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Alternative Healthy Eating Index may be associated with liver enzymes level among healthy adults

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Summary. *Background and aims:* Due to documented association between diet intake and liver enzymes level and also suggested role of AHEI in chronic disorders prevention, this study was conducted to investigate the association between AHEI and liver enzymes level. *Methods:* The study sample consisted of 256 subjects with a mean age of 34.93 (SD8.82) years, 126 men and 139 women. Dietary intake was evaluated by the use of a semi-quantitative food frequency questionnaire and AHEI-2010 was used to assess adherence to healthy eating index. All baseline blood samples were collected. All chemical and anthropometric measurements were performed at the EMRC laboratory of Shariatei hospital. All statistical analysis was performed using SPSS 16 for Windows. *Results:* Individuals in the highest tertile of AHEI-2010 were older and had significant lower weight (P=0.01), BMI (P=0.02), TG (P=0.02), total cholesterol (P=0.05), ALT (P=0.02) and AST (P=0.04) and higher fat percent (P=0.02) and AAR (P<0.01). Adherence to AHEI had a negative and significant association with AST after adjusting for age and weight (P value= 0.02 and 95%CI: 0.94, 0.99), while association with ALT was significant after adjusting for age and weight (P value= 0.02 and 95%CI: 0.94, 0.99). After adjusting for sex AHEI was inversely associated with ALT and AST, but it was not significant. *Conclusion:* In all, adherence to AHEI seems to be associated with lower levels of ALT and AST in participants. Prospective studies are required to confirm these associations.

Key words: liver enzymes, AHEI, ALT, AST

Introduction

Liver disease is regarded as a widespread disorder worldwide and imposes a severe burden on body health (1). High levels of liver enzymes have been documented as a risk factor for a wide range of diseases (2). Several studies have suggested increased levels of liver enzymes can result in type 2 diabetes mellitus (3). Moreover, diastolic blood pressure, chronic vascular disease(CVD), higher total cholesterol level and a lower high density lipoprotein cholesterol have been associated with liver enzymes level in previous studies (4, 5). Alanine transaminase(ALT) (6) and aspartate transaminase(AST) (7) are two reliable markers in hepatic dysfunction diagnosis (8). ALT is suggested as more reliable and more specific as a marker compared with AST since it is mainly in liver cytosol and lower elsewhere. AST has mitochondrial and systolic forms and present in liver, kidney, heart, pancreas, lungs, brain and red and white blood cells (9). Generally, the normal value of ALT is suggested less than19IU/L and less than 30 IU/L in women and men respectively. But, the value has different ranges and depends on the laboratories (10). Furthermore, less than 35 IU/L is regarded as a normal value for AST levels (11).

Previous studies have shown dietary component is associated with liver function. High fat diet, (12) alcohol intake (13) and vitamin A (14) have been shown to have an association with liver enzyme levels. Dietary approach to stop hypertension (DASH) diet has been shown to have protective effects on the liver and is associated with liver enzymes inversely (15). Alternative healthy eating index (AHEI) 2010 has 11 components involving 7 food groups (fruit, vegetables, whole grains, nuts and legumes, juices, alcohol and red/processed meat) and 4 nutrients (PUFAs, *trans* fat, long-chain n–3 FAs, and sodium) (16). AHEI extracted from healthy eating index(HEI) in 2002 (17). AHEI was shown to be stronger than the original HEI in predicting chronic disease risk. The difference comprises of higher consideration of fat quality in AHEI compare with the original HEI (6).

The present essay sought to explore the association between adherence to AHEI and liver enzymes through investigating the relationship between adherence to AHEI and ALT and AST levels in apparently healthy adults.

Method

The original cross-sectional study was performed to investigate the association between adherence to AHEI and liver enzymes and was conducted from July 2015 to June 2016. Among apparently healthy individuals who were invited to Shariati hospital, we selected 265 healthy individuals through convenience random sampling method. Participants were excluded if they consumed a specific drug with an effect on their liver enzymes level. Moreover, they were excluded if they consumed a special diet. All participants completed a written informed consent and this study was approved by ethics committee (Ethic Number: 93-04-161-277 22-149580) of Tehran University of medical sciences.

We evaluated dietary intake by the use of a semi-quantitative food frequency questionnaire (FFQ) that included 147 foods and beverages (with standard serving sizes) ordinarily consumed (based on their past year intake). Validity and reproducibility of this FFQ have been published in earlier studies (18). Respondents reported the frequency of each given serving that they consumed. The frequency of servings was classified into nine categories: less than once monthly, 1-3 times monthly, once a week, 2-4 times weekly, 5-6 times a week, once a day, 2-3 times daily, 3-5 times daily and 6 or more times daily. For each food item the portion size was categorized into three categories: small, medium and large, and also was converted to grams (19). Then, the portion size of the daily intake frequency was multiplied to determine Intake of each food item in grams. For seasonal food consumption, we considered the period of the year that these foods were available. The energy value of each food was added in the FFQ to estimate the total energy intake. The USDA Food Composition Data (20) and the Nutrients Composition of Foods (19) were used to estimate the value of food energy. The 147 food items were categorized into 25 food groups regarding their resemblance of nutrient content to construct dietary patterns (21).

We used AHEI-2010 to assess adherence to healthy eating index (22). AHEI-2010 included eleven components: vegetables, fruits, nuts and legumes, whole grains, long-chain n-3 fats (DHA and EPA), alcohol consumption, PUFA, red and processed meats, sugar-sweetened drinks and fruit juice, trans-fat and Na. We didn't included alcohol in the current study because of lack of information. We first constructed the mentioned groups and then adjusted for energy intake using residual method (23). Then, we classified participants in to deciles of mentioned energy-adjusted intake of these components we used deciles (instead of quantitative) to reduce misclassification probability as far as possible. Individuals in the highest deciles of vegetables, fruits, nuts and legumes, whole grains, PUFA and long-chain n-3 fats were given a score of 10 and score of 1 was given to those were in lowest deciles of this components. Participants in other deciles for these items were given corresponding scores respectively. Furthermore, dietary intake of red and processed meat, sugar-sweetened drinks and fruit juice and trans-fatty acids were given scores as highest deciles for these component assigned score of 1 and lowest deciles for mentioned items were given score of 10. Those in deciles of 2, 3, 4, 5, 6, 7, 8 and 9 were given score of 9, 8, 7, 6, 5, 4, 3 and 2 respectively. AHEI-2010 was calculated by summing up the scores of each item ranged from 10 to 100 (24).

All baseline blood samples were collected between 8:00 and 10:00 am following an overnight fasting. Serum was centrifuged, aliquoted and stored at a temperature of -80 °C. All samples were analyzed by means of a single assay. All measurements were performed at the EMRC laboratory of Shariati hospital. GOD/PAP method was used for the measurement of fasting serum glucose and triglyceride levels were measured by the GPO-PAP method and total cholesterol levels were measured by the Enzymatic Endpoint method, and direct high-density lipoprotein-cholesterol was measured using the enzymatic clearance assay. All measurements were done with the use of the Randox laboratories kit (Hitachi 902) (7).

Liver enzymes were measured using by the Enzymatic Endpoint method. AST/ALT ratio (AAR) was measured for each participant by dividing ALT level by AST. Body height (BH) and body weight (BW) were measured while the participants wore light underwear and no shoes. Then BMI expressed as: BMI = BW (kg)/ BH (m). A valid questionnaire (IPAQ) was used to obtain data on physical activity, which assesses the physical activity across a complete set of domains, including domestic, leisure time and gardening activities and work-related and transport-related activities.

For evaluating the normal distribution of quantitative variables Kolmogorov–Smirnov test was conducted and all of the quantitative variables were normal distribution. To compare presence of participants' characteristics significant difference across tertiles of AHEI score, one-way ANOVA was used. To compare amounts of nutrients and food groups among tertiles of AHEI score, ANOVA was used and re-analysis by ANCOVA to adjust for energy intake, age, sex and physical activity. Binary logistic regression model analysis was used to find the relationship between AHEI score and body liver enzymes. All statistical analysis was performed using SPSS 16 for Windows. The values were expressed as mean ± standard deviation. Statistical significance was defied as $P<.05$ for all tests.

Results

The study sample consisted of 256 subjects with a mean age of 34.93 (SD8.82) years, 126 men and 139 women. Anthropometric and biochemical characteristics of study participants across tertiles of AHEI-2010 are summarized in Table 1. Individuals in the highest tertile of AHEI-2010 were older and had significant lower weight (P=0.01), BMI (P=0.02), TG (P=0.02), total cholesterol (P=0.05), ALT (P=0.02) and AST (P=0.04) and higher fat percent (P=0.02) and AAR (P<0.01). Moreover, a positive relationship between AHEI score and HDL was observed, which was marginally significant.

Participants in the highest tertile of AHEI score had more consumption of fat compared to those in the lowest tertile (P=0.03) while carbohydrate consumption was more in the lowest tertile compared to the highest (P=0.01). Moreover, no significant difference was found for protein consumption and energy intake among individuals in different tertiles Greater adherence to AHEI was associated with more consumption of vegetables, fruits, Nuts, soya and legumes groups and grains (P=<0·001). Additionally, red meat and Sugar-sweetened beverages and fruit juice groups were inversely associated with greater adherence to AHEI (P=<0·001) (Table2).

Results from Table 3 shows adherence to AHEI diet and its relation to liver enzymes status through binary logistic regression model, which involves crude model, and model 1(adjusted for age), model 2 (adjusted for age and weight) and model 3 (Adjusted for age, weight, sex and physical activity). To conduct this analysis, we categorized ALT and AST into tertiles through rank case, then first and second tertiles combined and regarded as one single group third tertile also regarded as one other single group and then binary logistic regression conducted. As shown in table 3, before any adjustments adherence to AHEI had negative and significant association with ALT and AST. For ALT this significant association was remained after adjusting for age and weight (P value= 0.02 and β= -0.9 95%CI: 0.94, 0.99) while for AST this was only after adjusting for age (P value= 0.02 and β= -1.33 and 95%CI: 0.94, 0.99). No significant adjustment was observed in model 3.

Discussion

In summary as stated in the results participants with most adherences to AHEI had more consumption of fat and less carbohydrate and had lower serum status of ALT and AST compared to participants in lowest tertile for AHEI score.

Serum liver enzymes serve as prognostic factors and are associated to some disorders (25, 26). So, measurement of these enzymes has been considered to determine the health of the liver and to evaluate response to treatments. In routine measurements ALT and AST are more common biomarkers (27). Some studies have examined the association between liver enzymes and food groups, diet components and food items. In a recently published case control study it was shown that participants who received 25,000 IU/d vitamin A induced a mild elevation in liver enzymes status (14) While in our study fat consumption was more in the highest tertile of AHEI score, The effects of high fat diet on liver function was shown in a recent animal study, AST and ALT status were measured to determine liver function, results revealed a specific diet with increased levels of fat has augmented ALT and AST level (28). This may be in contrast to our study. Additionally, Purkins et al. in a randomized crossover study showed that status of liver enzymes (including ALT and AST) increased after consumption of high carbohydrate, high calorie (HCHC) and high fat, high calorie (HFHC) diet. Although the increased level of ALT and AST in both groups were considerable (compared to standard diet) but only in high carbohydrate diet the liver enzymes were above the normal range (7–56 defined as normal range for ALT and 5–40 for AST) (29). This is in agreement with our study as carbohydrate consumption in individuals with higher adherence to AHEI was less than participants with lower adherence. We also found that adherence to AHEI diet is significantly associated with more consumption of nuts and legumes, in line with our findings a randomized clinical trial has shown a hypocaloric almond enrich diet (AED) may decrease ALT and AST comparison to hypocaloric nut free diet (NFD) (30). Although it is useful to examine relation between nutrients and liver function, but willet M et al. stated that "epidemiologic analyses based on foods, as opposed to nutrients, are generally most directly related to dietary recommendations, because individuals and institutions ultimately modify their nutrient intakes primarily by their choice of foods" (31). On the other hand, as foods involve numerous ingredients and chemicals the reaction between these components may alter bioavailability and effectiveness of them so; it's preferred to survey the relation between food groups or dietary patterns and diseases. Azadbakht et al. in a randomized clinical trial showed that ALT and AST status had considerable decrease after consuming dietary approach to stop hypertension (DASH) diet (15). DASH diet rich in fruits and vegetable and restricted sodium, so a healthy diet.

In current study, high adherence to AHEI was inversely associated to liver enzymes status. Since , most of the ALT and AST values in the subjects are within normal ranges, and therefore variations of the ALT and AST values among the subjects should not be considered as biomarkers of liver damages, but may be related with hepatic adaptation for metabolic abnormality such as insulin resistance due to abdominal adiposity as suggested by recent studies (32). Furthermore, AHEI score was strongly associated with lower levels of AAR. As elevated levels of AAR are associated with a wide range of disorders and a good marker for diagnosing disorders such as liver damage (33, 34).

Lack of information about alcohol consumption in the original data which was leading to AHEI score from 10 food and nutrients was main limitation of our study. As far as our knowledge, the strength of this study is the first study that evaluates the relationship between AHEI and liver enzymes level and AAR.

In conclusion, participants who had high adherence to AHEI had lower levels of AST and ALT compared with those who had low adherence. Moreover, AAR which is a suggested index for a wide range of disorders seems to be associated with AHEI score. Further investigations are required to confirm this association.

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