carried out as part of the prospective epidemiological research studies in Iran (PERSIAN) [35], using data from the baseline phase of the Rafsanjan Cohort investigation (RCS) [36]. In Rafsanjan, a district in southeast Iran, the RCS recruiting phase began in August 2015 and completed in December 2017, having enrolled 9991 individuals between the ages of 35 and 70.

In the present research, pregnant women, participants who were under treatment for diabetes, hypertension, or hyperlipidemia, subjects with a history of cardiovascular disease, thyroid disorder, hepatitis B, hepatitis C, chronic kidney disease, and participants with an incomplete medical questionnaire were excluded, and finally, 5597 participants were included in the current study.

Consent to participate and ethics approval

Rafsanjan University of Medical Sciences' ethics committee granted approval for the current study (ethical code: IR.RUMS.REC.1400.215). For every subject, written informed permission was acquired.

Data collection

PERSIAN-validated questionnaires were used by skilled interviewers to interview each participant [35]. The questionnaire asked about physical activity, smoking, opium and alcohol usage, food, and past medical history in addition to sociodemographic information. A trained individual measured the subjects' weight and height in accordance with the RCS methodology [36]. The use of opiates, alcohol, and cigarettes was also self-reported. Reporting opium usage at least once a week for six months was considered to be the definition of opium consumption [37]. A standardized 22-item questionnaire and daily physical activity were used to calculate each participant's physical activity.

Additionally, each physical activity was given a weight based on its proportional metabolic cost in order to determine its metabolic equivalent (MET). MET-hours per day were then computed. The Wealth Score Index was employed to determine socioeconomic status (WSI). Multiple correspondence analysis (MCA) of the economic characteristics of the participants was used to measure this index. The formula for calculating body mass index (BMI) was to divide weight in kilograms by height in meters squared.

Evaluation of pistachio consumption

In this study, the standardized food frequency questionnaire (FFQ) was employed to assess pistachio consumption. Two questions concerning the participants' nutritional consumption from the previous year were asked during the interview: (1) how often they had eaten pistachios each month, week, or day; and (2) the quantity of pistachios that are every time consumed. Using the average household portion sizes of pistachios consumed, all reported intakes were translated to grams per day. Then, pistachio consumption was categorized into quartiles (Qs) including Q1: <0.546, Q2: 0.547-1.342, Q3: 1.343-2.771, Q4: >2.771 gr/day. The validity and reliability of the FFQ were confirmed in a previous study in Iran [38].

Laboratory assessment and definitions

All subjects had their blood drawn by a qualified individual between 7:00 and 9:00 AM following a minimum 12-hour fast. A biotecnica analyzer (BT 1500, Italy) was used in the cohort center's central laboratory to assess the serum levels of BUN, Cr, AST, ALT, ALP, and GGT. Serum AST and ALT activity were measured using the kinetic technique (Pars Azmoon Co., Tehran, Iran). Additionally, serum ALP activity was measured using p-nitrophenol phosphate as a substrate, while serum GGT activity was measured using p-glutamyl-3-carboxy-4-nitroanilide phosphate (kinetic technique, Pars Azmoon Co, Tehran, Iran). Abnormal BUN, Cr, AST, ALT, ALP, and GGT values were established based on the reference range of the central laboratory in the cohort center.

Serum GGT level greater than 54 U/L in males and 37 U/L in females was defined as elevated GGT. Also, elevated ALP was considered a serum level higher than 306 U/L in both genders. Serum CR and BUN levels higher than 1.4 mg/dl and 23 mg/dl were considered as elevated CR and BUN, respectively.

Glomerular filtration rate (GFR) was estimated from serum creatinine using the MDRD formula:

$$GFR\ (ml/min/1.73\ m^2) = 186 \times SCr\ (mg/dl)^{-1.154} \times age^{-0.203} \times 0.742\ (\text{if woman})$$

GFR less than 60 mL/min/1.73 m2 was considered a reduced GFR [39].

Statistical analyses

Continuous data were shown as mean ± standard deviation (SD), whereas categorical variables were expressed as frequency (%). Using chi-square and one-way ANOVA testing for categorical and continuous variables, respectively, different quartiles of pistachio consumption were compared in terms of sociodemographic, personal habits, and specific laboratory characteristics. Furthermore, the study employed multiple logistic regression models to evaluate the correlation between pistachio consumption and indicators related to liver as well as kidney function. Two basic and adjusted models were employed. On the basis of pistachio consumption, the crude model was stratified. Confounding variables such as age, gender (male/female), education, physical activity, BMI, WSI, fatty liver, alcohol consumption, cigarette smoking, opium consumption, total fruits and vegetables, and total energy intake were taken into account when adjusting the adjusted model. The statistical analyses were conducted using SPSS software version 22, with a significance level of P-value less than or equal to 0.05 (two-tailed).

3. Results:

This study recruited 5597 participants including 3020 males and 2577 females, aged 35-70 years old. Table 1 presents the demographic and personal habits of participants. The mean consumption of pistachio in the total population was 2.27 ± 2.99 gr/day. The mean consumption of pistachio in men was higher than in women (2.55 ± 3.38 gr/day vs 1.93 ± 2.41 gr/day). The participants' average age was 46.68 ± 8.75 years. The mean age of participants in the various quartiles of pistachio consumption differed statistically significantly (P <0.001). Between the various quartiles of pistachio consumption, there were also noteworthy variations in gender, education, WSI, alcohol intake, and cigarette smoking (P<0.001). Individuals who consumed more pistachios were more likely to be male, had greater levels of education and WSI, and their mean age was far lower.

Table 1. Demographic and personal habits of study participants by quartiles of pistachio consumption (n=5597).

Characteristics	Total	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P-Value
Gender-n (%)						<0.001
Male	3020(100)	617(20.4)	706(23.4)	801(26.5)	896(29.7)	
Female	2577(100)	665(25.8)	718(27.9)	630(24.4)	564(21.9)	
Age- year						<0.001
Mean ± SD	46.68±8.75	47.70±9.21	46.66±8.73	46.30±8.35	46.17±8.66	
Education-year						<0.001
Mean ± SD	9.36±4.76	7.93±4.87	9.14±4.53	9.78±4.68	10.41±4.64	
Physical activity						0.502
Mean ± SD	39.56±6.91	39.43±6.87	39.43±6.66	39.60±6.77	39.77±7.29	
WSI						<0.001

Mean ± SD	0.047±0.979	0.353±1.028	0.014±0.922	0.155±0.916	0.323±0.929	
Alcohol consumption-n (%)						<0.001
No	4891(100)	1144(23.4)	1283(26.2)	1244(25.4)	1220(24.9)	
Yes	692(100)	134(19.4)	139(20.1)	186(26.9)	233(33.7)	
Cigarette smoking-n (%)						<0.001
NO	3975(100)	910(22.9)	1066(26.8)	1013(25.5)	986(24.8)	
Yes	1608(100)	368(22.9)	356(22.1)	417(25.9)	467(29.0)	
Opium consumption-n (%)						0.204
No	4160(100)	956(23.0)	1085(26.1)	1060(25.5)	1059(25.5)	
Yes	1423(100)	322(22.6)	337(23.7)	370(26.0)	394(27.7)	
BMI-kg/m^2						0.054
Mean ± SD	26.93±4.69	26.74±5.20	26.93±4.51	27.20±4.62	26.83±4.45	
Fatty liver-n (%)						0.171
No	5229(100)	1211(23.2)	1337(25.6)	1326(25.4)	1355(25.9)	
Yes	368(100)	71(19.3)	87(23.6)	105(28.5)	105(28.5)	
Total energy-gr/day						<0.001
Mean ± SD	2129.95±751.80	1807.97±648.48	1989.29±611.24	2191.67±689.49	2489.36±851.39	
Total fruits and vegetables-Kcal/day						<0.001
Mean ± SD	641.26±348.69	481.31±280.37	584.06±274.61	674.97±319.33	804.45±412.78	

Abbreviations: Wealth score index (WSI), Body mass index (BMI), gr/day: grams per day, Kcal/day: Kilocalories per day.

Table 2 outlines liver and kidney function parameters in different quartiles of pistachio consumption among participants of the study. There were statistically significant differences in the mean value of Cr (P <0.001) and ALP (P <0.001). Furthermore, there was a significant difference in the subjects with normal and elevated GGT (P=0.047) among different quartiles of pistachio consumption. In terms of serum levels of BUN, GFR, AST, and ALT, there was no significant difference among different quartiles of pistachio consumption.

Table 2. Liver and kidney function parameters in study participants by quartiles of pistachio consumption (n=5597).

Parameters	Total	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P-Value
BUN-n (%)						0.451
Normal	5528(100%)	1264(22.9%)	1408(25.5%)	1419(25.7%)	1437(26.0%)	
Elevated	38(100%)	6(15.8%)	9(23.7%)	9(23.7%)	14(36.8%)	
Mean ± SD	13.54 ± 3.54	13.49 ± 3.54	13.46 ± 3.52	13.60 ± 3.51	13.63 ± 3.58	0.527
Cr-n (%)						0.716

Normal	5494 (100%)	1255(22.8%)	1402(25.5%)	1407(25.6%)	1430(26.0%)	
Elevated	72 (100%)	15(20.8%)	15(20.8%)	21(29.2%)	21(29.2%)	
Mean ± SD	1.03 ± 0.16	1.01 ± 0.16	1.02 ± 0.16	1.04 ± 0.16	1.05 ± 0.17	<0.001
AST-n (%)						0.913
Normal	5417 (100%)	1237(22.8%)	1380(25.5%)	1386(25.6%)	1414(26.1%)	
Elevated	149 (100%)	33(22.1%)	37(24.8%)	42(28.2%)	37(24.8%)	
Mean ± SD	19.66 ± 9.23	19.68 ± 8.39	19.55 ± 10.19	19.79 ± 9.55	19.62 ± 8.60	0.911
ALT-n (%)						0.973
Normal	5061(100%)	1156(22.8%)	1286(25.4%)	1296(25.6%)	1323(26.1%)	
Elevated	505 (100%)	114(22.6%)	131(25.9%)	132(26.1%)	128(25.3%)	
Mean ± SD	21.47 ± 16.07	20.77 ± 14.11	21.24 ± 16.24	21.92 ± 17.04	21.88 ± 16.50	0.192
ALP-n (%)						0.083
Normal	5142(100%)	1154(22.4%)	1313(25.5%)	1319(25.7%)	1356(26.4%)	
Elevated	424(100%)	116(27.4%)	104(24.5%)	109(25.7%)	95(22.4%)	
Mean ± SD	219.09±63.02	225.75±65.24	218.30±64.66	217.23±61.76	215.85±60.23	<0.001
GGT-n (%)						0.047
Normal	5099(100%)	1140(22.4%)	1309(25.7%)	1309(25.7%)	1341(26.3%)	
Elevated	467(100%)	130(27.8%)	108(23.1%)	119(25.5%)	110(23.6%)	
Mean ± SD	26.49 ± 24.56	27.34 ± 23.40	25.78 ± 24.05	26.70 ± 28.71	26.21 ± 21.41	0.394
GFR-n (%)						0.241
Normal	5022(100%)	1129(22.5%)	1292(25.7%)	1287(25.6%)	1314(26.2%)	
Decreased	544(100%)	141(25.9%)	125(23.0%)	141(25.9%)	137(25.2%)	
Mean ± SD	73.63 ± 11.37	73.63 ± 11.97	73.66 ± 11.35	73.09 ± 10.72	74.12 ± 11.46	0.115

Abbreviations: Blood urea nitrogen (BUN), Creatinine (Cr), Aspartate transaminase (AST), Alanine transaminase (ALT), Alkaline phosphatase (ALP), Gamma-glutamyl transpeptidase (GGT), Glomerular filtration rate (GFR).

Table 3 reports the association between pistachio consumption and liver plus kidney function parameters using the crude and adjusted models. After adjusting for confounding variables, no significant association was seen between abnormal BUN, Cr, GFR, AST, ALT, ALP, and GGT levels and any quartile of pistachio consumption (P>0.05).

Table 3. The association between pistachio consumption and liver and kidney function parameters using crude and adjusted models.

Liver and kidney function parameters	Pistachio consumption	Crude model OR (95%CI)	Adjusted model OR (95%CI)
Elevated BUN	Quartile 1	1	1
	Quartile 2	1.34(0.47-3.79)	1.39(0.49-4.01)
	Quartile 3	1.33(0.47-3.76)	1.37(0.47-4.01)
	Quartile 4	2.05(0.48-5.35)	2.13(0.73-6.14)
Elevated Cr	Quartile 1	1	1

	Quartile 2	0.89(0.43-1.83)	0.92(0.43-1.94)
	Quartile 3	1.24(0.64-2.43)	1.13(0.55-2.32)
	Quartile 4	1.22(0.63-2.39)	1.05(0.50-2.24)
Decreased GFR	Quartile 1	1	1
	Quartile 2	**0.77(0.60-0.99)**	0.85(0.65-1.11)
	Quartile 3	0.87(0.68-1.12)	1.03(0.79-1.35)
	Quartile 4	0.83(0.65-1.07)	0.99(0.75-1.32)
Elevated AST	Quartile 1	1	1
	Quartile 2	1.00(0.62-1.61)	1.03(0.63-1.70)
	Quartile 3	1.13(0.71-1.80)	1.13(0.69-1.84)
	Quartile 4	0.98(0.61-1.57)	0.90(0.53-1.53)
Elevated ALT	Quartile 1	1	1
	Quartile 2	1.03(0.79-1.34)	0.99(0.75-1.31)
	Quartile 3	1.03(0.79-1.34)	0.90(0.67-1.19)
	Quartile 4	0.98(0.75-1.27)	0.79(0.59-1.07)
Elevated ALP	Quartile 1	1	1
	Quartile 2	0.78(0.59-1.03)	0.88(0.67-1.17)
	Quartile 3	0.82(0.62-1.08)	0.94(0.70-1.25)
	Quartile 4	**0.69(0.52-0.92)**	0.82(0.60-1.13)
Elevated GGT	Quartile 1	1	1
	Quartile 2	**0.72(0.55-0.94)**	0.77(0.59-1.02)
	Quartile 3	0.79(0.61-1.03)	0.85(0.64-1.11)
	Quartile 4	0.71(0.55-0.93)	0.79(0.59-1.07)

The crude model remained unaltered.

Confounding factors such as age (continuous variable), gender (male/female), education (continuous variable), physical activity (continuous variable), BMI (continuous variable), WSI (continuous variable), fatty liver (yes/no), alcohol consumption (yes/no), cigarette smoking (yes/no), opium consumption (yes/no), total energy (continuous variable), and total fruits and vegetables (continuous variable) were adjusted in the adjusted model.

The following are abbreviations: GFR (globular filtration rate), gamma-glutamyl transpeptidase (GGT), aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), blood urea nitrogen (BUN), and creatinine (Cr).

4. Discussion

The current investigation, which involved 2577 females and 3020 males with a mean age of 46.68 ± 8.75 years, was carried out during the Rafsanjan adult cohort study's baseline phase. Individuals who consumed more pistachios were more likely to be male, had greater levels of education and WSI, and their mean age was far lower.

After adjusting for confounding variables, no significant association was observed between abnormal BUN, Cr, GFR, AST, ALT, ALP, and GGT levels and any quartile of pistachio consumption.

The relationship between pistachio consumption and indicators of liver plus renal function in humans is based on very scant evidence. The results of this study were in line with those of an earlier study conducted by Jamshidi et al., which found no evidence of a substantial impact of wild pistachio oils on liver enzymes and oxidative stress in rats [28]. Several experimental research have shown that pistachios have beneficial effects on the liver function, which contradicts our findings [11, 27, 40]. The administration of hydroalcoholic pistachio extract resulted in a reduction in the serum levels of AST, ALP, and ALT in a study conducted by Hakimizadeh et al on male mice exhibiting liver damage [40].

Iranmanesh et al. demonstrated that pistachio hydro-alcoholic extract gavaged continuously to rats with liver damage results in lower levels of AST, ALT, and LDL; however, levels of ALP, total protein, and HDL were unaffected [11].

Also, in contrast with our results, some studies have revealed the nephroprotective effect of pistachio in rats [27, 29-31]. Ehsani et al observed a reduction in the serum Cr, BUN, urine volume, and glucose plus an increase of GFR after administration of pistachio extract in an experimental study in rats. According to the author, pistachios have a protective effect on renal function by lowering inflammation and oxidative stress in the kidney [29].

Also, in another investigation by Hakimizadeh et al., pistachio had a favorable effect on nephrotoxicity in mice and lowered the levels of serum Cr, and BUN [32]. Rats' biochemical parameters were examined in relation to the Pistacia Atlantica extract by Jafarian Dehkord et al. Pistacia Atlantica extract reduced significantly triglycerides (TG), cholesterol, AST, GGT, CR, BUN, and total bilirubin and elevated HDL-C levels, while this extract had no significant effect on fasting plasma glucose (FPG) and ALT levels [41]. The discrepancy between the current study's results and those of previous research could be attributed to variations in the study population (human versus animal) and research design (observational versus experimental).

Free radicals damage cell membranes by initiating lipid peroxidation, which causes kidney and liver damage [42, 43]. Pistachios are plants that have compounds with antioxidant properties such as vitamins E and C, beta-carotene, iron, copper, and selenium, and are also a rich source of coenzyme 10. Coenzyme 10 is found in the inner membrane of the mitochondria of all tissues, especially in the heart, liver, and kidney [44, 45]. It has been shown that pistachios are rich in phenolic compounds, which are considered strong antioxidants [46, 47]. Tomaino et al showed that phenolic compounds of Pistachia such as gallic acid, cyanidin-3-O-galactoside, eriodictyol-7-O-glucoside, catechin, and epicatechin have the most antioxidant effects [48].

Extracts of Pistacia lentiscus fruits (PF) and leaves (PL) have shown hepatoprotective and antioxidant properties against liver injury in rats, according to a study by Mehenni et al. [49]. Chios mastic (Pistacia lentiscus var. chia) was consumed for eighteen months by healthy volunteers in a study by Triantafyllou et al., which showed a reduction in liver enzymes and a hypolipidemic effect [50]. A diet high in pistachios had positive effects on insulin resistance, glucose metabolism, and metabolic risk factors in prediabetic patients in a randomized clinical trial [13]. A cross-sectional study involving 9660 randomly chosen Iranian participants who were at least 19 years old revealed that eating nuts (walnuts, almonds, pistachios, and hazelnuts), especially three to four times a week, may help reduce dyslipidemia and cardiometabolic risk factors [51].

The current investigation has had certain shortcomings. First, the statistics cannot be applied to the broader public because of the participants' diverse lifestyles and age range of 35 to 70 years. Secondly, the analysis did not take into account other nuts possibly consumed in the diet of participants. There's also a chance that the memory bias regarding pistachio eating exists. A further drawback is that because the study was cross-sectional, it is possible that some participants began eating pistachios after their illness first manifested. Consequently, the follow-up stage of the study ought to look into this association. However, large sample size, the use of standardized questionnaires, and the fact that the study was papulation-based were some of its benefits.

5. Conclusion

According to the results, there were significant differences in gender, education, Wealth Status Index, alcohol consumption, and cigarette smoking between different quartiles of pistachio consumption. Also, the present study revealed that after adjusting for confounding variables, no significant association was seen between abnormal BUN, Cr, GFR, AST, ALT, ALP, and GGT levels and any quartile of pistachio consumption. Accordingly, investigation of this association in the follow-up phase is suggested.

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The Rafsanjan University of Medical Sciences Ethics Committee accepted the study protocol, which was created in accordance with the Persian cohort study (Ethical codes: IR.RUMS.REC.1400.215).

Conflict of Interest

None of the authors of the present study declared a conflict of interest.

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