

## Research Article

# Dietary Patterns and Nutrient Intakes in SLE Patients in Oman

Asma Al Kindi<sup>1</sup>, A'Shaima Al Kindi<sup>2</sup>, Batool Hassan<sup>3</sup>, Saied Al Yahyai<sup>4</sup>, Mostafa Waly<sup>5</sup>, Aliya Alansari<sup>1\*</sup>

<sup>1</sup>Department of biology, College of Science, Sultan Qaboos University, Oman

<sup>2</sup>Department of Nutrition and Dietetics, Sultan Qaboos University Hospital, Oman

<sup>3</sup>Department of Medicine, College of Medicine and Health Sciences, Sultan Qaboos University, Oman

<sup>4</sup>Department of Genetics, College of Medicine and Health Sciences, Sultan Qaboos University, Oman

<sup>5</sup>Department of Food Science and Nutrition, College of Agriculture and Marine Sciences, Sultan Qaboos University, Oman

**\*Corresponding Author:** Aliya Al Ansari, Department of Biology, College of Science, Sultan Qaboos University, Oman, Tel: 00968 24146825; E-mail: [alansari@squ.edu.om](mailto:alansari@squ.edu.om)

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## Abstract

Systemic lupus erythematosus is an autoimmune disease with unexpected flares that is thought to be affected by dietary habits. In order to explore the dietary habits of Omani patients, we analyzed the intake of nutrients based on the assessment of diet from the semi-quantitative FFQ. Dietary patterns of sixty Omani cases and sixty age-gender-and origin- matched controls were assessed in terms of the recommended number of servings per day according to the Omani healthy plate for the main food groups and compared to the recommended dietary allowances (RDA) per day. Cases were found to consume proteins, fats and carbohydrates

higher than RDA per day. Micronutrient intakes by cases showed that the intake of calcium, magnesium, iron, selenium, iodine, vitamins B6, D and E were lower than RDA, while phosphorous and vitamin B12 intake were higher. These observations were similar to previous studies except for B12 that was reported to be lower in SLE cases. However, this is considered as pilot study and the findings need to be confirmed by larger size study.

**Keywords:** Systemic Lupus Erythematosus; Dietary patterns; Nutrients intake; Semi-quantitative food

frequency questionnaire; Oman

## **Abbreviations**

SLE-Systemic lupus erythematosus; FFQ-Food Frequency Questionnaire; SFFQ-Semi-Quantitative Food Frequency Questionnaire, RDA-Recommended daily allowances; AI-Adequate Intake

## **1. Introduction**

Systemic lupus erythematosus (SLE) is a chronic, autoimmune disease characterized by autoantibodies production and immune complex deposition resulting in inflammation of some tissues and organs [1]. The disease runs with unpredictable course of flare and remission. There is an increasing interest in understanding the relationship between diet and SLE since there are significant differences in some vitamin levels between SLE patients and healthy people. Although diet alterations can reduce the risk of associated conditions such as atherosclerosis and metabolic syndrome [2], there is no clear evidences showing the effect of dietary changes in the SLE development and disease activity in humans [2].

### **1.1 Dietary patterns**

Dietary pattern analysis for food items or food groups are important for examining the relationship between food or nutrients and the risk of chronic disease development [3]. Some studies linked the development of SLE to meat [4] and milk [5] consumption and classified them as strong and significant risk factor, whereas fish a weak and not significant risk factor [6]. Mediterranean diet, which is rich in vegetables, fruits, seeds, grains, nuts, two portions of fish per week and a small amount of meat and dairy, is recommended for SLE patients [7].

### **1.2 Nutrient Intakes**

Nutrients are divided into macronutrients (carbohydrates, proteins and fat) and micronutrients

(such as vitamins, selenium and iron). Specific nutrients were found to be associated with increasing SLE flares such as excess calories, fats, proteins, iron and zinc, while some micronutrients reported to have beneficial effects on SLE cases such as vitamin A, vitamin B, vitamin C, vitamin D, vitamin E, selenium, calcium [8]. For example, vitamin A level in SLE patients found to be significantly lower compared to healthy controls ( $p=0.001$ ) [9]. Furthermore, they reported that 77.77% of the recruited patients had lower than 30 mcg/dl of vitamin A, i.e. hypovitaminosis. In animal models, vitamin A supplementation has shown to decrease SLE pathogenesis through the reduction of proteinuria and glomerulonephritis [10]. One of the potential mechanisms through which vitamin A can reduce pathogenesis is by modulating the Th17/ Treg balance by increasing Treg cells and decreasing Th17 cells and therefore reducing the inflammatory response. Handono et al. [11] found that the supplementation of CD4+ T cell cultures with vitamin A can modulate the ratio of Th17/ Treg [11].

In SLE patients, vitamin B complex intake reduces triglycerides and LDL-C and improves clinical symptoms [12] such as fatigue, fever and cardiovascular diseases [13]. In a study on Japanese SLE patients, increased doses of Vitamin B6 and folate were able to reduce disease severity regardless of the non-dietary factors [14]. Vitamin D deficiency is associated with severity and disease activity of SLE [15]. In addition, vitamin D has an immunomodulatory role on adaptive immune response by inhibiting Th1 and Th17 cells in humans and mice. It can also stimulate the differentiation of T cells towards Treg cells and maintain their induction [16].

### **1.3 Diet and microbiome**

Dietary patterns are also important due to their influence on the microbiota diversity. For example, low fat/ high

fiber diet was reported to be positively associated with *Firmicutes* levels [17, 18]. The gut microbiota helps the host in extracting and digesting nutrients from their diets, protect against enteropathogens and for normal immune functions and responses, especially the development of T helper (Th) cell lineages [19, 20]. Any significant change in the composition of microbiota may lead to autoimmune diseases such as rheumatoid arthritis, inflammatory bowel disease (IBD) and SLE [21, 22]. The influence of gut microbiota was reported by López et al. [23] when the differentiation of Th17 was increased in naïve T cells when co-cultured with stool microbiota from SLE patients and not seen with healthy controls [23]. This increase in Th17 was also linked to calcium/calmodulin-dependent proteinase kinase IV(CAMK4) and serine/threonine kinase, which is present at high levels in T cells in SLE patients [24]. As the diet and nutrient intakes of patients with SLE appear to play an important role in the disease development and complications [25], we investigated the dietary patterns and nutritional status of Omani females in the age range of 19-50 years based on case-control design.

## **2. Materials and Methods**

### **2.1 Dietary patterns and nutrients Intake**

The questionnaire was designed to provide data about the frequency of intake of a variety of food items as standardized portion sizes. Development of semi-quantitative food frequency questionnaire (SFFQ) went through four main steps. First step was the construction of food list based on other validated FFQ according to Block et al. [26] and previously used at SQU, which is based on the Omani food consumption patterns (Appendix 1). The Omani healthy plate is structured on 6-11 servings of grains and potatoes, 3-5 servings of vegetables, 2-4 servings of fruits, one serving of legumes and one serving of milk and dairy products [27]. Then portion sizes were defined for all food items.

After that, the categories to assess the frequency of consumption were set from never to more than 6 times per day. At last, the FFQ was administered to a small group of patients and controls to determine the completeness of food list and to guide the generation of shorter food list for SFFQ by eliminating less commonly consumed food items from the questionnaire. Similar method was used by Dehghan et al. [28] to develop SFFQ based on local food types in United Arab Emirates and Kuwait. The average frequency of consumption in SFFQ was assessed by five categories (never, rarely, monthly, weekly and daily) that are based on the mid-point of the frequencies used in FFQ; for example, daily is equivalent to 4 servings per day.

Ethical approval for conducting the study was obtained from the ethics committee at the college of medicine and health sciences, Sultan Qaboos University (MERC# 1418). This part of the questionnaire was interviewer-administered for all cases to reduce the errors comes from weak understanding of the serving sizes and to clarify any other questions regarding the food types. For 95% of controls, the questionnaire was self-administered and a supplementary sheet was sent to explain the portion sizes for each food item and extra details regarding some food items (Appendix 2). Participants that were admixed or males were excluded from the study.

The semi-quantitative FFQ assessed the intake of 30 food items and the participants indicated their average intake for each food item over the last 3 months of a specified serving size. Nutrient intake was then calculated using computerized software program (Micro.diet V4, publisher Downlee System Limited) in collaboration with SQUH dietitians that multiply the reported frequency of each food item by the amount of nutrients in a serving of that food item. The nutrients analysis covered both macro and micronutrients

including; protein, fat, carbohydrate, sugar, sodium, potassium, calcium, water-soluble vitamins (B6, B12, C) and fat-soluble vitamin (D). The frequency of consumption recorded in five categories (once a month, weekly, daily and rarely, never). For the analysis of the FFQ, survey answers were converted into numeric factors that represent the frequency of consumption per week. These numbers were then plugged in the food intake frequency template (Appendix 3) that is used to calculate the total intake of nutrients in all food items per week for each participant. After that, the average of total intake of nutrients of patients was compared with controls.

## **2.2 Data Analysis**

**2.2.1 Dietary patterns:** Principle component analysis (PCA) was carried to predict food groups as possible risk factors for SLE [6].

**2.2.2 Nutrient Intakes:** The frequency of each nutrient was calculated as described above and compared to the accepted reference used by SQUH, “Oman Food Based Dietary Guidelines” published by Ministry of Health in Cooperation with UNICEF and international standards. It is also coupled with the Adequate Intake (AI) and Recommended daily allowances (RDAs) international standards that both could be used as a reference of daily intake of macro and micronutrients [29]. The intake of

macronutrients was compared between cases and controls using ANNOVA, multiple t tests.

## **3. Results**

One hundred and twenty participants (60 cases and 60 controls) completed a data collection of their dietary intake using a semi-quantitative food frequency questionnaire (SFFQ). The PCA figure showed a trend of cases clustering with high intake of beef, oil and fruits (Percentage of variance of PC1 is 16.176 PC2 11.659) (Figure 1).

### **3.1 Nutrient intakes**

The analysis of the intake of nutrients was based on the assessment of diet from the semi-quantitative FFQ (Table 1 and Table 2). Macronutrients analysis did not show any significant differences between cases and controls. Therefore, the levels of macronutrients will be compared to RDAs and AI to evaluate the results. The energy intake of cases (1505.88 Kcal/d) was lower than RDA (2200 Kcal/d) while proteins and fats intake were higher than RDA (Table 1). Carbohydrates intake was higher than the recommended AI (130 g/day) as reflected by the assessment of dietary intake from semi quantitative questionnaire. Micronutrient intakes by cases showed that the intake of calcium, magnesium, iron, selenium, iodine, vitamins B6, D and E was lower than RDA. Whereas phosphorous and vitamin B12 intake was higher than RDA (Table 2).

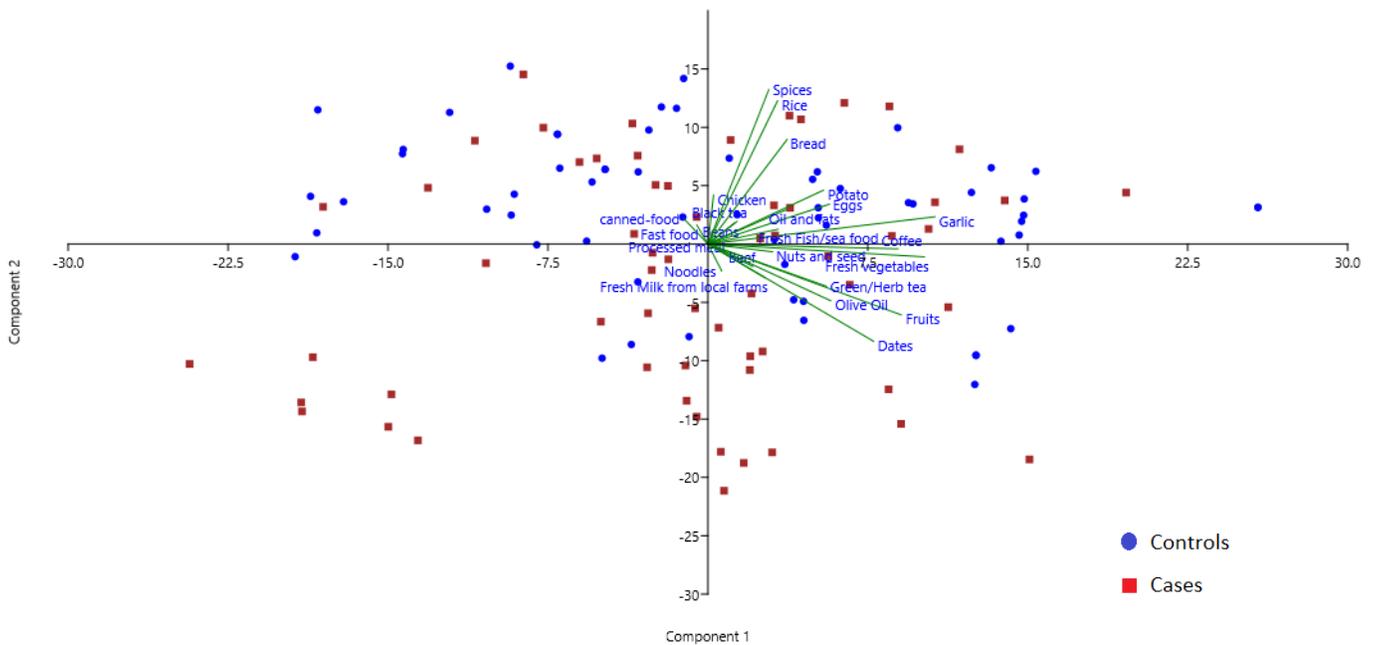


Figure 1: PCA of the intake of 30 food items by cases and controls.

Group Nutrient	Cases N=60	Control N=60	t-test, P values
Carbohydrates	139.77 ± 63.03	147.227 ± 58.624	t= 0.6708, P=0.503673
Protein	72.80 ± 35.93	70.742 ± 38.512	t= 0.3020, P=0.763158
Fats	78.20 ± 38.17	76.769 ± 44.828	t=0.1886, P=0.850732
Energy	1505.88 ± 662.91	1515.854 ± 717.375	t=0.07906, P=0.937120

Data are expressed as mean ± S.D; Recommended dietary allowances (RDA) for Caloric requirements (2200.00-2600.00 kcal/day), Protein requirements (46 g/day), Carbohydrate requirements (130 g/day), Fat (AI) (25 g/day)

Table 1: Average Daily Macronutrient Intakes of Study Subjects.

Group Micronutrient	Cases (n=60)	Controls (n=60)	P value	RDA
Na (mg/d)	1501.333	1391.223	0.265	1600
Ca mg/d	437.6276	245.067	0.351	1000
Mg mg	181.8647	186.072	0.746	320
P (mg/d)	867.4423	807.3	0.118	700
Iron (mg/d)	9.805529	9.428	0.251	18
Se (mg/d)	18.39314	17.958	0.742	55
Iodine (mg /d)	47.72675	48.104	0.650	150

VitB6 mg/d	1.042937	1.049	0.597	1.3
VitB12 mg /d	5.345708	3.933	0.006	2.4
VitC mg/d	57.97084	52.172	0.153	75
VitD mg /d	2.743525	1.926	0.006	15
VitE mg/d	0.854426	0.895	0.843	15

AI for sodium is shown in bold

**Table 2:** Nutrients differences between cases and controls.

#### 4. Discussion

SLE is a multifactorial disease affected by genetic, environmental and hormonal factors. Therefore it is hard to establish relationship between nutrition and SLE activity although there are evidence for the influence of diet quality in the development of clinical complications, such as low bone mineral density and cardiovascular diseases, in SLE cases [30]. Nutrients like selenium, calcium,  $\omega$ -3 fatty acids, vitamins E, A and D reported to have beneficial effects on disease symptoms. On the other hand, high intake of fats, calories, protein, zinc and iron can worsen disease symptoms [31]. SFFQ found to be easier to administer and more reliable as reported by others [28]. Pre-specified serving sizes was incorporated in the SFFQ instead of giving the participants the opportunity to specify their portion sizes to make the calculations easier and more consistent. Although self-administration of the questionnaire to controls might have biased the results, but this was the only way to include participants from different backgrounds and educational levels instead of focusing on the university students and staff. Three dietary patterns of cases were determined; meat, fats and fruits. High meat dietary pattern was reported earlier in Japanese SLE females but did not have measurable association with SLE risk [6].

The adequate caloric intake for SLE cases is 1,200-1,400 kcal/day for men and 1,000-1,200 kcal/day for women [12, 33], which is lower than energy intake of

the cases in our study that is 1505.88 Kcal/day. It is known that the progression of autoimmune diseases is altered by the restriction of calories in the diet [33]. Energy restriction prevent the reduced production of CD4+ and CD8+ T lymphocytes and increased Th1 cytokines (IL2 and IFN-g) in NZB/NZW mice [8]. In addition, Calories restriction can induce changes in the gut microbiota that was proven to benefit the immune system [33]. In humans, the risk of fetal loss in women with SLE and antiphospholipid syndrome was reduced when their diet included higher levels of polyunsaturated fatty acids (PUFA) [34].

In our study, the results showed high daily intake of proteins and fat by both cases and controls compared to RDA. Although there are no significant differences between the two groups but the average daily intake of proteins and fats by cases is more than controls. There are studies suggesting the association of proteins with complications of SLE diseases. In NZB/NZW mice, studies have revealed that moderate-protein diet-fed mice had a delay in autoimmunity and complication of SLE compared with normal-protein diet- fed mice. In addition, a restricted diet of phenylalanine and tyrosine amino acids was associated with beneficial effects on these mice [12]. Excessive protein intake lead to constant bone mineral loss in patients with juvenile SLE, whereas the consumption of 0.6 g/kg/day in a protein-restricted diet has enhanced the glomerular

filtration rate in pre-dialytic chronic kidney disease of patients with systemic diseases [8].

Changes in the metabolism of lipoproteins and lipid profile in SLE patients is related to autoimmunity and inflammation in the disease. It was reported that both active and remission status of SLE, have higher levels of triglycerides (TG) and very low-density lipoprotein cholesterol (VLDL-C), which is associated with lower levels of high-density lipoprotein cholesterol (HDL-C). The enzymatic activity of lipoprotein lipase is reduced in SLE leading to reduced catabolism of TG-rich lipoproteins by either the presence of anti-lipoprotein lipase antibodies (anti-LPL) or tumor necrosis factor- $\alpha$  (TNF-  $\alpha$ ) action [8]. This suggest that high consumption of fat seen in this study can elaborate the problems associated with lipid metabolism in SLE cases. Balanced diet is important to avoid complications associated with SLE such as cardiovascular diseases, diabetes, obesity, metabolic syndrome and dyslipidemia [8, 12].

The intake of vitamin B12 is usually associated with the consumption of animal origin foods that are the only dietary sources of this vitamin [35]. Although there was no measurement of vitamin B12 concentration in plasma, participants in our study had high levels of vitamin B12 as reflected by the data analysis of dietary intake in the SFFQ unlike other studies showing low vitamin B12 in cases due to low intake of meat and beans [35]. This is due to the higher intake of food from animal origin by our study group. The recommended daily intake of vitamin B12 is 2-3 mg that balanced diet could easily provide [36, 37]. Some studies discussed the fact that the recommended value (2-3 mg/d) is not sufficient to maintain genomic stability recommending to increase the daily intake to 7 mg/day. This daily intake is probably sufficient for a plasma level of 400

pg/ml [38] which is known to decrease micronucleus formation in lymphocytes [36, 39].

Deficiency or low levels of vitamin D was linked with increased susceptibility of SLE and increased activity-SLEDAI [40]. Nutrient analysis of cases participating in this study showed low levels of vitamin D of 2.74 mg/d compared to RDA of 15 mg/d. The steroid hormone vitamin D have essential role in immune system homeostasis and mineral metabolism [41, 42]. The active form of vitamin D (calcitriol) regulate T and B cell responses and boost the innate immune response. In this sense, low levels of vitamin D in the body is a possible trigger for SLE and other autoimmune disease [43, 44]. Low levels of vitamin D is seen in cases and controls in this study as this is one of the common deficiencies in Oman especially in females [45]. This could be due to the low intake of milk and dairy products as part of the dietary habits in the country as we found 72% of the total participants in this study are consuming less than 2 portions of milk per day. The general practice for SLE patients at SQUH is supplementation with vitamin D and monitoring its levels between routine visits. Supplementation with vitamin D have significant beneficial effects on the maturation and activation of dendritic cells [46] in addition to bone mineral density when the plasma level reaches  $>36.8$  ng/l [47].

The intake of vitamin E by cases (0.854 mg/d) was very low compared to RDA that can worsen disease status in these cases since it is known for the ability to decrease the levels of inflammatory cytokines, IL-2, IL-4 and TNF- $\alpha$  when combined with omega3 PUFA from fish oil [8]. The study showed that the average intakes of calcium, iron, selenium, magnesium, Iodine, vitamins B6, D and E for cases are lower than RDA. Selenium is an important antioxidant and critical component in a number of antioxidant enzymes and immune functions.

In autoimmune diseases, selenium serum levels were lower than healthy controls is possibly associated with the initiation of inflammation and auto immunity [48]. Similar observations for calcium and iron were reported earlier in patients compared to healthy controls [35].

## 5. Conclusion

The dietary habits of the Omani females in this study showed high protein and fat intake with low levels of important micronutrients like vitamin C, vitamin D, calcium and selenium, which may be associated with SLE complications in the long term. Replication of the questionnaire recruiting more number of SLE cases and healthy controls will help in confirming the findings. This will help in suggesting healthy dietary plan for patients aiming for better management of the disease and possibly prolongs the remission status of patients.

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## Conflicts of Interest

The authors declare that they have no conflict of interest.

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