Is The Healthy Eating Index-2015 Associated With Rheumatoid Arthritis?

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Abstract

Objective: Healthy Eating Index-2015 (HEI-2015) is a multidimensional criterion of diet quality utilized to evaluate how well people's dietary behaviors align with major recommendations of the 2015–2020 Dietary Guidelines for Americans. We aim to investigate the association between the diet quality and Rheumatoid arthritis (RA) activity.

Design: Cross-sectional study

Setting: This study was done on 184 patients with RA in rheumatology clinic in Kermanshah city, Iran, in 2020. RA was diagnosed according to the criteria of the 2010 American College of Rheumatology/ European League against Rheumatism. The overall quality diet was extracted from a validated 168-item food frequency questioner (FFQ) to calculate the HEI-2015 score. RA disease activity was assessed using Disease Activity Score 28 (DAS28) scores. One-way ANOVA and ANCOVA were done to find the associations.

Participants: RA patients

Results: Individuals in the highest HEI-2015 quartile had a lower mean Erythrocyte Sedimentation Rate (ESR) than those in the lowest quartiles of the HEI scores (P-value: 0.014). A linear trend towards decreasing waist circumference in patients was observed with increasing quartiles of the HEI-2015 scores (P-value= 0.005). After controlling for all potential confounders, patients in the highest HEI-2015 quartile had the lowest DAS28 scores than those in the lowest quartile of the HEI-2015 scores (Q_1= 3.65; 95% CI= 3.29 – 4.02 vs. Q_4= 2.35; 95% CI= 1.94 - 2.67; P-value<0.001).

Conclusion: Our results indicated that following a high diet quality might be one of the therapeutic strategies to control or reduce the disease activity in RA patients.

Introduction

Rheumatoid arthritis (RA) is an inflammatory autoimmune disease that affects about 0.25% of the world's population (1). Epidemiological studies show that women are two to three times more at risk of RA than men, but the reasons are unknown (2). Chronic inflammation of the synovial tissue in the joints, stiffness, swelling, and joint pain are the main clinical features of patients with RA (3). RA is a lifelong disease and causes disabilities that have deteriorative impact on patients' daily activities (4). These patients also have a higher risk of cardiovascular disease (CVD) events due to excessive inflammatory mediators' release (5). Since RA is a multifactorial disease, further perceiving of the factors contributing to disease progression or improvement leads to the development of treatment approaches.

Diets have a significant role in regulating mechanisms underlying RA development particularly inflammatory pathways, owing to their pro- or anti-inflammatory attributes. For instance, dietary fish intake is inversely associated with the risk and disease activity of RA (6). A lot of evidence shows that higher red meat consumption is associated with an increased risk of autoimmune diseases such as RA (7, 8). A recent cross-sectional study also shows the relationship of red meats with the early onset of RA (9). Furthermore, there is evidence that dietary intakes of antioxidants, fiber, vitamins C, D, and E, omega-3 fatty acids, flavonoids, and carotenoids have been associated with less levels of chronic systemic inflammation (10). However, due to the interactive of food and nutrients in the diet and their cumulative health effect, it has been recommended to assess dietary eating pattern rather than only 1 dietary components (11). The Healthy Eating Index-2015 (HEI-2015) is a dietary quality index that measures compliance with the 2015-2020 Dietary Guidelines for Americans (DGA) (12).The HEI-2015 has 13 dietary components including nine healthy components (total fruits, whole fruits, total vegetables, greens and beans, whole grains, total protein foods, dairy, seafood and plant proteins, and fatty acids) and four unhealthy components (sodium, refined grains, saturated fats, and added sugars) (12). Various studies have examined the relationship between HEI and chronic diseases (13), while only four papers were published on HEI and RA. Two cross-sectional studies were conducted in the United State indicated that RA patients had significantly lower adherence to HEI-2010 (14) and HEI-2005 (15). In a prospective cohort of the Nurses' Health Study and the Nurses' Health Study II, with the aim of evaluating the relationship between long-term diet quality, was measured by the 2010 Alternative Healthy Eating Index and the risk of RA in women, it was shown that a healthier diet was associated with a reduced risk of RA (16). In cross-sectional study conducted in US adult from National Health and Nutrition Examination Survey 2011–2016 to assay dietary quality measured by Healthy Eating Index (HEI)- 2015, it was shown that adherence to a poor quality dietary pattern was related to odds of RA among older adults (17). Previous studies have examined the relationship between HEI and the odds of RA and it should be mentioned that to our knowledge there is no data on the association of the HEI-2015 and RA disease activity. With considering the increasing prevalence of RA, identifying associations between RA disease activity and diet quality can help dietary recommendations for these patients (18-20). Therefore, this study aimed to investigate that whether higher HEI-2015 scores would be associated with decreased activity of RA.

Materials And Methods

Study design and patients

All of the patients in this cross-sectional study were recruited based on a representative sample of outpatients with RA at the rheumatology clinic in 2020, Kermanshah, Iran. From each patient, written informed consent was obtained. The study protocol was approved by the research council and ethical committee of Kermanshah University of Medical Sciences in accordance with the principle of the Helsinki Declaration (ID: IR.KUMS.REC.1400.219). Certain rheumatoid arthritis based on the criteria of the 2010 American College of Rheumatology/ European League against Rheumatism (ACR/EULAR) was a key inclusion criterion (3). The 2010 ACR/EULAR criteria for Rheumatoid arthritis contains the number and site of involved joints (score range from 0 to 5), serologic abnormality (score range from 0 to 3), increased acute-phase response (score range from 0 to 1), and symptom duration (score range from 0 to 1). Individuals were diagnosed as definite RA who had at least a score of six with the confirmed presence of synovitis in at least one joint which is not better explained by another disease. Age of 18 years or older, female gender, and written informed consent were other inclusion criteria. Diseases such as cancer, renal failure, and heart failure, other connective tissue or joint diseases such as gout, lupus, and ankylosing spondylitis, Cushing's syndrome, inflammatory bowel disease bone or joint surgery, pregnancy, lactation, and adherence to any particular dietary regimen were considered as exclusion criteria.

Disease activity score 28

To monitor RA disease activity, there is a valid indicator called Disease Activity Score 28 (DAS28). This index is a multi-dimensional appliance that uses a physician's assessment of the number of tender and swollen joints, the levels of an acute phase reactant (CRP or ESR), and the total self-assessment of disease activity by visual analogue scale (VAS) of general health. The study rheumatologist examined all patients to determine the number of tender joints (TJ) and swollen joints (SJ), and then DAS28 scores were calculated with the following formula (21):

$$\text{DAS-28} = [0.56 \sqrt{TJ}] + [0.28 \sqrt{SJ}] + [0.7 \ln(ESR)] + [0.014\ VAS]$$

Dietary intake assessment

In this study, a credible and valid 168-item semi-quantitative food frequency questionnaire (FFQ) was used to evaluate usual dietary intake (21). FFQs assess dietary intake during the last year ranking frequency of each food/beverage on a scale from "never or < 1 serving per month" to "≥ 6 servings per day". Participants reported the daily, weekly, monthly, or annual consumption of each food item according to its portion size in the questionnaire. Dietary data from each participant through face-to-face interviews were collected by a trained dietitian. Using of the Iranian household measures, the amount of each food item was converted to weight (grams/day). Then, the data obtained from the questionnaire were analyzed using the Nutritionist IV software (First Databank Inc., Hearst Corp., San Bruno, CA, USA), and the average daily energy and nutrients consumed were calculated. Participants with a daily energy intake outside of predefined limits (800 and 4200 kcal) were excluded from the final analysis.

Healthy Eating Index-2015

The HEI-2015 components and scoring standards evaluated using the standardized cup and ounce equivalents from the MyPyramid Equivalents Database (22). In summary, the HEI-2015 contains 13 different components which are scored one by one and summed up together to obtain a maximum overall score of 100. Adequacy components include the components capture the balance among food groups, subgroups, and dietary elements containing those to encourage, and moderation components include those for which there are limits. Higher scores for the nine adequacy components (i.e., total fruits, whole fruits, total vegetables, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, and fatty acids) reflect higher intakes that meet or exceed the standards and higher scores for the four moderation components (i.e., refined grains, sodium, added sugars, and saturated fats) reflect lower intakes because lower intakes are more favorable. The component scores display the composition of the dietary patterns, and the overall score is demonstrator of the overall diet quality. Overall higher HEI-

2015 score indicated adherence to a high diet quality and healthy dietary pattern based on the 2015–2020 DGA (23). The more detailed information on content, construct, and criterion validity and reliability of the HEI-2015 and its development are available elsewhere (12, 24, 25).

Anthropometric assessments

Weight was measured using digital scales with minimal clothing. While the patients were standing in a normal position, height was measured using a tape measure. Then, body mass index (BMI) was calculated by dividing weight (kg) by height (m) squared. Without any pressure to the body surface and using an unstretched tape, waist circumference (WC) was measured at the narrowest level with light clothing. Measurements were noted to the nearest 0.1 cm (26). Body fat-free mass (FFM) and Body fat mass (FM) was measured using the bioelectrical impedance analysis (BIA) method with a Tanita BC- 418 machine (Tanita Corp., Tokyo, Japan). A trained dietitian performed all measurements.

Biochemical assessment

At the beginning of the study, blood samples were obtained from all patients. Erythrocyte Sedimentation Rate (ESR) was measured with the Westergren technique. The samples using ethylene-diamine tetraacetate potassium anticoagulant were coagulated and with 0.85% NaCl solution diluted and poured into Westergren pipe with ant "0" (1 mm) sample. Within 1 h/mm, the distance between the plasma meniscus and the top of the deposited erythrocyte column was recorded. The samples for measuring the titration of anti-nuclear antibodies (ANA) and antibodies against cyclic citrulline peptide (anti-CCP) using the ELISA method were centrifuged at 3000 rpm for 15 min (Seramun Diagnostica GmbH, Heidesee, Germany). Also, rheumatoid factor (RF) and C-reactive protein (CRP) assays were performed using the latex agglutination turbidimetric immunoassay.

Statistical methods

SPSS software version 16.0 (SPSS, Inc., Chicago IL, USA) was utilized for all statistical analyses. To determine the normality of quantitative variables, the Kolmogorov-Smirnov test was used. Quantitative variables with normal distribution as mean ± standard deviation (SD) are shown, and to analyze these variables one-way ANOVA with Tukey's Post-hoc test was used. Quantitative variables with non-normal distribution as median ± interquartile range (IQR) are shown, and to analyze these variables with Kruskal–Wallis H test and Mann–Whitney U test were used. Other variables are shown as numbers (%) and were analyzed using the Chi-square test/Fisher exact test. For adjusting effects of the confounding variables (e.g. energy intake and age) on comparison of means of DAS-28 score across quartiles of the healthy eating index-2015, analysis of covariance (ANCOVA) was used. P-value less than 0.05 were considered as statistically significant.

Results

This study included 184 eligible patients with RA based on the inclusion and exclusion criteria. All patients received medication for the treatment of rheumatoid arthritis, including Corticosteroids, Disease modifying anti-rheumatic drugs (DMARDs) such as Methotrexate, Hydroxychloroquine, Sulfasalazine, Azathioprine, and biological DMARDs. The mean age was 49.1 years (SD: 12.91), mean weight was 69.21 kg (SD: 13.34), and mean BMI was 27.25 kg/m^2 (SD: 5.11). The most of the patients were a housekeeper (90.8%) and had a positive CRP test (85.3%).

The general characteristics of the patients according to the quartiles of the HEI-2015 scores are shown in **Table 1**. The mean age and median duration of disease did not differ significantly among the quartiles of the HEI-2015 scores (P-value =0.357, P-value=0.670, respectively). The distributions of the patients in the terms of having a positive ANA, a positive anti-CCP, a positive RF, and university education and using dietary supplements were not significantly different between the quartiles of the HEI-2015 scores. The mean ESR showed a significant difference between the quartiles of the healthy eating index-2015 scores (P-value =0.015). In other words, the patients in the highest HEI-2015 quartile (Higher Quality Diet) had a lower mean ESR than those in the lowest quartiles of the HEI scores (P-value: 0.014). Also, a significant linear trend in the mean ESR was observed across the quartiles of the HEI scores (P-value= 0.003). This linear association was illustrated in **Figure 1** using Pearson correlation analysis (correlation coefficient: -0.213; P-value: 0.004).

Statistical comparisons of the anthropometric characteristics of participants according to the quartiles of the HEI-2015 scores were shown in **Table 2**. The mean of WC showed a significant difference between the quartiles of HEI-2015 (P-value=0.028). Other anthropometric variables were not significantly different between the quartiles of the HEI-2015 scores. The further analysis only showed a linear trend towards decreasing waist circumference in patients with increasing quartiles of the HEI-2015 scores (P-value= 0.005).

The mean of DAS-28 scores of patients with RA according to the quartiles (Q) of the HEI scores was shown in **Figure 2**. In the crude model, the patients in the highest HEI-2015 quartile had the lowest DAS-28 scores than those in the lowest quartile of the HEI-2015 scores (Q_1= 3.63; 95% CI= 3.28 – 3.97 vs. Q_4= 2.48; 95% CI = 2.14 - 2.83; P-value<0.001). In model 1 after adjusting of energy-adjusted, the patients in the highest HEI-2015 quartile had the lowest DAS-28 scores than those in the lowest quartile of the HEI-2015 scores (Q_1= 3.67; 95% CI= 3.31 – 4.04 vs. Q_4= 2.28; 95% CI= 1.92 - 2.65; P-value<0.001). Finally, after the adjustment of potential confounding factors including energy intake, WC, age, fat mass, duration of disease, and supplement use in model 2, the patients in the highest HEI-2015 quartile had the lowest DAS-28 scores than those in the lowest quartile of the HEI-2015 scores (Q_1= 3.65; 95% CI= 3.29 – 4.02 vs. Q_4= 2.35; 95% CI= 1.94 - 2.67; P-value<0.001). In addition, linear trend of mean of DAS-28 and the quartiles of the HEI was significant for all of the models (P-values<0.001).

Discussion

The main finding of this study was a high diet quality associated with the lower activity of rheumatoid arthritis disease, independent of potential confounding factors. Also, adherence to a healthy diet is associated with a reduction in ESR and waist circumference.

Several studies suggested a relationship between atherosclerosis and RA disease activity (27, 28). Moreover, a cohort study in patients with RA showed a significant trend toward a decreased risk of CVD incidents with improved disease activity, which emphasizes on the importance of sustained control of RA disease activity means improvement in pain and function for reduced CVD risk (29). In the current study, we found an inverse association between greater adherence to a healthy diet and disease activity in patients with RA. As far as we know, no other study has been done in this field, but there are others studies that have examined the association HEI and risk of RA. A cross-sectional study was conducted in New York in 2017 to evaluate the adherence to the Healthy Nutrition Index (HEI)-2010 in patients with RA, found that RA patient did not needs adhere to HEI-2010, which was probably related to RA-related functional disability (14). In a prospective cohort study, followed 76 597 women aged 30–55 years in the Nurses’ Health Study and 93 392 women aged 25–42 years in the Nurses’ Health Study II for 21.6 years. The study indicated that long-term adherence to Alternative Healthy Eating Index-2010 was associated with a reduced risk of RA happening at age of 55 years or younger, specially seropositive RA (16). In a cross-sectional study in Arizona, USA in 2009 with aim of assessing the dietary quality of older women (≥55 years) with RA and healthy controls using the Healthy Eating Index-2005 (HEI-2005), it was shown that patients with RA had significantly lower dietary quality (30). In cross-sectional study conducted in 11,768 US adult from National Health and Nutrition Examination Survey 2011–2016 to assay dietary quality measured by Healthy Eating Index (HEI)-2015 and self-reported disease status for RA, showed that a poor overall quality of dietary pattern was related with RA among older adults aged 60 years and older (17). Indeed, it seems that following a healthier dietary pattern could reduce the chance or developing RA.

The current study also provided additional evidence of the relationship of HEI-2015 with inflammatory markers (ESR) and waist circumference (WC). Higher HEI-2015 score that indicates a Higher Quality Diet associated with a lower ESR. ESR is common laboratory test for evaluation of acute phase response to inflammation and diagnosis and monitoring of inflammatory condition (31). Changes of ESR at the first stage of treatment predict treatment response and evaluation of serum ESR provides a valid quantitative tools for early anticipation of treatment response (32). Also, increased risk of cardiovascular events in RA patients correlates both with traditional CVD risk factors and with markers of inflammation, such as the ESR (33). As far as we know, no study has been conducted to investigate the relationship between HEI and ESR and the present study is the first study has been conducted in this field. On the other hand, our results showed that the amount of WC significantly decreases with elevating adherence to HEI-2015. In line with this result, the previous studies showed better measures of body adiposity (lower BMI and WC) in the individuals with the highest HEI values (34, 35). Several studies show that dietary patterns rich in saturated fatty acids and added sugar cause adipose tissue accumulation in various body sites, especially intra-abdominal fat (36, 37). Obesity, determined as excessive fat accumulation leads to the accumulation of white adipose tissue (WAT) and systemic inflammation. WAT acts as an “endocrine organ" releasing pro-inflammatory mediators such as tumor necrosis factor-α (TNF-α), interleukin- 6 (IL-6), leptin, resistin, and C-reactive protein (CRP) (38). As well, in a cohort of 200 RA patients, abdominal obesity is related with high disease activity, physical inactivity, high disability and poor mental health recently (39). Therefore, adherence to HEI-2015 could decrease RA disease activity through reduction in ESR and WC.

This disease is an inflammatory autoimmune disease. Objective indicators of systemic and localized inflammation are signs of disease activity in RA. Increased pro-inflammatory biomarkers (e.g., hs-CRP and ESR) are signs of systemic inflammation in RA (14). RA is related to the increased production of adipokines, ROS, and pro-inflammatory cytokines like TNFα, IL-1, and IL-6 (40). These metabolites degrade the main components of cartilage and bone, such as collagen and hyaluronic acid, and have been attributed to contribute towards the destructive, proliferative synovitis directly, which have major roles in elevating DAS-28 scores (41). There was a significant correlation between antioxidant intake and signs of anti-inflammatory status in RA (e.g., measured via DAS-28) (42). Adherence to HEI-2015 means consuming a healthy diet rich in fruits, vegetables, whole grains, low-fat dairies, and healthy fats and less consumption of foods that are high in refined grains, red meat, added sugar, sodium, and solid fats. Evidence suggested that a diet rich in healthy foods and low in unhealthy food decline overproduction of free radicals and pro-inflammatory cytokines (43-46). These results point to the key role of inflammation in developing RA and it can be concluded that the overall quality of the diet is important for modulating the risk of RA.

There are some strengths in this study such as adjusting effects of potential confounding factors and the similarity among HEI quartiles in terms of general characteristics. However, the limitation of this study was a cross-sectional analysis. Hence, it could not evaluate causal relations. Also, present study was done only among women, and the results may not be extensible to men. The effectiveness of nutrition interventions on improving diet quality in individuals with RA should be evaluated in future studies.

Conclusion

The current study showed that adherence to a diet with a high adherence to HEI-2015 was associated with decreasing the level of inflammatory factors and reduce the activity of RA. These results highlight the important role of habitual eating patterns in controlling RA and encourage clinicians to put special emphasis on the quality of individuals' diet as an effective strategy for performing RA preventive programs. Prospective longitudinal studies or clinical trials are needed to clarify whether the high HEI scores can induce relevant improvements in RA disease activity.

Declarations

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Conflict of interest disclosure:

The authors have declared no conflict of interest.

Authors' Contribution:

Conceptualization: Seyed Mostafa Nachvak; Funding acquisition: Seyed Mostafa Nachvak,; Methodology: Seyed Mostafa Nachvak; Resources: Seyed Mostafa Nachvak; Project administration: Seyed Mostafa Nachvak, Amir Bagheri and Atiyeh Nayebi. Data curation: Negin Elahi and Homayoun Elahi. Formal analysis: Shayan Mostafaei and Davood Soleimani. Writing-original draft of the manuscript: Atiyeh Nayebi, Davood Soleimani. Writing-review & editing: Amir Bagheri, Mahdi Mahmoudi and Seyed Mostafa Nachvak. All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work.

Ethical Standards Disclosure:

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the ethics committee at the Kermanshah University of Medical Sciences (ID: IR.KUMS.REC.1400.219). Written informed consent was obtained from all patients.

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Tables

Table 1. General Characteristics of the RA patients across quartiles (Q) of the healthy eating index-2015 scores.

Variables	Quartiles of the Healthy eating index-2015 scores				P-value
	Q1 **Lower Quality Diet**	Q2	Q3	Q4 **Higher Quality Diet**	
HEI-2015 score	< 42	42 - 51	51 – 60	≥ 60	-
Number	46	46	46	46	-
Age; years	48.36 ± 12.17	49.89 ± 11.59	51.39 ± 15.42	46.78 ± 12.08	0.357†
Positive ANA; n (%)	34 (73.9%)	33 (71.7%)	24 (52.2%)	32 (69.6%)	0.104‡
Positive anti-CCP; n (%)	44 (95.7%)	45 (97.8%)	41 (89.1%)	43 (93.5%)	0.336‡
Positive RF; n (%)	45 (97.8%)	43 (93.5%)	42 (91.3%)	42 (91.3%)	0.544‡
Use of Supplement; n (%)	32 (69.6%)	32 (69.6%)	36 (78.3%)	37 (80.4%)	0.499‡
University education, n (%)	4 (8.7%)	6 (13%)	9 (19.6%)	11 (23.9%)	0.202‡
Duration of disease; years	10.56 ± 9.33	8.88 ± 8.35	8.75 ± 6.24	9.27 ± 6.92	0.670†
ESR; mm/h	26 ± 14.56	26.28 ± 18.67	19.45 ± 15.56	17.96 ± 12.87	0.015†

Abbreviations. ANA: anti-nuclear antibodies, CCP: cyclic citrulline peptide, RF: rheumatoid factor, CRP: C-reactive protein.

Notes. Data are presented as a mean ± standard deviation and frequency (%).

† P-value was obtained from the one-way ANOVA test.

‡ P-values were obtained from the chi-squared test.

Table 2. Anthropometric characteristics of the RA patients across quartiles (Q) of the healthy eating index-2015 scores.

Variables	Quartiles of the Healthy eating index-2015 scores				P-value†
	Q1	Q2	Q3	Q4	
	Lower Quality Diet			**Higher Quality Diet**	
HEI-2015 score	< 42	42 - 51	51 – 60	≥ 60	-
Number	46	46	46	46	-
Weight; kg	72.23 ± 15.00	69.58 ± 14.76	67.50 ± 10.98	67.51 ± 12.01	0.273
Body mass index; kg/m^2	28.48 ± 5.61	27.48 ± 5.34	26.75 ± 4.19	26.26 ± 5.05	0.178
Fat mass; kg	24.14 ± 9.51	25.18 ± 8.86	23.87 ± 6.67	22.5 ± 8.40	0.501
Fat free mass; kg	46.25 ± 6.18	44.53 ± 6.79	43.76 ± 5.30	44.85 ± 5.19	0.236
Waist circumference; cm	97.21 ± 9.87	94.93± 9.95	94.78 ± 8.42	90.80 ± 12.44	0.028

Abbreviation. HEI-2015: healthy eating index.

Notes. Data are presented as a mean ± standard deviation.

† P-value was obtained from the one-way ANOVA test.

Figures

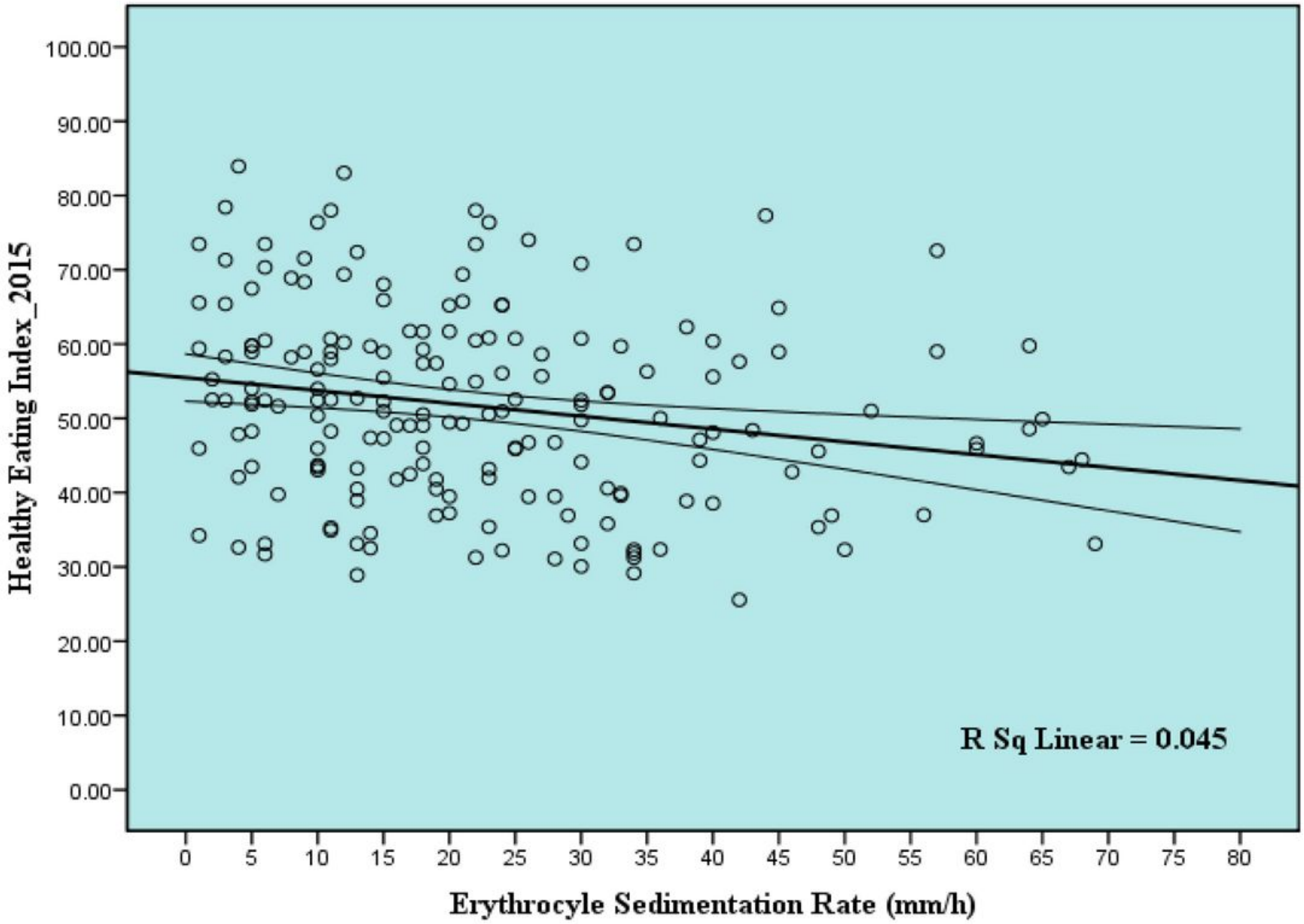

Figure 1

Significant correlation between ESR and healthy eating index-2015 score (correlation coefficient: -0.213; P-value: 0.004).

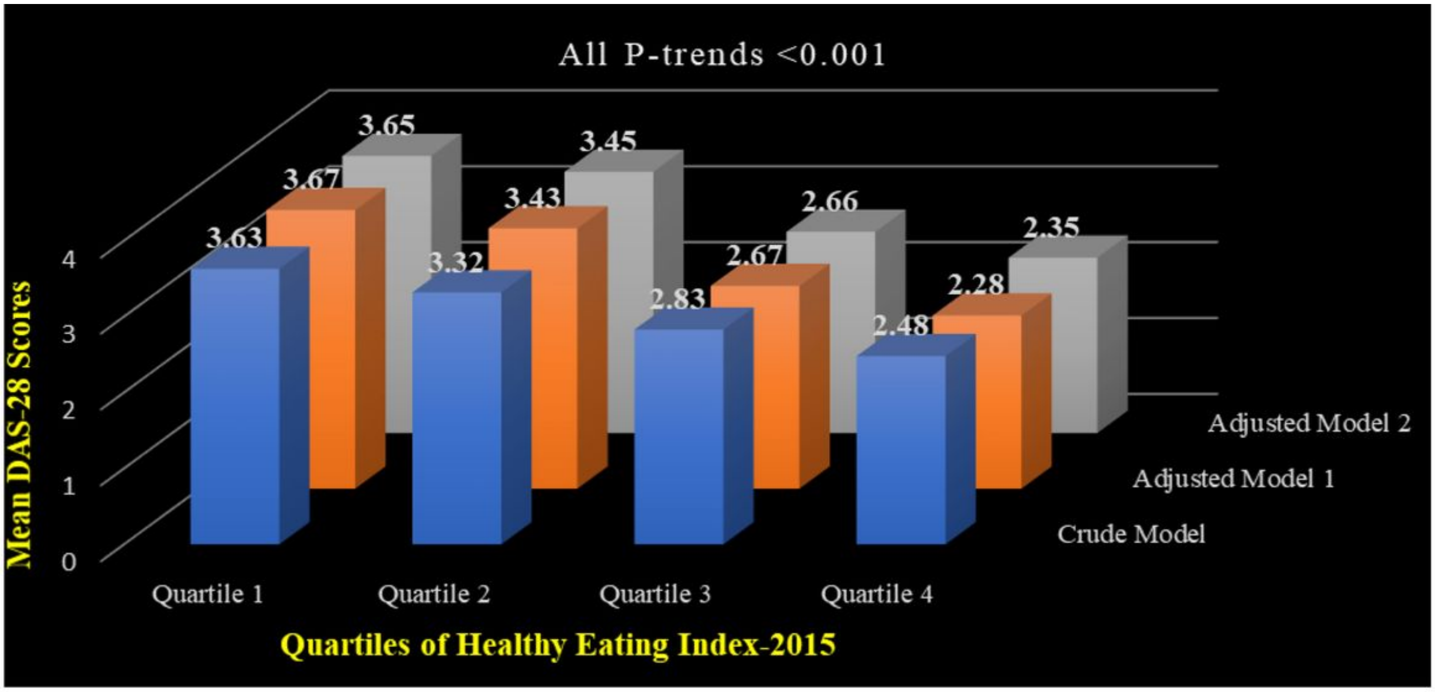

Figure 2

The mean of DAS-28 scores across the quartiles of healthy eating index 2015. Crude model: Comparison of mean of DAS-28 scores across the quartiles of HEI-2015 without any adjustment (Comparison's P-value<0.001). Model 1: Adjusted for energy intake (Comparison's P-value<0.001). Model 2: Adjusted for energy intake, WC, age, fat Mass, duration of disease, and supplement used (Comparison's P-value<0.001). P-value of trends for each of the model were obtained from the analysis of covariance (P-values<0.001).