Assessment of nutritional status and physical activity in systemic lupus erythematosus patients

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ABSTRACT

Introduction: Patients with systemic lupus erythematosus (SLE) may present nutritional changes triggered by disease or treatment, and these conditions may interfere with prognosis. **Objective:** Assess the nutritional status, physical activity and associated factors in patients with SLE under treatment at the Service of Rheumatology of Hospital das Clínicas/ Universidade Federal de Minas Gerais. **Methods:** A cross-sectional study evaluating the nutritional status, clinical laboratory findings, sociodemographic, and treatment characteristics of 170 SLE female patients. **Results:** Patients aged between 18 and 60 years were included. The mean (SD) age of patients and duration of SLE was 39.1 (10.0) and 9.9 (6.2) years, respectively. Two (1.2%) patients were classified as grade I underweight, 59 (34.7%) eutrophic, 61 (35.9%) as overweight, 37 (21.8%) as grade I obesity, seven (4,1%) as grade II obesity, and four (2,4%) as grade III obesity. Overweight and obesity were significantly associated with older age, lower education, higher SLE damage index, higher serum concentration of complement, higher incidence of hypertension and *diabetes mellitus*, presence of ovarian failure, and less frequent use of antimalarials Regarding physical activity, 39 patients (22.9%) were classified as inactive, 100 (58.8%) insufficiently active, and 31 (18.2%) active. Of the latter, 13 (43.3%) were in the eutrophic group. **Conclusion:** Excess weight was high in this population and associated with some traditional risk factors for cardiovascular disease and SLE poor prognosis. Therefore, encouraging weight control must be part of the main goals in treating SLE patients.

Keywords: systemic lupus erythematosus, nutritional status, exercise.

INTRODUCTION

The integration between nutritional status and immunity, which is beneficial to health in certain physiological conditions, could be detrimental in some situations. Malnutrition, which causes immunosuppression, and obesity, which triggers systemic inflammation, are conditions that can modify the individual's response to a particular disease.[1,2]

In Brazil, the records show a decrease in the occurrence of malnutrition at the same time that there is significant increase in the prevalence of obesity.[3] In developed countries this transition in nutrition profile has already occurred, and programs to control overweight are performed in order to stabilize the obesity rate and, thereby, reduce costs, morbidity and mortality.[4] Systemic lupus erythematosus (SLE) is a multisystem inflammatory disease of connective tissue, characterized by immune system imbalance with periods of exacerbation and remission.[5] Currently, the most common nutritional disorder described in SLE patients is the excess weight. However, the causes and consequences have not yet been studied.[6]

Submitted in 06/10/2010. Approved on 08/26/2010. This research was funded by Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG). We declare no conflicts of interest.
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This study aims to evaluate the nutritional status and physical activity in patients with SLE treated at the Rheumatology Department, *Hospital das Clínicas, Universidade Federal de Minas Gerais* (HC/UFMG) and analyze the main characteristics associated with nutritional disorders.

PATIENTS AND METHODS

Patients

This is a cross-sectional clinical study conducted at the Rheumatology Department, HC/ UFMG, from February 2008 to May 2009. Female patients with SLE diagnosis, according to classification criteria of 1982 (revised 1997) by the American College of Rheumatology (ACR),[7,8] aged between 18 and 60 years and who agreed to sign an informed consent were included. Exclusion criteria were pregnancy, severe hepatic dysfunction not associated with SLE, patients on dialysis, unable to stay upright or in supine position to perform nutritional assessment, and disease duration less than one year.

Among the 400 subjects treated at the Rheumatology Department in the same study period, 170 patients were selected for the study. The sample was selected for convenience, and the patients were invited to participate in the study on the routine visit day, according to the order of service attendance.

The sample size calculation was performed with an estimated 2% error; 95% confidence interval; and 30% expected prevalence of obesity in SLE patients.[9]

METHODS

Sociodemographic data and clinical characteristics

A questionnaire containing socioeconomic data, clinical and laboratory changes, defined according to the classification criteria of SLE/ACR,[7,8] and treatment was applied. Presence of systemic hypertension (SH) (SBP ≥ 140 mmHg or DBP ≥ 90 mmHg in at least two occasions, or use of antihypertensive drugs),[10] *diabetes mellitus* (DM) (fasting glucose ≥ 126 mg/dL on at least two occasions, or oral hypoglycemic agents, or insulin),[11] and ovarian failure (last spontaneous menstruation for more than a year, or use of hormone replacement therapy [HRT], or menstrual irregularity, or amenorrhea for less than one year, and serum FSH > 20 mUI/mL)[12] was considered.

Disease activity and damage index

Disease activity was measured by Systemic Lupus Erythematosus Disease score Index 2000 (SLEDAI-2K)[13] and cumulative irreversible damage by Systemic Lupus International Collaborating Clinics/ACR Damage Index (SLICC-ACR/DI).[14]

Physical activity

The International Physical Activity Questionnaire (IPAQ), short version, already translated into Portuguese and validated for the Brazilian population[15,16] was used to determine the level of physical activity. The questionnaire was individually applied by the main investigator, and consisted of questions about the frequency (days per week) and time (minutes per day) spent on walks and performing activities involving moderate and intense physical effort in four domains (work, commuting to work, household duties, leisure). We use the consensus proposed by the Laboratory Center for the Study of Physical Fitness of São Caetano do Sul (CELAFISCS)[17] for habitual physical activity categorization, considering three categories:

- *Active*: ≥ 20 minutes/session of vigorous activity ≥ 3 days/week, and/or ≥ 30 minutes per session of moderate activity, or walking ≥ 5 days/week, and/or ≥ 150 minutes/week of any of the activities combined (vigorous + moderate + walking);
- *Irregularly active*: < 150 and > 10 minutes/week of any of the activities combined (vigorous + moderate + walking);
- *Sedentary*: ≤ 10 minutes/week of any of the activities combined (vigorous + moderate + walking).

Nutritional status

Nutritional status was determined by subjective global assessment (SGA) and anthropometric measurements (body mass index). SGA was performed by interview and physical examination according to standard protocol; witch consisted of questions about weight changes and dietary habits, gastrointestinal symptoms, changes in functional capacity, disease metabolic demands, and patients' physical evaluation (presence of edema and loss of subcutaneous fat).

Weight loss less than 5% in six months was considered mild, between 5% and 10% moderate, and greater than 10% severe.[18] The patient was then classified as nourished, moderately malnourished or with suspected or severe malnutrition. Weight and height were measured with a mechanical platform scale (Welmy®), and the attained results placed in a formula for body mass index (BMI) calculation.

Statistical analysis

Database was assembled in the program EpiData® version 3.1 (EpiData Association, Odense, Denmark), and the software Statistical Package for Social Sciences (SPSS®) version 16.0 (SPSS Inc., Chicago, IL USA.) was used for statistical analysis.

Categorical variables were described as proportions and continuous variables as mean and standard deviation (SD) when distribution was normal, or median and interquartile range (IQR) when distribution was not normal.

To perform the analysis, patients were divided into three groups: eutrophic, overweight, and obese. For continuous variables, Student t-test was used when there was evidence of normality, and nonparametric Mann-Whitney test when the variable did not show evidence of normal distribution. Chi-square or Fisher's exact test was used, when appropriate, to test categorical variables.

The variables with significant differences between groups in univariate analysis were analyzed to identify in which groups the statistical difference was found. We used standardized residual analysis for categorical variables, post hoc analysis with Least Significant Difference (LSD) correction for normal continuous variables, and Mann Whitney test with Bonferroni correction for continuous non-normal. For all analysis, a significance level of 5% ($P < 0.05$) was considered.

The project was approved by the Ethics Committee of UFMG and the *Diretoria de Ensino, Pesquisa e Extensão do HC/UFMG* (Board of Education, Research and Extension of HC/UFMG), and funded by *Fundação de Amparo à Pesquisa do Estado de Minas Gerais* (FAPEMIG) — (Research Support Foundation of Minas Gerais).

RESULTS

The sociodemographic characteristics of 170 patients included in the study are described in Table 1. Hematologic abnormalities, as a group, were the clinical and laboratory manifestations frequently observed in 150 (88.2%) patients; followed by mucocutaneous manifestations in 147 (86.5%), arthritis in 129 (75.9%), immune disorders in 127 (74.7%), serositis (pleuritis and pericarditis) in 46 (27.1 %), and neuropsychiatric disorders (psychosis and seizures) in 31 (18.2%). Assessment of 167 patients showed SLICC median (IQR) of 1.0 (0.0 to 2.0) and SLEDAI-2K of 0.0 (0.0 to 2.0). Ovarian function was evaluated in 161 patients and 59 (36.6%) had ovarian failure.

Table 1
Sociodemographic characteristics of 170 SLE patients

Variables	Median (SD) (years)
Age	39.1 (10.0)
Age at diagnosis	28.7 (9.4)
Disease duration	9.9 (6.2)
Education*	8.0 (5.0-11.0)
Individual monthly income	N (%)
No income	38 (22.4)
< 1 MW	53 (31.2)
≥ 1 MW e < 4 MW	77 (45.3)
≥ 4 MW	2 (1.2)
Marital status	N (%)
Single	55 (32.4)
Married	87 (51.2)
Divorced	22 (12.9)
Widowed	6 (3.5)

SLE: systemic lupus erythematosus; MW: minimum wage, *median (IQR).

Most patients (73%) were taking corticosteroids, antimalarials (61.7%), and some type of immunosuppressant (57.7%). The median (IQR) dose of corticosteroids was 5.0 mg (0.0 to 10.0) and mean (SD) cumulative dose, measured in 164 patients, was 35.8 g (26.1). Azathioprine was the immunosuppressant most used (27.1%); followed by cyclophosphamide (17.1%), and methotrexate (12.3%). Only six patients were taking thalidomide.

According to subjective global assessment (SGA), 91.8% of patients were classified as malnourished, 6.5% have suspected malnutrition or were moderately malnourished, and 1.8% severely malnourished. According to the World Health Organization classification criteria for BMI,[19] two patients (1.2%) were classified as grade I underweight (BMI 17.00 to 18.49 kg/m^2), 59 (34.7%) eutrophic (18.50 to 24.9 kg/m^2), 61 (35.9%) overweight (25.0 to 29.9 kg/m^2), 37 (21.8%) class I obesity (30.0 to 34.9 kg/m^2), seven (4.1%) grade II obesity (35.0 to 39.0 kg/m^2), and four (2.4%) morbid obesity (≥ 40.0 kg/m^2).

Patients classified as grade I underweight were excluded from the univariate analysis because the group was very small and would invalidate statistical analyses.

Univariate analysis of the remaining 168 patients studied included three groups divided into: eutrophic (BMI 18.5 to 24.49 kg/m^2), overweight (25-29.9 kg/m^2), and obese (≥ 30.0 kg/m^2). Comparison of sociodemographic, clinical, and laboratory characteristics and use of medications between groups is listed in Table 2.

Obese patients were older than those with overweight and eutrophic, with a mean (SD) age for each group of 43.44 (7.76), 41.52 (9.33), and 33.69 (9.59) years, respectively, ($P < 0.001$). Eutrophic patients had more years of education (11 years on average). Overweight and obese patients had higher rates of

Table 2
Sociodemographic, clinical, and laboratory characteristics and use of medication in 168 SLE patients according to BMI classification

Sociodemographic characteristics	Eutrophic (N = 59)	Overweight (N = 61)	Obese (N = 48)	P
Age (years)*	33.7 (9.6)	41.5 (9.3)	43.4 (7.8)	< 0.001[1]
Education (years)**	11.0 (7.0-11.0)	6.0 (4.0-11.0)	8.0 (4.0-11.0)	< 0.001[2]
Individual monthly income ≥ 1 MW < 1 MW	27.0 (45.8) 32.0 (54.2)	25.0 (41.0) 36.0 (59.0)	26.0 (54.2) 22.0 (45.9)	NS[3]
Clinical				
Disease duration*	9.2 (6.1)	10.8 (6.5)	9.9 (5.8)	NS[1]
Mucocutaneous	47.0 (79.7)	55.0 (90.2)	44.0 (91.7)	NS[3]
Arthritis	44.0 (74.6)	47.0 (77.0)	36.0 (75.0)	NS[3]
Serositis	19.0 (32.2)	16.0 (26.2)	10.0 (20.8)	NS[3]
Nephritis	37.0 (62.7)	35.0 (57.4)	29.0 (60.4)	NS[3]
Neuropsychiatric	8.0 (13.6)	12.0 (19.7)	11.0 (22.9)	NS[3]
Hematologic	52.0 (88.1)	57.0 (93.4)	41.0 (85.4)	NS[3]
SLEDAI-2K[a**]	0.0 (0.0-4.0)	0.5 (0.0-2.0)	1.0 (0.0-4.0)	NS[2]
SLICC**	0.0 (0.0-1.0)	1.0 (0.0-2.0)	1.0 (0.0-2.0)	0.034[2]
C3**	87.2 (73.1-112.8)	106.7 (88.2-125.0)	97.0 (59.1-126.0)	0.031[2]
C4**	15.2 (11.8-21.9)	19.8 (14.6-27.1)	16.2 (11.1-22.7)	0.036[2]
SAH	24.0 (40.7)	34.0 (55.7)	33.0 (68.8)	0.014[3]
DM	1.0 (1.7)	4.0 (6.6)	9.0 (18.8)	0.014[3]
Ovarian failure[b]	11.0 (18.6)	25.0 (41.0)	23.0 (47.9)	0.003[3]
Laboratory				
Hemoglobin (g/dL)**	12.8 (12.0-13.4)	12.9 (11.8-13.6)	13.2 (12.3-13.9)	NS[2]
Creatinine**	0.8 (0.7-0.92)	0.9 (0.75-1.00)	0.9 (0.79-0.93)	0.028[2]
Glucose (mg/dL)**	73.0 (68.0-81.0)	78.0 (70.5-89.0)	80.0 (73.0-98.0)	0.005[2]
Albumin[c**]	4.0 (3.8-4.5)	4.0 (3.9-4.5)	5.0 (3.9-4.3)	NS[2]
Total cholesterol ≥ 200 mg/dL[d]	18.0 (31.0)	21.0 (34.4)	16.0 (33.4)	NS[3]
LDL-c ≥ 130 mg/dL[d]	15.0 (25.4)	14.0 (23.0)	13.0 (27.1)	NS[3]
HDL-c < 40 mg/dL[d]	9.0 (15.3)	13.0 (21.3)	7.0 (14.6)	NS[3]
Triglycerides ≥ 150 mg/dL[d]	10.0 (17.0)	18.0 (29.5)	16.0 (33.4)	NS[3]
Drugs				
Immunosuppressive	35.0 (59.3)	33.0 (54.1)	29.0 (60.4)	NS[3]
Cyclophosphamide	10.0 (16.9)	13.0 (21.3)	5.0 (10.4)	NS[3]
Azathioprine	14.0 (23.7)	14.0 (23.0)	18.0 (37.5)	NS[3]
Methotrexate	11.0 (18.6)	3.0 (4.9)	7.0 (14.6)	NS[3]
Antimalarial	44.0 (74.6)	31.0 (50.8)	29.0 (60.4)	0.027[3]
Current corticosteroid dose**	5.0 (2.5-15.0)	5.0 (0.0-10.0)	5.0 (0.0-10.0)	NS[2]
Cumulative corticosteroid dose (g)[e*]	32.9 (27.4)	39.2 (26.1)	35.4 (24.5)	NS[1]
Simvastatin use	5.0 (8.5)	8.0 (13.1)	8.0 (16.7)	NS[3]

The results are presented as n(%) unless otherwise indicated.
*, Mean (SD); **, median (IQR); SLE: systemic lupus erythematosus; MW: minimum wage; SLEDAI-2K: Systemic Lupus Erythematosus Activity Index; SLICC: Systemic Lupus International Collaboration Clinics; C3: serum complement C3; C4: serum complement C4; SAH: systemic arterial hypertension; DM, *diabetes mellitus*; c-LDL: low density cholesterol; HDL-c: high density cholesterol;
1: Anova; 2: Kruskal Wallis test; 3: Person chi-square test;
[a]167 patients; [b]161 patients; [c]163 patients; [d]166 patients; [e]164 patients.

SLE damage (SLICC) than eutrophic patients. Serum concentration of C3 and C4 was higher among overweight patients; and the frequency of hypertension, diabetes and ovarian failure was higher among the obese. There was no statistical difference among the three groups concerning individual monthly income, SLE duration, clinical characteristics, disease activity, and number of patients with high cholesterol and triglycerides (Table 2). Regarding the use of medication, there was no statistically significant difference with antimalarial use, which was more frequent in patients with normal weight.

The assessment of physical activity showed that 100 patients (58.8%) were classified as insufficiently active,

39 (22.9%) sedentary or inactive, and 31 (18.2%) active. Distribution of active patients among those classified as eutrophic, overweight, and obese was not statistically different (P = NS).

Individuals with higher BMI had a higher average age. In post hoc analysis, it was observed difference between patients considered eutrophic and overweight and between eutrophic and obese patients (Table 3).

It was not possible to identify between which groups there was no statistical differences for SAH and antimalarial drugs, according to standardized residual analysis, considering a significance level of 0.05. Regarding DM and ovarian failure, statistical difference was observed between obese and nourished. Table 4 presents the results of multiple comparisons of continuous variables for BMI classification using Mann-Whitney test with Bonferroni correction.

Table 3
Post hoc analysis of the continuous variable age with LSD test

Variables		P
Eutrophic	Overweight	< 0.001
	Obese	< 0.001
Overweight	Eutrophic	< 0.001
	Obese	NS
Obese	Eutrophic	< 0.001
	Overweight	NS

P: P value.

Table 4
Results of continuous variable multiple comparisons for BMI classification, using Bonferroni correction in Mann-Whitney test

Variables	Eutrophic x Overweight P	Eutrophic x Obese P	Overweight x Obese P
Education	< 0.001*	0.003*	NS
C_3	0.006*	NS	0.001*
C_4	NS	NS	NS
Creatinine	0.016	NS	NS
Glucose	NS	0.002*	NS
SLICC	NS	0.008*	NS

P: P value; C3 and C4: serum complement; SLICC: Systemic Lupus International Collaboration Clinics; *: statistical significance according to Bonferroni correction (P < 0.017).

DISCUSSION

In this study, the frequency of malnutrition was 1.2%, which is lower than stated by the Household Budget Survey (HBS) conducted by *Instituto Brasileiro de Geografia e Estatística (IBGE)* — (Brazilian Institute of Geography and Statistics). In this research, 5% of malnutrition was seen among healthy women over 20 years of age.[20] Prevalence of social malnutrition in individuals with SLE is rarely described in literature. In the Brazilian study by Caetano *et al*. of 22 children and adolescents with SLE, malnutrition was present in 4.5%.[21] However, other studies have shown that adult patients with SLE may have deficiencies of micronutrients, such as retinol, beta carotene, and vitamin D, which were not object of this research.[22,23]

In our study, 109 (64.2%) patients were identified as overweight. Research has shown the occurrence of this nutritional disorder in general population and LES patients.[6,24,25,26] However, the relationship between obesity, sociodemographic and clinical characteristics and use of medication, as well as physical activity in individuals with LES has not been extensively studied.

Analysis of 172 SLE patients (95.9% women) performed at the same service of *Hospital das Clínicas*, UFMG, in 2005, identified 20.9% of obesity, according to IMC classification.[24] This frequency was lower than that found in our study (28.3%), suggesting an increase in the number of patients with BMI ≥ 30 attended at this service. The prevalence of obesity in adult women in Brazil in 2006, 2007, and 2008 was 11.5%, 12.0%, and 13.8%, respectively; showing a relative increase of obese women.[26] In the U.S. population, between 2007 and 2008, obesity was found in 35.5% of adult women. Although this index is high, the increased rate of obesity prevalence in adult American women during the last 10 years does not seem to be increasing, as shown in comparative analysis by Flegal *et al*.,[27] different from what has happened in Brazil.[26]

Some studies comprising healthy individuals and lupus patients have shown an increase in BMI with increasing age.[26,28,29] In our study, the mean age was higher among patients with higher BMI, especially when eutrophic patients are compared with overweight and obese patients. Hormonal factors and reduction of daily energy expenditure are related to age and may contribute to weight gain in these patients.[30]

Loistein *et al*. evaluated the BMI and socioeconomic characteristics of 100 women with SLE, and found a positive association between low socioeconomic status and higher BMI.[31] In LUMINA study, a multicenter cohort study conducted with 365 SLE individuals, an inverse relationship was found between the number of years of education and BMI, similar to that observed in our study.[6] This relationship does not seems to be found only in individuals with SLE. A Brazilian study showed that healthy women with up to four years of education are twice as likely to be obese than those with 12 or more years of education.[28]

Persistence and severity of SLE inflammatory activity are important determinants of damage index, according to SLICC/ACR. In this study, we observed in univariate analysis higher values of damage index in overweight and obese patients than in eutrophic patients. Oeser *et al*. did not observe the same association in a sample of 100 patients. However, they observed high concentrations of inflammatory markers in patients with a higher mean BMI, suggesting greater inflammatory activity in patients with adipose tissue accumulation.[29]

Cross-sectional studies assessing metabolic syndrome frequency in SLE patients showed an independent correlation between presence of metabolic syndrome and worst damage index score.[24,32] Because these patients had higher inflammatory activity, they may have greater potential for developing end-organ damage, Therefore, more studies are needed to evaluate the possible association between cumulative damage caused by SLE and overweight.

According to Gabrielsson *et al*., healthy overweight or obese individuals often have high concentrations of C3 and C4 due to increased gene expression of these factors in visceral adipose tissue.[33] A study with 93 SLE patients compared the average concentration of CH50 from three distinct groups with BMI and showed that those with BMI greater than or equal to 30 had higher concentrations of CH50.[29] In our study, the median concentrations of C3 and C4 complements were higher in overweight patients. Decreased serum complement is one of the factors assessed in SLE activity index (SLEDAI-2K) and contributes to behavior management during treatment. Therefore, when analyzing complement fraction concentration or CH50 in SLE patients, BMI should be considered.

Estrogen receptors from hypothalamus act as switches controlling food intake, energy consumption, and body fat distribution. In ovarian failure there is a decrease of estrogen concentration and, consequently, body weight may increase. In our research, women with ovarian failure had higher BMI, which is in agreement with published data.[29,34,35]

Antimalarial drug is indicated for SLE treatment because it improves survival and reduces disease recurrence.[36,37] In our study, it was observed by univariate analysis that eutrophic patients where those using antimalarial drugs more frequently, compared with individuals with excess weight (overweight and obese). However, it was not possible to identify among which group there was a statistical difference, probably due to reduced number of patients in each group. Because multivariate analysis was not performed, other confounding factors that may affect this association were not excluded. We found no publications in literature describing the relationship between lupus patients' nutritional status and use of antimalarial drug; therefore, further studies are needed to better understand this observation.

Chaiamnuay *et al*. and Oeser *et al*., in cross-sectional studies involving SLE patients,[6,29] found no association between current and cumulative dose of corticosteroids versus BMI, similar to what was identified in this study. Mok *et al*. assessed the body composition of 29 SLE patients using high doses of corticosteroids for six months, and observed an increase in fat percentage, reduced lean body mass in trunk, and reduced bone mineral density with, however, no change in BMI.[35] Therefore, it is noteworthy that patients using corticosteroids may produce modification of body composition with no change in BMI.

Body composition of lupus patients may be improved by physical activity, as well as exercise tolerance, muscle strength, aerobic capacity, quality of life, depression, and fatigue without worsening disease inflammatory activity.[38,39] In the present study, we found that only 31 patients (18.2%) were considered sufficiently active according to IPAQ. Furthermore, there was no association between physical activity and BMI, possibly due to the very small number of active individuals compared with total sample. Another factor that may have contributed to this non-association was the lack of body composition assessment, which could better discriminate the percentage of fat mass and lean mass of these individuals and, thus, enable a more detailed analysis of the association between the level of physical activity and nutritional status of this population. Studies with more patients and with body composition analysis should be conducted.

This study presents some limitations. We performed a cross-sectional evaluation, in which the direction of causality could not be established. In addition, multivariate analysis was not performed. Therefore, the association of variables could not be independently assessed. Still, the findings observed should be considered, as they are an alert to the presence of factors related to obesity that may worsen lupus patient's prognosis. It is well known that both obesity and SLE, individually, are already associated with increased morbidity and mortality and, when combined, may trigger medical conditions poorly studied.

In conclusion, this study showed that overweight was the primary nutritional disorder seen in SLE patients; the frequency was high, being greater than that observed in general population. Excess weight was associated with patient's older age; low level of education; higher cumulative damage of disease, complement concentration, and frequency of hypertension and diabetes; presence of ovarian failure; and lower frequency of

antimalarial use. Therefore, assessment of nutritional status and physical activity is routinely paramount in these patients for early detection of these changes. The physician can and should intervene in order to improve patients treatment and quality of life.

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