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The Association between Dietary Patterns and a doctor diagnosis of Systemic Lupus Erythematosus: the Adventist Health Study-2

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Abstract

Objective: The aim of our study was to assess the association between a diagnosis of Systemic Lupus Erythematosus (SLE) and dietary pattern as well as demographic factors among subjects in the Adventist Health Study-2 (AHS-2) cohort.

Methods: Multivariable logistic regression modeling was used to assess the association between prevalence of self-reported SLE and dietary patterns (vegetarian, pesco-vegetarian and non-vegetarian). Potential confounding variables included were age, gender, race, education, and smoking history among 77,795 AHS-2 participants.

Results: There was a dose-response association between the prevalence of SLE with vegetarian diets, ordered by content of animal meats. The stricter vegetarians had 25% lower odds of reporting that they were currently being treated for SLE (OR=0.75, 95% CI 0.56, 1.02) with intermediate levels for the pesco-vegetarians who eat fish (OR 0.88, 95% CI 0.57, 1.36), compared to non-vegetarians. As expected, there were also significant associations between the prevalence of SLE with sex, race, age, and smoking. Significantly fewer men were diagnosed with SLE compared to women (OR=0.14, 95% CI: 0.08, 0.22). Compared to non-Hispanic Whites, non-Hispanic Blacks were significantly more likely to report a diagnosis of SLE (OR 1.69, 95% CI 1.29, 2.21). A significantly lower proportion of 30–39 year olds (OR 0.51, 95% CI 0.29, 0.90) reported a diagnosis of SLE when compared to those 60 or older. Also, ever smokers were more likely to report prevalent SLE than those who had never smoked (OR 1.71, 95% CI 1.27, 2.31).

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Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Conclusion: We found that vegetarians had lower odds of doctor-diagnosed SLE with an increasing trend in prevalence from stricter vegetarians to pesco-vegetarians to non-vegetarians. We also note that the association with other demographic factors in AHS-2 was similar to that found in other studies. Future studies may focus on assessing the incidence and severity of the disease among vegetarians and non-vegetarians.

Keywords

Systemic Lupus Erythematosus; SLE; diet; vegetarians

Introduction

Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease affecting both genders, all age-groups, race/ethnicities, and socioeconomic statuses. The Lupus Foundation of America estimates that 1.5 million Americans have SLE, with more than 90 percent being women.¹ African American women are about three times more likely to be diagnosed with SLE than Caucasian women.² Symptoms and diagnoses occur most often when women are in their child-bearing age, between the ages of 15 and 45.³

A definite cause of SLE is still unknown, but the pathogenesis is believed to include genetic, environmental, nutritional, hormonal, and immunologic factors.⁴ It was reported that adherence to pro-inflammatory diet was associated with increased risk of chronic diseases, such as all cancer types, cardiovascular diseases, and metabolic syndrome.⁵ In line with this, researchers postulated that diet might be a possible future therapy for people with SLE.⁶ Animal studies have demonstrated that lack of important dietary factors, such as omega-3 fatty acids, affected the onset of SLE and caused primary symptoms leading to a diagnosis of SLE.⁷ A systematic review reported that a low-calorie and low-protein diet with high contents of polyunsaturated fatty acids, vitamins, and minerals contain sufficient macronutrients to regulate the activity of the disease by modulating the inflammation and immune functions of SLE.⁴ Vegetarian diets have been proposed as protective for SLE due to their lower levels of protein, fat, and calories.⁸ The aim of this study was to investigate the association between a self-reported, doctor-told SLE diagnosis and dietary patterns.

Methods

Study Population

This study is based on data from the Adventist Health Study-2 (AHS-2),⁹ a large prospective, epidemiologic cohort study of mostly Non-Hispanic Black and White Adventists living in the United States and Canada who were 30 years or older at enrollment between 2002–2007. Adventists have a wide range of dietary habits with about 50% being either vegetarians (fish, poultry, red meats <1/month) or pesco-vegetarians (consume fish once or more per month, but all other meats less than once per month) while the rest consume meat 1/week. As a result, the AHS-2 cohort provides strong power to assess the relationship between dietary practices and various chronic diseases.

Since the vast majority, 85,766 (89%) among the 96,741 participants in the AHS-2, were either non-Hispanic Black or White, we excluded other races from the analyses due to low power. After case-wise deletion due to missing values among the covariates (n=7,971), the final analytic dataset contained 77,795 participants. Among these, 50,542 were women, of whom 220 reported doctor-diagnosed SLE and 27,253 were men where 17 reported a SLE diagnosis

Study Design

This is a cross-sectional study using data collected at enrollment into the AHS-2 cohort.

Survey Tool: The mailed baseline questionnaire contained information on demographics, medical history, and lifestyle including physical activity and diet measured by a validated comprehensive food frequency questionnaire.¹⁰

Outcome measure: Identification of SLE was ascertained through self-report on the baseline questionnaire by two level verification. Each subject replied yes or no to a question on whether they “had ever been diagnosed by a physician with any of the following diseases?” where one answer option was SLE and a follow-up question on whether they “had been treated for this condition over the last 12 months? Those who indicated having been treated during the last 12 months were considered as prevalent cases of SLE.

Independent Variables: The main exposure was dietary pattern defined based on frequency of meat/fish/poultry, dairy and egg consumption. To assess the impact of dietary pattern on health outcomes, the AHS-2 food frequency questionnaire included assessments of 130 food items of which 26 were used to define subjects as following one of three dietary habits: vegetarians (consuming fish, poultry, and meat combined <1/month); pesco-vegetarians (consuming fish freely, but poultry and other meat <1/month); and non-vegetarians (consuming non-fish meats once a month or more and all meats combined (fish included) more than once a week). In our calibration studies, validity coefficients were moderate to high for macronutrients, fatty acids, vitamins, minerals, and fiber when comparing the food frequency questionnaire with the repeated 24 hour recalls.¹⁰ When we analyzed differences in nutrient intakes by dietary patterns it was found that nutrient profiles varied markedly among dietary patterns that were defined by animal-derived foods.¹¹

Potential confounding variables were identified through literature review and included age, race, gender, smoking history, and highest level of education achieved (a proxy for socio-economic status). Smokers were classified as either ever or never smokers with the latter as the reference. This classification was chosen as only 1% were current smokers, 19% were past smokers and about 80% were never smokers.

Statistical Analysis

Univariate analyses were conducted to compare cases and non-cases with respect to dietary patterns, demographic characteristics, and candidate covariates using chi-square test. Multivariable logistic regression was used to assess the multivariable-adjusted association between dietary patterns (vegetarian, pesco-vegetarian and non-vegetarian) and prevalence

of SLE. For dietary patterns and ordinal variables, p-values for trend were calculated while adjusting for the other covariates. Effect modification was also tested by adding an interaction term to the model for vegetarian status with each covariate. No effect modification was found so all analyses were conducted on the entire study population without stratifications. Since BMI could potentially be a mediator between dietary patterns and risk of SLE, we ran a sensitivity analysis excluding BMI. This did not change the main result so BMI was not retained in the final multivariable model. All analyses were performed using R version 2.4.0.

This study was approved by the Institutional Review Board of Loma Linda University (IRB #48134). Written, signed, and dated informed consent forms were obtained from all study participants.

Results

Only 237 subjects (0.3%) in this study reported a diagnosis of SLE which had been treated during the previous 12 months. Of these, 68 (29%) were vegetarians, 24 (10%) were pesco-vegetarians and 145 (61%) were non-vegetarians (Table 1). Thus, vegetarians were less likely to report SLE than the non-vegetarians. Smoking is very rare among Adventists, and of the 62,115 participants who reported having never smoked, 173 (0.3%) had been treated for SLE. Of the 14,865 past smokers, 58 (0.4%) reported SLE. Only 815 (1.0%) were current smokers and 6 (0.7%) of these reported SLE. So, the prevalence of SLE increased monotonically with smoking status: never (0.3%), past (0.4%) and current (0.7%).

Multivariable analyses found that both vegetarians and pesco-vegetarians had decreased odds of being diagnosed with SLE compared to non-vegetarians (OR=0.75, 95% CI: 0.56, 1.02) and (OR=0.88, 95% CI: 0.57, 1.36), respectively. Significantly fewer men were diagnosed with SLE compared to women (OR=0.14, 95% CI: 0.08, 0.22) and Blacks were 69% more likely to report a diagnosis of SLE compared to Whites (OR=1.69, 95% CI: 1.29, 2.21). Younger age (30–39 years old) was protective against SLE with OR of 0.51 (95% CI: 0.29, 0.90) compared to those 60+ years. Ever smokers showed a significantly elevated odds ratio compared with those who had never smoked (OR=1.71, 95% CI: 1.27, 2.31).

Discussion

We found that vegetarians had lower odds of self-reported doctor-told SLE with an increasing trend from vegetarians to pesco-vegetarians to non-vegetarians. Unfortunately, only a small proportion of participants were pesco-vegetarians, giving us low power and thus relatively wide confidence intervals for this group.

There are no current dietary recommendations for decreasing the risk of developing SLE; however, diet has been hypothesized as a possible therapeutic option.¹² Lupus is an autoimmune disease, so maintaining good nutritional habits may help the body remain as healthy as possible. A healthy diet in SLE may help preserve the body's homeostasis, prevent adverse effects of medication, increase the periodic remission, and improve the patient's physical and mental well-being.¹³ Multiple studies, reviewed briefly below, have found that nutritional interventions can alleviate chronic and acute symptoms of SLE¹⁴,

consistent with the inverse trend we found in the prevalence of SLE by degree of vegetarian diet.

A comprehensive review of nutritional factors reported positive associations with SLE, including excess energy, excess protein, high fat diets, zinc, and iron, all of which are commonly associated with meat-containing diets.⁴ Nutritional factors reported to be inversely associated with SLE include vitamins E and A, fish oils, and flaxseed, which are typically found in vegetarian and fish-based diets.⁸ This supports our study finding that people with plant- and fish-based diets were less likely to report SLE compared to non-vegetarians.

A possible mechanism for how nutrition affects SLE development is likely through the effect of dietary factors on apoptosis.¹⁵ Our study subjects reporting a vegetarian diet have lower intake of total fat, especially animal fat, compared with the non-vegetarian subjects.¹¹ This difference may have a beneficial effect on the rate of apoptosis as vegetarian diets have been proposed as a way of regulating apoptosis and treating autoimmune diseases such as SLE.¹⁵ The abnormal accumulation of cells as a result of the suppression of apoptosis leads to the development of autoimmune diseases such as SLE where there is an increased development of auto-antibodies.¹⁵

Our findings of an association of SLE with race, age, sex, and education are in line with what other studies have reported.³ In 2007, a medical review of inpatient hospital databases of women in California found that age, sex, and race/ethnicity adjusted SLE prevalence among those 18+ years was 184.2 per 100,000, 164.4 for all White women and 406.3 for all Black women. The prevalence for women aged 18–44 years, 45–64 years, and 65+ were 162.5, 272.5 and 107.6 per 100,000, respectively.¹⁶ These prevalences are similar to our findings.

Adventists are a health-conscious population with significant proportions of vegetarians and pesco-vegetarians. Because the Adventist church recommends eating a plant-based diet, members who eat meat tend to eat meat in much smaller quantities and on fewer occasions than the general population.⁹ Since our study population is a low meat-eating population, it is possible that the beneficial association with a vegetarian diet is underestimated compared to a comparison group with a higher meat intake. Also, it is possible that subjects may choose to change their diet toward a more vegetarian diet when diagnosed with a chronic disease believed to be related to lifestyle. Then, reverse causation would bias our results toward the null.

Our findings of lower prevalence of SLE among vegetarians may be due to a truly lower incidence or could also be a result of less severe SLE with fewer symptoms. Since remissions may be related to dietary interventions, it is possible that dietary habits may also prevent a mild case from ever being diagnosed. Thus, following a vegetarian diet may have been an effective prevention strategy for those who adhere to the diet.

Strengths and limitations

One of the main strengths of this study is the large proportion of participants who follow a vegetarian dietary pattern. This gives reasonable power to observe an association between this rather uncommon disorder and various diets if it exists. Further, our study includes a large number of Blacks who have the highest risk of SLE, allowing us to investigate associations by race. Another strength is that, although this is a cross-sectional study, the reliability/validity of diet patterns in this population has been assessed and found to be good.¹⁰

Study limitations include the validity of a self-reported SLE diagnosis. However, identification of SLE was ascertained through self-report by two level verification. The question was if the participants had ever been diagnosed by a physician with SLE and whether they had been treated for this condition over the last 12 months. One would not expect many false positive since the assessment includes not only doctor-told diagnosis, but also current treatment for SLE. In the Women's Health Initiative, verification of self-reported SLE was improved 4-fold by adding medication to doctor-told diagnosis of SLE.¹⁷ There may also be healthy volunteer bias. Since SLE can be a debilitating disease with severe joint pain, subjects may have problems with writing and therefore not enroll in a study requiring completing a lengthy self-administered survey. Thus, a systematic inclusion of less severe cases and exclusion of more severe cases may attenuate the measures of association we studied. Lastly, since the study was cross sectional in nature, causality cannot be established and it does not present evidence of which factors in a vegetarian diet would be protective. Due to these limitations, this study can be considered preliminary or hypothesis-generating.

Future Studies

For future references on this matter, we would recommend assessing the severity of the disease among vegetarians and non-vegetarians to investigate the difference in the prognosis of the disease among the different dietary patterns. Tedeschi et al.² recently reported no difference between risk of SLE and either prudent or Western dietary pattern score in women. When sufficient follow-up time has accrued in this study population, there will hopefully be sufficient number of incident cases of SLE to assess the relative risk in the various dietary patterns. It will also be promising to study the association between various components of diet, such as omega-3 fatty acids, as they relate to SLE.

Conclusions

Both the vegetarian and the pesco-vegetarian diet were associated with lower odds of reporting a diagnosis of SLE compared to non-vegetarians. In spite of the uniqueness of this population, we believe our findings of potential benefits of a plant-based diet are applicable to the general population of Blacks and non-Blacks as the association with other demographic factors was similar to that found in other studies with respect to a higher prevalence among women, Blacks, ever smokers and among those with higher education.

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Table 1.

Characteristics of the sample population for SLE cases versus non-cases.

Sample Population Characteristics	SLE (%) N = 237	No SLE (%) N = 77,558	χ^2 p-value
Dietary Patterns			
Vegetarians	68 (29%)	29,782 (38%)	
Pesco-Vegetarians	24 (10%)	7,457 (10%)	
Non-Vegetarians	145 (61%)	40,319 (52%)	0.0078
Age			
60 years or older	97 (41%)	34,752 (45%)	
40–59 years old	126 (53%)	35,187 (45%)	
30–39 years old	14 (6%)	7,619 (Wo)	0.0218
Race			
Non-Hispanic Black	97 (41%)	20,822 (27%)	
Non-Hispanic White	140 (59%)	56,736 (73%)	<0.0001
Gender			
Male	17 (7%)	27,236 (35%)	
Female	220 (93%)	50,322 (65%)	<0.0001
Smoking History			
Past or Current Smokers	64 (27%)	15,616 (20%)	
Never Smokers	173 (73%)	61,942 (80%)	0.0107
Education			
Bachelor's Degree or Higher	84 (35%)	29,682 (38%)	
Some college	105 (44%)	30,943 (40%)	
High School Graduation or Less	48 (20%)	16,933 (22%)	0.3841

Table 2.

Multivariable adjusted Odds Ratios (OR) for the association between SLE and dietary patterns in the Adventist Health Study-2

	Basic^a	Final Model^b
	OR (95% CL)	OR (95% CL)
Dietary Patterns		
Vegetarians	0.73 (0.54, 0.98)	0.75 (0.56, 1.02)
Pesco-Vegetarians	0.85 (0.55, 1.32)	0.88 (0.57, 1.36)
Non-Vegetarians	Ref	Ref
	p(trend)=0.03	p(trend)=0.06
Age		
30–39 years old	0.52 (0.30, 0.92)	0.51 (0.29, 0.90)
40–59 years old	1.14 (0.87, 1.49)	1.08 (0.82, 1.42)
60 years or older	Ref	Ref
	p(trend)=0.27	p(trend) = 0.46
Race		
Non-Hispanic Black	1.67 (1.27, 2.20)	1.69 (1.29, 2.21)
Non-Hispanic White	Ref	Ref
Gender		
Male	0.15 (0.09, 0.24)	0.14 (0.08, 0.22)
Female	Ref	Ref
Smoking History		
Past or Current Smokers		1.71 (1.27, 2.31)
Never Smokers		Ref
Education		
High School Graduate or Less		0.72 (0.49, 1.04)
Some College		0.87 (0.65, 1.17)
Bachelor's Degree or Higher		Ref
		p(trend) = 0.08

^aAdjusted for Age, Race, Gender

^bAdjusted for Age, Race, Gender, Smoking, and Education