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ORIGINAL ARTICLE

Observational Study

Dietary phytochemical consumption is inversely associated with liver alkaline phosphatase in Middle Eastern adults

Zahra Darabi, Richard James Webb, Hassan Mozaffari-Khosravi, Masoud Mirzaei, Ian Glynn Davies, Sayyed Saeid Khayyatzadeh, Mohsen Mazidi

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Abstract

BACKGROUND

The hepatoprotective effects of phytochemicals are controversial. A dietary phytochemical index (DPI) has been suggested as an alternative method for quantifying the phytochemical content of foods.

AIM

To assess the DPI in relation to liver function tests among a representative sample of Iranian adults.

METHODS
A total of 5111 participants aged 35-70 years old were included in this cross-sectional study by a multistage cluster random sampling method. Dietary intakes were collected by a validated and reliable food frequency questionnaire with 121 items. DPI was calculated by the percent of daily energy intake taken from phytochemical-rich foods. Fasting serum concentrations of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and gamma glutamyl transferase (GGT) were determined. Linear regression was used to investigate the association between DPI and levels of liver enzymes using crude and adjusted models.

RESULTS
There was an inverse association between DPI score and serum ALP in the crude model (β = -0.05; $P < 0.001$). This association remained significant after adjustment for body mass index, age, smoking, energy intake, history of diabetes, and education (β = -0.03; $P = 0.01$). No significant associations were found between DPI score and serum levels of AST, ALT, and GGT. The individuals with the highest DPI scores consumed significantly higher amounts of fruits, vegetables, legumes, nuts, and cereals, yet were shown to have significantly higher serum total cholesterol and low-density lipoprotein cholesterol, as well as several other metabolic abnormalities.

CONCLUSION
Higher adherence to phytochemical-rich foods was associated with lower levels of ALP, but no change in other liver enzymes. Those with higher DPI scores also consumed food items associated with a healthier overall dietary pattern; however, they also presented several unexpected metabolic derangements. Additional randomised trials are needed to better determine the effects of phytochemical-rich foods on liver function.

Key Words: Diet; Phytochemical; Liver; Dietary phytochemical index; Dietary pattern; Phytochemical index; Iran; Middle East; Nutrition

Core Tip: It has been debated whether phytochemicals are hepatoprotective. Furthermore, to the authors knowledge, this has not previously been researched in an Iranian population. In our study we used a dietary phytochemical index to categorise participants in terms of their intake of dietary phytochemicals. We found that participants with higher intakes of phytochemicals had a healthier overall dietary pattern and lower levels of alanine aminotransferase, which may be suggestive of improved liver function. Despite this, several metabolic disturbances were also revealed in these participants.

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INTRODUCTION

The hepatoprotective effects of phytochemicals have been the subject of recent debate. This has stemmed from increasing evidence concerning the ability of these plant-derived bioactive components to beneficially modulate metabolic processes. Favourable changes have been previously demonstrated in a variety of disease states, including Type 2 diabetes, obesity and cardiovascular and renal disease[1]. Given the links of these metabolic aberrations with liver pathology it is reasonable to suggest that phytochemicals might infer a degree of hepatoprotection[1].

More specifically, studies investigating potential links between dietary phytochemicals and liver function have shown that compounds such as polyphenols, flavonoids, carotenoid and terpenoids, contained in food items such as grapes, tea, olives, nuts and legumes, may favourably mediate liver function when consumed, especially in the context of a low-calorie diet[2,3]. Several proposed mechanisms responsible for these effects may include the ability of phytochemicals to act as natural ligands for peroxisome proliferator-activated receptors, as well as favourably impacting upon mitochondrial beta-oxidation[4]. Furthermore, the ability of phytochemicals to reduce oxidative stress

and decrease transaminase activity are also thought to be influencing factors[1,5].

The Iranian population has high rates of hepatic abnormalities, such as non-alcoholic fatty liver disease (NAFLD), which affects approximately 4.1% of the population[6]. It is thought that this is perpetuated by concurrent high rates of metabolic syndrome; a cluster of risk factors known to be strongly associated with the development of NAFLD[7]. In addition to this, recent findings have also revealed that NAFLD is more likely to be present in Iranians with a higher socioeconomic class and is exacerbated by a Western dietary pattern, whereas a healthier traditional Iranian dietary pattern, presumably richer in dietary phytochemical-containing foods, is likely to be more protective[8]. Although there is evidence concerning the beneficial impact of dietary phytochemicals upon cardiometabolic risk, there are no studies to date which focus specifically on liver function in Iranian adults[9].

We aimed to determine, for the first time, the association between dietary phytochemical index (DPI) and liver function in Iranian adults. We used data derived from the Prospective Epidemiological Research Studies in Iran (PERSIAN) Cohort Study to create a 'dietary phytochemical index' (DPI), based on the work of McCarty, which takes into account the health promoting properties of phytochemicals [10]. This enabled us to test the hypothesis that higher DPI scores would equate to improved liver function.

MATERIALS AND METHODS

Study population

The present cross-sectional study is reported based on the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guideline[11]. The study was conducted in the context of the baseline data of Shahedieh Cohort Study, which is a part of the PERSIAN multicenter cohort study which was conducted using a representative sample of the Iranian adult population aged 35-70 years old[12]. The Shahedieh cohort study recruited about 10000 adults older than 35 living in two municipal areas of Yazd city (Zarch and Shahedieh), Yazd province, Iran. The study protocol of the PERSIAN cohort is provided in detail elsewhere[12,13]. In brief, healthy participants were selected by a multistage cluster random sampling method after they provided written informed consent. The eligible participants were invited to give blood samples and provide data on general characteristics, demographic, dietary intake, smoking, and other lifestyle related data. Anthropometric and blood pressure measurements were also conducted for all attendants. All data were collected by trained interviewers[12,13]. Data on 10,113 adults were provided. Participants with a history of current pregnancy, ovary removal, cardiac ischemia, myocardial infarction, stroke, renal failure, hepatitis B and C, and different types of cancer such as skin cancer, breast cancer, stomach cancer, colorectal cancer, and bladder cancer along with the history of hematopoietic cancers were excluded from the current study because of the possibility of an adjustment in diet (n = 1189). Data for participants with a history of alcohol consumption, fatty liver, and diabetes (n = 2241) were also omitted. Furthermore, we excluded those who left > 70 items unanswered on the food frequency questionnaire (FFQ) and those who under and over reported their dietary intake (daily energy intake less than 800 kcal/d or more than 7000 kcal/d) (n = 1433). The missing data consisted of n = 139 participants who were also excluded from the study. After the mentioned exclusions, 5111 participants remained for the present analysis. The study was also approved by the ethics committee of Shahid Sadoughi University of Medical Sciences (approval code: IR.SSU.SPH.REC.1397.161).

Laboratory assessment

Blood samples (25 mL) were taken when participants were in the fasted state (8 to 12 h before blood sampling). The blood was aliquoted into serum, buffy coat, and whole blood samples. Serum gamma-glutamyltransferase (GGT), alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) were determined from serum samples by an auto-analyser (Analyzer BT1500) using Pars Azmun standard kits.

Dietary intake assessment

The study participants were interviewed by trained nutritionists to complete a semi-quantitative FFQ with 121 items, which asked about dietary intake over the past year[12]. To complete the information, two questions were asked from the participants about each food item: (1) The frequency of food consumption (number of times per month, week, or day the food was consumed) in the previous year, and (2) the amount of the food that was usually consumed every time (portion size based on the standard serving sizes commonly consumed by Iranians). All reported intakes were converted to g/day by using household portion sizes of consumed foods[14]. The USDA food database was used to calculate nutrient intakes[15].

Dietary phytochemical index calculation

The DPI score was computed based on the method presented by McCarty as follows: DPI = [daily energy derived from phytochemical-rich foods (kcal)/total daily energy intake (kcal)] × 100[10]. Fruits, vegetables, legumes, whole grains, nuts, soy products, seeds and olive oil were considered phytochemical-rich foods. The phytochemical content of potatoes is low and so potatoes were not included[16].

Anthropometric measurement

Anthropometric parameters (weight, height) were measured by a trained investigator. Weight was measured while the participants were wearing minimum clothing and without shoes using a digital scale (SECA, model 755, Germany). Participants' height was measured using a stadiometer with a precision of 0.5 cm. Body mass index (BMI) was calculated by dividing weight (kg) by height (meters) squared.

Assessment of other variables

Data on additional variables including marital status, smoking (never smoker/current smoker/ex-smoker), and multivitamin-mineral supplements use (yes/no) were obtained using questionnaires. People were asked about their usual physical activity in the last year and if they had seasonal jobs. The information gathered in the questionnaire was converted to the metabolic equivalent of task hours per week [metabolic equivalent of task (MET)-h/wk][17].

Statistical methods

Continuous and categorical variables were compared across quartiles of DPI scores using analysis of variance (ANOVA) and chi-square tests, respectively. Linear regression was applied in crude and different multi-variable adjusted models to examine the linear association between DPI scores and serum liver enzyme levels. Age, sex (male/female) and the energy intake (kcal/day) were adjusted in the first model; the second model also included BMI (kg/m^2). Additional adjustments were performed for physical activity, smoking and multivitamin supplement use in third model. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS, version 23.0 for Windows, 2006, SPSS, Inc, Chicago, IL, United States). *P* values less than 0.05 were considered statistically significant.

RESULTS

General characteristics of the study participants across quartile scores of DPI are shown in Table 1. There were no significant differences in BMI (P = 0.647), multivitamin mineral supplement use (P = 0.211) and gender (P = 0.071). However, individuals in the first quartile of DPI scores were significantly younger than those in the fourth quartile of DPI scores (46.4 ± 9.1 and 47.5 ± 9.5 y respectively (P < 0.001)) and had significantly lower systolic blood pressure (107.4 ± 16.2 and 109.1 ± 16.4 mm/Hg respectively (P < 0.001)). Those in the first quartile of DPI score also had significantly lower MET than those in the fourth quartile of DPI score (41.3 ± 6.8 and 42.0 ± 6.5 h/week respectively (P < 0.01)). Table 2 shows that there were also no significant differences in the levels of serum ALT (P = 0.225), AST (P = 0.562) and GGT (P = 0.338) between the quartiles of DPI scores. However, the participants in the first quartile of DPI scores had higher ALP levels compared to participants in the fourth quartile (185.7 ± 59.3 and 176.8 ± 52.7 U/L respectively (P < 0.01)). There were also significant differences in serum total cholesterol and low-density lipoprotein cholesterol (LDL-C) concentrations between those with the lowest DPI scores compared to those with the highest (189.9 ± 59.8 and 195.4 ± 39.0 mg/dL and 106.7 ± 55.1 and 111.4 ± 31.2 mg/dL respectively) (both P < 0.01). Fasting blood sugar was also lower in those with the lowest DPI scores compared to those with higher scores (96.0 ± 21.9 and 97.6 ± 32.7 mg/dL (P < 0.01)). Dietary intakes of study participants by quartile score of DPI is shown in Supplementary Table 1. Participants with greater DPI scores had higher intakes of vegetable, fruits, legumes, nuts, olive oils and olives, dairy, and dietary cholesterol (all P < 0.001). In addition, intakes of energy, carbohydrate, protein, fat, monounsaturated fatty acids (MUFA), saturated fatty acids (SFAs), and polyunsaturated fatty acids (PUFAs) were significantly lower among the subjects within the fourth quartile of DPI score compared to the first quartile (all P < 0.001). Vitamin B12, vitamin A and vitamin C intake were significantly higher among individuals in the fourth quartile of DPI score in comparison to the first quartile (all P < 0.001), but folate, magnesium, calcium, iron, vitamins B6, Niacin, Riboflavin and Thiamin intake were significantly higher among individuals in the first quartile of DPI score in comparison to the fourth quartile (all P < 0.001). The relationships between score of DPI and levels of liver enzymes are presented in Table 3. There was an inverse association between score of DPI and serum ALP levels in our unadjusted model (β = -0.05; 95%CI (-0.43 to -0.15) P < 0.001). Additionally, this inverse correlation remained significant after adjustment for confounding factors in Model I (β = -0.04 95%CI (-0.39 to -0.07); P < 0.01), Model II (β = -0.04 95%CI (-0.39 to -0.08); P < 0.01), Model III (β = -0.03 95%CI (-0.34 to -0.03); P < 0.019) and Model IV (β = -0.03 95%CI (-0.35 to -0.04) P = 0.014. No statistically significant

Table 1 General characteristics of study participants by quartiles score of dietary phytochemical index

	Q4 (N = 1278)	Q3 (N = 1278)	Q2 (N = 1278)	Q1 (N = 1277)	*P* value[1]
Age (Yr)	47.5 ± 9.5	45.9 ± 8.8	45.5 ± 8.8	46.4 ± 9.1	< 0.001
BMI (kg/m^2)	28.2 ± 4.9	28.3 ± 7.7	28.2 ± 10.9	27.9 ± 5.0	0.647
Waist circumference (cm)	94.1 ± 11.8	94.3 ± 11.5	94.2 ± 11.4	94.7 ± 12.1	0.668
WHR	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.8	0.9 ± 0.3	0.021
Systolic blood pressure (mm/Hg)	109.1 ± 16.4	106.8 ± 15.8	106.7 ± 15.1	107.4 ± 16.2	< 0.001
Diastolic blood pressure (mm/Hg)	67.3 ± 11.0	66.8 ± 11.0	66.8 ± 10.3	67.2 ± 10.6	0.451
Metabolic equivalent of task (h/wk)	42.0 ± 6.5	41.0 ± 6.6	41.6 ± 7.2	41.3 ± 6.8	< 0.01
WSI	0.2 ± 0.7	0.2 ± 0.7	0.2 ± 0.7	0.1 ± 0.7	< 0.001
Gender men (%)	578 (45.2)	543 (42.5)	609 (47.7)	548 (45.7)	0.071
Smoking					< 0.01
Never smoker (%)	1086 (85.0)	1088 (85.1)	1045(81.8)	1052 (82.4)	
Current smoker (%)	106 (8.3)	128 (10.0)	161 (12.6)	140 (11.0)	
Ex_smoker (%)	86 (6.7)	62 (4.9)	72 (5.6)	85 (6.7)	
Education					< 0.001
Uneducated and elementary (%)	536 (41.9)	506 (39.6)	501 (39.2)	612 (48.0)	
Middle and high school	487 (38.2)	535 (38.2)	541 (42.3)	472 (37.0)	
University or college degree	224 (17.5)	212 (16.6)	195 (15.3)	168 (13.2)	
Postgraduate	31 (2.4)	25 (2.0)	40 (3.1)	24 (1.9)	
Multivitamin mineral use					0.211
Never (%)	1244 (97.4)	1242 (97.2)	1231 (96.5)	1245 (97.6)	
Daily (%)	1 (0.1)	0	2 (0.2)	1 (0.1)	
Weekly (%)	4 (0.3)	1 (0.1)	1 (0.1)	0	
Monthly (%)	1 (0.1)	4 (0.3)	2 (0.2)	0	
Yearly (%)	27 (2.1)	31(2.4)	39 (3.1)	30 (2.4)	
Metabolic syndrome	213 (16.7)	225 (17.6)	216 (16.9)	233 (18.2)	0.713

[1]Obtained from one way Anova or Chi-squared tests for continuous and categorical variables, respectively.
Values are means ± SDs or *n* (%).
DPI: Dietary phytochemical index; BMI: Body mass index; WHR: Waist-to-hip ratio; WSI: Wealth score index.

association was found between levels of ALT, AST, GGT and score of DPI in the crude mode, which remained non-significant after adjustment for potential confounders.

DISCUSSION

In this study we aimed to determine if increased phytochemical consumption, consequently resulting in an increased 'dietary phytochemical index' (DPI) score, would be predictive of improved liver function in Iranian adults. Our principal finding was that DPI score was inversely related to ALP and that this relationship persisted, even after adjusting for multiple variables. No such relationship existed with the other liver enzymes, which were similar across the DPI quartile scores. Furthermore, perhaps unsurprisingly, there were also several differences in the overall dietary intake of the participants. Principally, those with higher DPI scores consumed more foods and nutrients suggestive of largely 'healthy' dietary patterns, as opposed to those with lower scores, who consumed greater quantities of foods and nutrients often associated with 'unhealthy' dietary patterns.

The homogeneity in levels of ALT, AST and GGT between those with varied DPI scores is a finding which is not in agreement with the literature. Previous studies have suggested that phytochemical consumption is associated with improvements in these particular liver enzymes[1]; however, this was

Table 2 Biochemical parameters of study participants by quartiles score of dietary phytochemical index

	Q4 (N = 1278)	Q3 (N = 1278)	Q2 (N = 1278)	Q1 (N = 1277)	*P* value[1,2]
ALT (U/L)	22.6 ± 15.4	22.3 ± 17.1	23.2 ± 17.3	21.9 ± 16.7	0.225
AST (U/L)	19.0 ± 7.4	19.0 ± 10.32	19.4 ± 8.5	19.1 ± 7.5	0.562
GGT (U/L)	27.9 ± 22.8	26.5 ± 23.5	27.2 ± 23.0	26.2 ± 27.7	0.338
ALP (U/L)	176.8 ± 52.7	180.5 ± 50.3	181.0 ± 49.7	185.7 ± 59.3	< 0.01
Cholesterol (mg/dL)	195.4 ± 39.0	191.9 ± 40.6	189.5 ± 38.8	189.9 ± 59.8	< 0.01
Triglyceride (mg/dL)	162.4 ± 96.4	155.0 ± 100.8	157.5 ± 99.8	152.5 ± 96.2	0.075
HDL-C (mg/dL)	53.6 ± 12.3	54.0 ± 12.1	52.9 ± 12.0	53.8 ± 12.4	0.116
LDL-C (mg/dL)	111.4 ± 31.2	107.9 ± 31.2	106.4 ± 30.9	106.7 ± 55.1	< 0.01
FBS (mg/dL)	97.6 ± 32.7	95.5 ± 20.0	94.4 ± 15.9	96.0 ± 21.8	< 0.01
BUN (mg/dL)	27.3 ± 7.6	27.0 ± 7.3	26.9 ± 7.1	27.4 ± 7.0	0.241
Creatinine (mg/dL)	1.1 ± 0.2	1.1 ± 0.2	1.1 ± 0.2	1.1 ± 0.2	0.135

[1]Values are means ± SDs.
[2]Obtained from one way Anova.
DPI: Dietary phytochemical index; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; GGT: Gamma-glutamyl transferase; ALP: Alkaline phosphatase; HDL: High-density lipoprotein; LDL: Low density lipoprotein; FBS: Fast blood sugar; BUN: Blood urea nitrogen.

not the case in the present study for reasons which are not entirely clear. This is also unexpected given the higher proportion of foods such as fruits, vegetables and nuts which were consumed by those with the highest DPI scores. Food items such as these have previously been associated with a more favourable overall dietary pattern; a feature associated with a decreased risk of NAFLD[18-21]. Furthermore, a reduction in calorie intake accompanied by a concomitant decrease in carbohydrate consumption, both factors which occurred in those with higher DPI scores in the present study, has also been previously associated with improvements in transaminase levels[20].

Despite the unexpected similarities in most liver enzymes, it is important to note that the concentration of ALP was significantly lower in those with higher DPI scores, even after adjusting for energy intake. This aligns with previous literature which also demonstrated that the consumption of phytochemicals is associated with improvements in ALP[22-27]. However, these studies have typically been carried out in animal models with the aim of alleviating hepatic damage resulting from aging and/or pharmacological agents *via* the delivery of phytochemical rich extracts as opposed to the dietary consumption of these compounds per se. Furthermore, as there is a dearth of human studies comparing the impact of dietary phytochemicals upon markers of liver damage it is difficult to make direct comparisons with the improvements in ALP shown by us. Despite this, it is noteworthy that this finding persisted after adjusting for a range of other variables, including metabolic syndrome. This is important, especially given the high rates of the disorder in Iran, its suspected role in NAFLD and because ALP is routinely utilised as a marker for liver disease[7,28]. More specifically, elevated ALP of hepatic origin is used as a marker of primary biliary cirrhosis which can indicate cholestatic liver disease[29]. This is possibly perpetuated by a decline in the tissue-specific environment, such as a deterioration of the HCO_3 umbrella; however, the exact mechanisms have yet to be fully elucidated[29]. As such, the driving factors underpinning the inverse association between DPI score and ALP found in the present study remain unknown.

While there are potentially hepatoprotective benefits of consuming a diet rich in dietary phytochemicals, it is noteworthy that those with higher DPI scores also had increased levels of serum cholesterol and LDL-C, as well as higher levels of fasting blood sugar and systolic blood pressure, even when these individuals were comprised of fewer current smokers and had similar rates of metabolic syndrome compared to those with lower DPI scores. These abnormalities associated with phytochemical consumption are not in agreement with previous research, with a recent review of the literature highlighting how these compounds are generally considered to infer positive effects upon a range of clinical markers including body weight, waist circumference and blood pressure and glucose[1]. Therefore, perhaps some of the observed cardiometabolic abnormalities may be related to other less favourable dietary factors. For example, those with higher DPI scores consumed a higher proportion of total dietary fats than those with lower scores and a smaller quantity of MUFA and PUFA per gram. Consumption of MUFA and PUFA are well known to favourably modulate both the concentration and size of LDL particles[30,31]. However, in the case of the current study it could be hypothesised that perhaps the reduced intake per gram of these fatty acids, along with the percentage increase in SFA intake may override any benefits normally attributed to MUFA and PUFA, leading to a net increase in

Table 3 Linear regression analysis of the correlations between score of dietary phytochemical index and levels of liver enzymes.

	P value	B (95%CI)
ALT		
Crude	0.474	0.02 (-0.002 to 0.06)
Model I	0.063	0.02 (-0.002 to 0.09)
Model II	0.109	0.02 (-0.009 to 0.08)
Model III	0.1	0.02 (-0.008 to 0.08)
Model IV	0.097	0.02 (-0.007 to 0.08)
AST		
Crude	0.751	-0.004 (-0.02 to -0.01)
Model I	0.902	-0.002 (-0.02 to 0.02)
Model II	0.773	-0.005 (-0.02 to 0.02)
Model III	0.9	-0.002 (-0.02 to 0.02)
Model IV	0.917	-0.002 (-0.02 to 0.02)
GGT		
Crude	0.154	0.02 (-0.01 to 0.11)
Model I	0.328	0.01 (-0.03 to 0.10)
Model II	0.433	0.01 (-0.04 to 0.09)
Model III	0.366	0.01 (-0.03 to 0.10)
Model IV	0.365	0.01 (-0.03 to 0.10)
ALP		
Crude	< 0.001	-0.05 (-0.43 to -0.15)
Model I	< 0.01	-0.04 (-0.39 to -0.07)
Model II	< 0.01	-0.04 (-0.39 to -0.08)
Model III	0.019	-0.03 (-0.34 to -0.03)
Model IV	0.014	-0.03 (-0.35 to -0.04)

Model I: Adjusted for energy intake, age and gender; Model II: Additionally adjusted for body mass index; Model III: Additionally adjusted for physical activity, supplement or multivitamin use, smoking, education and wealth score index; Model IV: Additionally adjusted for metabolic syndrome. DPI: Dietary phytochemical index; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; GGT: Gamma-glutamyl transferase; ALP: Alkaline phosphatase.

LDL-C.

Limitations and strengths

This study has several strengths. These being that the study is the first of its kind to investigate the associations between DPI score and liver function in an Iranian adult population, using a large sample size. Despite this our study has several limitations. These being that the study design is cross-sectional in nature, meaning that the findings cannot detect changes across time, which is important since the impact of diet is often only detected through longitudinal measurements. Similarly, as the participants in the study resided in a single province it is unlikely that our findings are extrapolatable to the Iranian population. Furthermore, the DPI scoring technique only creates an approximate estimation of the consumption of dietary phytochemicals and excludes certain items, which have no calorific value, such as tea, which is consumed in high quantities in Iran[10,32]. Also, the scoring technique fails to consider that the ratio of phytochemicals to calories varies greatly in plant foods, as do the health promoting properties of individual phytochemicals[10]. In addition to this, the logistic regression analysis, although offering insights into the relationship between dietary phytochemical intake and liver function, can succumb to high intercorrelations as well as residual confounding, potentially leading to the production of spurious relationships. It is also important to remember that certain medications may also have impacted upon our findings and although a medication history was taken when the PERSIAN cohort study was conducted this data was not included in our analysis. Finally, as our study is

ecological in nature, the exact biological mechanisms underpinning our findings are subject to speculation and further research to elucidate these aspects is therefore warranted.

CONCLUSION

To summarise, our findings reveal that an increased consumption of dietary phytochemicals is associated with beneficial reductions in serum ALP in an Iranian adult population. Furthermore, we also demonstrate that a higher DPI score is also accompanied with an overall increase in consumption of food items and nutrients associated with healthier dietary patterns. Despite these positive aspects, our findings also showed that those with higher DPI scores presented several metabolic disturbances compared to counterparts with lower scores. This suggests that there may be hepatoprotective effects associated with increased consumption of phytochemicals, but further research is required to determine the validity of these findings as well as any factors that may be driving unexpected metabolic abnormalities.

ARTICLE HIGHLIGHTS

Research background

Dietary phytochemicals are plant-derived bioactive compounds. It has been previously suggested that these compounds may be hepatoprotective; however, the existing literature concerning this is equivocal.

Research motivation

In addition to the debatable hepatoprotective nature of dietary phytochemicals, there has been little research investigating this specifically in an Iranian population.

Research objectives

To determine the if the intake of dietary phytochemicals is hepatoprotective.

Research methods

Participants recruited to the PERSIAN cohort study were asked to complete a validated food frequency questionnaire. We applied a dietary phytochemical index to this data in order to categorise participants based upon their phytochemical intake. We then used linear regression to investigate the association between the dietary phytochemical index and levels of liver enzymes using both crude and adjusted models.

Research results

We found significant and inverse associations between dietary phytochemical intake and alkaline phosphatase. This is possibly indicative of improved liver function. We also found that participants with higher intakes of dietary phytochemicals also had an overall healthier dietary pattern yet increased levels of serum cholesterol, low-density lipoprotein cholesterol, blood pressure and blood glucose.

Research conclusions

Although there may be hepatoprotective effects associated with increased dietary phytochemical intake in addition to a healthier overall dietary pattern, these may be accompanied by a a number of metabolic abnormalities.

Research perspectives

Future research should seek to determine the validity of our findings and to elucidate any factors which may be responsible for any metabolic abnormalities associated with an increased intake of dietary phytochemicals.

FOOTNOTES

Author contributions: Darabi Z, Mozaffari-Khosravi H, Mirzaei M, Khayyatzadeh SS, and Mazidi M conceived and designed the study, acquired and analysed the data; Darabi Z and Webb RJ interpreted the data and wrote the first draft of the manuscript; All authors critically revised the manuscript.

Institutional review board statement: The study was also approved by the ethics committee of Shahid Sadoughi University of Medical Sciences (approval code: IR.SSU.SPH.REC.1397.161).

Informed consent statement: All involved persons gave their informed consent prior to study inclusion.

Conflict-of-interest statement: The authors know of no conflicts of interest associated with this publication, and there has been no significant financial support for this work that could have influenced its outcome.

Data sharing statement: Technical appendix, statistical code, and dataset available from the corresponding author at mohsen.mazidi@ndph.ox.ac.uk.

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