REVISTA BRASILEIRA DE REUMATOLOGIA

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SOCIEDADE BRASILEIRA DE REUMATOLOGIA

Original article

Risk factors for cardiovascular disease in rheumatoid arthritis patients from Mato Grosso do Sul

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ARTICLE INFO

Article history:
Received 24 October 2013
Accepted 2 February 2015
Available online 3 September 2015

Keywords:
Rheumatoid arthritis
Autoantibodies
Comorbidities

ABSTRACT

Objective: To identify risk factors for cardiovascular disease in patients with Rheumatoid Arthritis (RA).

Material and methods: A descriptive cross-sectional study with 71 patients with established RA. The instruments used were: DAS-28, HAQ and SF-36, and the following parameters were determined: the erythrocyte sedimentation rate, capillary blood glucose; total cholesterol (TC) and its fractions, thyroid hormones, antinuclear antibodies (ANA), rheumatoid factor (RF) and antibodies against citrullinated proteins (ACPAs). Patients were classified into groups HAQ ≤ 1 (mild dysfunction) and HAQ > 1 (moderate and severe dysfunction) and, according to the HAQ scores, in groups treated with corticosteroids (CS) and without CS.

Results: 9 patients were male and 62 female with mean age and duration of disease of 53.45 ($\pm$10.7) and 9.9 ($\pm$8.6), respectively. RF was positive in 52 (76%), ACPAs in 54 (76.1%) and ANA in 12 (16.9%). Thirty-six patients (50.7%) had systemic hypertension, 9 (12.68%) diabetes mellitus, 16 (22.5%) hypothyroidism, 33 (46.5%) dyslipidemia and 8 (11.27%) were smokers. The results of TC > 240 were found in 53.8% for group HAQ > 1 (26) and in 24.4% for group HAQ ≤ 1 (45) ($p = 0.020$). These groups did not differ as to presence of comorbidities or drug treatment. Triglyceride levels >200 for the group with CS (42.4%) *versus* without CS (18.42%) were significant ($p = 0.025$).

Conclusion: An association of increased TC and triglycerides with results of HAQ ≤ 1 and with CS use was noted, reinforcing the importance of screening risk factors associated with cardiovascular disease in RA.

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http://dx.doi.org/10.1016/j.rbre.2015.07.012

Caracterização de pacientes com artrite reumatoide quanto a fatores de risco para doenças vasculares cardíacas no Mato Grosso do Sul

Palavras-chave:
Artrite reumatoide
Autoanticorpos
Comorbidades

RESUMO

Objetivo: Caracterizar pacientes com Artrite Reumatoide (AR) quanto à presença de fatores de risco para doenças cardiovasculares.

Material e métodos: Estudo transversal descritivo com 71 pacientes diagnosticados com AR definida. Foram utilizados os instrumentos: DAS-28, HAQ e SF-36 e determinados os parâmetros: velocidade de hemossedimentação, glicemia capilar; colesterol total (CT) e suas frações, hormônios tiroidianos, anticorpos antinúcleo (ANA), fator reumatoide (FR) e anticorpos contra proteínas citrulinadas (ACPAs). Os pacientes foram classificados em grupos HAQ ≤1 (disfunção leve) e HAQ >1 (disfunção moderada e grave) e, segundo os escores do HAQ, em grupo tratado com corticosteroides (CE) e sem CE.

Resultados: Proporção de 9 homens para 62 mulheres com idade e tempo médio de doença de 53,45 (± 10,7) e 9,9 (± 8,6), respectivamente. O FR foi positivo em 52 (76%), os ACPAs em 54 (76,1%) e ANA em 12 (16,9%). Trinta e seis pacientes (50,7%) apresentaram hipertensão arterial sistêmica, 9 (12,68%) *Diabetes mellitus*, 16 (22,5%) hipotireoidismo, 33 (46,5%) dislipidemia e 8 (11,27%) tabagismo. O grupo HAQ >1 (26) apresentou resultados de CT >240 (53,8%) e o grupo com HAQ ≤1 (45) (24,4%) (p = 0,020). Os grupos não diferiram quanto à presença de comorbidades ou tratamento farmacológico. Os níveis de triglicérides >200 (42,4%) entre os grupos em uso de CE e sem uso (18,42%) foi significativo (p = 0,025).

Conclusão: Houve associação do aumento CT e triglicerídeos com resultados de HAQ ≤1 e com uso de CE, reforçando a importância do rastreamento de fatores de risco associados às doenças cardiovasculares na AR.

Introduction

Rheumatoid Arthritis (RA) is a chronic, inflammatory, autoimmune disease, with unknown etiology, associated with progressive joint dysfunction, whose consequence for patients is functional limitation for their daily and professional activities. Furthermore, RA can lead to systemic complications and early mortality.[1]

The pharmacological research involving RA has changed considerably, and the current treatment recommends the introduction of an early and aggressive therapeutic action, guided by disease activity indexes. However, what has been observed is that some patients do not present effective results to available treatments.[2]

In addition, higher severity and early mortality from cardiovascular disease in these patients, when compared to the healthy population,[3] remains a challenge for physicians who are monitoring these patients.

Current published literature advocates the identification of subgroups of patients with different prognosis and therapeutic responses.[4] Thus, this study aimed to characterize patients diagnosed with RA in terms of risk factors for cardiovascular disease, identifying possible markers that show those patients with worse prognosis, treated or not treated with corticosteroids, such as: IgM class rheumatoid factor antibodies (RF), antibodies against citrullinated proteins (ACPAs), and antinuclear antibodies (ANA); presence of comorbidities: systemic hypertension (SH), diabetes mellitus (DM), hypo- or hyperthyroidism and dyslipidemias, and to correlate these markers with clinical activity of disease, functional status and quality of life.

Material and methods

This is a descriptive cross-sectional study that evaluated consecutive patients from July 2012 to February 2013, attended at the Rheumatoid Arthritis Outpatient Clinic, Department of Rheumatology, University Hospital (UH) of Universidade Federal de Grande Dourados (UFGD). The study included 71 patients of both genders previously diagnosed with RA, who met the 1987 American College of Rheumatology criteria for RA.[5] Patients who agreed to participate in this study signed an informed consent form. The project was approved by the Research Ethics Committee of UFGD, protocol number 14136013.0.0000.5160. Patients were clinically assessed by rheumatologists who calculated disease activity with the Disease Activity Score for 28 joints (DAS-28), using as laboratory parameter the erythrocyte sedimentation rate.[6]

Clinical evaluation included the body mass index (BMI) that was computed as weight divided by height squared. Individuals were weighed barefoot wearing light clothes t, using a scale and stadiometer (WELMY). Patients with a previous diagnosis and in use of antihypertensive medication, as well as those with an elevated blood pressure at the time of measurement were considered hypertensive. Later, the diagnosis of hypertension was confirmed during follow-up, according to Brazilian Society of Hypertension guidelines.[7] We considered as diabetic those patients being treated for the disease and

also those showing changes in blood glucose at the diagnosis, later confirmed according to Brazilian Society of Diabetes guidelines.[8]

In tests for plasma lipids, we considered as dyslipidemic those patients in use of medication for this condition and/or with dietary measures recommended for the disease, as well as those who had their results for dyslipidemia confirmed during follow-up in at least one more laboratory analysis.

Functional status was assessed using the Health Assessment Questionnaire (HAQ) (simplified) validated and translated into Portuguese.[9] The parameters were correlated with HAQ results associated with use or not use of corticosteroids; and patients were classified according to the score in groups HAQ ≤ 1 (mild dysfunction) and HAQ > 1 (moderate and severe dysfunction), considering the reduced number of patients with severe dysfunction in this study.

Quality of life was analyzed by the instrument The Short Form (36) Health Survey (SF-36) validated and translated into Portuguese.[10]

We collected 15 mL of each patient's blood on clinical evaluation day, for performing an erythrocyte sedimentation rate (ESR) test by Westergreen method (mm/1st hour) in the same day of collection.

For determining blood glucose, a drop of blood was deposited in the blood glucose test strip meter (G-TECH model Free1).

To test anti-nuclear antibodies (ANA), HEp-2 cells were used (EUROIMMUN, Germany) and analyzed by indirect immunofluorescence according to the protocol suggested by the manufacturer.

The enzyme-linked immunosorbent assay (ELISA) was used to identify the presence of anti-cyclic citrullinated peptide (Anti-CCP-3) (INOVA), rheumatoid factor (RF) (ORGENTEC), and anti-mutated citrullinated vimentin (Anti-MCV) (ORGENTEC). Triiodothyronine (T3 and free T3) and thyroxine (T4 and free T4) hormones were measured by electrochemiluminescence with the use of a Cobas E411 (ROCHE LTD.) analyzer and using kits supplied by the manufacturer.

Total cholesterol and its fractions were performed in a Cobas Integra E400 plus (ROCHE Ltd.) analyzer, also using kits supplied by the manufacturer.

The presence of rheumatoid factor was evaluated by latex agglutination, but also by Waaler–Rose test, for IgM isotypes, according to manufacturer's protocols.

Statistical analysis was performed with SPSS (Statistical Package for Social Sciences) version 20.0. To characterize the sample, we used descriptive statistics; and data are presented as mean (X) ± standard deviation (SD) for quantitative variables, and absolute (*f*) and relative (%) frequencies for qualitative variables. Statistical inference was used for the remaining analyzes. To compare continuous variables with normal distribution, Student's *t*-test was performed; otherwise Mann Whitney test was used. Categorical variables were compared using Fisher exact test. The significance level was set at $p < 0.05$.

Results

Seventy-one patients of both genders, previously diagnosed with RA, were evaluated; of these, 62 (87.32%) were female and 9 (12.68%) were male, an approximate ratio of 7:1. The mean age of patients was 53.4 (±10.8) years. The mean disease duration was 9.9 (±8.4) years, with a median of 7 years, ranging from 1 to 42 years. The mean for disease onset was 43.5 (±11.5) years, with a median of 43 years, ranging from 17 to 73 years old (more demographics data in Table 1).

Table 1 – Demographics and clinical data of patients with RA.

Demographics and clinical data	
Gender, *n* (%)	62♂–9♀
Age, (±SD)	53.4 (±10.8)
Disease duration, (±SD)	9.9 (±8.4)
Disease onset, (±SD)	43.5 (±11.5)
Smoking, *n* (%)	18 (23.35)
BMI, X (±SD)	27.63 (±4.61)
Hypertension, *n* (%)	36 (50.07)
Diabetes, *n* (%)	9 (12.68)
Hypothyroidism, *n* (%)	16 (22.57)
RF positive, *n* (%)	54 (76.1)
ACPA positive, *n* (%)	52 (73.2)
ANA positive, *n* (%)	12 (16.9)
DAS-28, (±SD)	0.84 (1.53)
HAQ, (±SD)	1.36 (0.90)
SF-36, (±SD)	53.45 (10.75)
TC > 240, *n* (%)	24 (33.80)
LDL > 160, *n* (%)	15 (21.12)
Triglycerides > 200, *n* (%)	21 (29.57)
HDL > 35, *n* (%)	8 (11.26)
TC/HDL, *n* (%)	31 (43.66)

TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

Ten (14.08%) of 71 patients were smokers, while eight (11.27%) of 71 were former smokers, totaling 18/71 (25.35%) patients that had had contact with tobacco. Sera from 15 of these patients were positive for anti-citrullinated protein antibodies (ACPAs). Of the three negative sera for these antibodies, one came from a former smoker and two from current smokers.

The mean BMI was 27.63 ± 4.61. About 1/3 of patients (30.98%) had an adequate weight/height relation in the period of data collection. The others were distributed into overweight (28/71, 40%) or obese (21/71, 29.58%) category.

As for systemic hypertension (SH), 35/71 (49.29%) patients had this disease diagnosed and were using antihypertensive medication. During the screening tests, 32 (44.44%) patients presented with elevated blood pressure. Of these 32 patients, two had no previous diagnosis of hypertension. SH was confirmed in another patient during the implementation period of the study, totaling 36/71 (50.7%) patients with a diagnosis of hypertension.

As for glycemic profile, 7/71 (9.86%) patients had a previous diagnosis of diabetes mellitus (DM). However, 22 (30.98%) patients exhibited elevated fasting glucose in screening tests performed on the day of blood collection. Of these, only two had a previous diagnosis of DM. Later, three of the other 20 patients had a confirmed diagnosis of DM, totaling 12.68% (9/71) patients with this disease. Of these 22 patients, five were corticosteroid users, including 2 patients with a previous diagnosis of DM.

Table 2 – Medications used in patients with RA (*n* = 71).

Medications	*n* (%)
Non-steroidal anti-inflammatory drugs (NSAIDs)	27 (38.03)
Corticosteroids	33 (46.47)
Chloroquine/sulfasalazine	29 (40.84)
MTX	32 (45.07)
Leflunomide	27 (38.03)
MTX + Leflunomide	1 (1.40)
Anti-TNF	34 (47.89)
MTX/Leflunomide + anti-TNF	32 (45.07)
MTX/Leflunomide + anti-TNF or leflunomide + chloroquine/sulfasalazine	10 (14.84)

MTX, metotrexate; Anti-TNF, anti-tumor necrosis factor.

As for thyroid disease, 13/71 (18.30%) were on thyroid hormone replacement therapy, while 2/71 (2.81%) were being treated for hyperthyroidism. However, according to results of laboratory tests, four patients showed serological changes consistent with hypothyroidism and only one of these patients had been already in treatment, totaling 16/71 (22.53%) patients with hypothyroidism.

Seropositivity was characterized as follows: 37/71 (52.1%) patients were positive for rheumatoid factor (RF) by ELISA, and 9/71 (12.67%) were positive only for RF. Using the latex method, positivity was of only 28/71 (39.4%) and 17 of these patients were also positive by Waaler–Rose method. The positivity for RF was of 54/71 (76.1%), and those patients who had their results confirmed by the same method, or who were positive by two different methods, were regarded as positive cases.

As to anti-cyclic Citrullinated Peptide (Anti-CCP) by Elisa, 36/71 (50.70%) patients were positive, and 3/71 (4.22%) were positive only for anti-CCP. As to anti-mutated citrullinated vimentin (anti-MCV) by Elisa, 48/71 (67.60%) patients were positive, with 11/71 (15.49%) positive only for anti-MCV. Thus, 52/71 (73.2%) were positive for anti-citrullinated protein antibodies (ACPAs).

Positivity for RF and ACPA was diagnosed in 34/71 (47.9%) of sera.

Serological analysis for antinuclear antibodies (ANA) resulted in 12/71 (16.90%) positive results, and no patient was positive exclusively for these antibodies.

Regarding the positivity association for autoantibodies, 7/71 (9.9%) patients were positive for all analyzed antibodies. The same number was negative for RF and ACPAs.

As for prescription drugs for treatment of RA, Table 2 shows that 27/71 (38.03%) and 33/71 (46.47%) patients had nonsteroidal anti-inflammatory drugs and corticosteroids prescribed, respectively. Leflunomide was taken by 27/71 (38.03%) and methotrexate (MTX) by 32/71 (45.07%); and in 1/71 (1.40%) both medications were used. 34/71 (47.89) patients had prescription for biologicals (anti-TNF blockers), and 32/34 (94.11%) were associated with leflunomide or MTX.

Regarding dyslipidemia, 6/71 (8.45%) of patients had been previously diagnosed, and four were taking medication (two treated with simvastatin, one with atorvastatin and one with benzafibrate) and two other were in dietary therapy. Only 1/6 (16.7%) had normal lipid levels. However, according to screening tests, 33/71 (46.5%) had some type of dyslipidemia (Table 3), confirmed in at least one previous test, or subsequently during follow-up.

Table 3 – Association of clinical and laboratory parameters with HAQ.

	HAQ ≤ 1 (45)	HAQ > 1 (26)	*p*
Age, (±SD)	52.91 ± 10.62	54.38 ± 11.31	0.47
Disease duration, (±SD)	9.76 ± 7.32	10.31 ± 10.29	0.64
Disease onset, (±SD)	43.16 ± 11.43	44.08 ± 11.72	0.73
Smoking (*f*)	13 (28.88)	5 (19.23)	0.37
Body mass index, (±SD)	27.22 ± 4.42	28.11 ± 5.84	0.39
Systemic hypertension (*f*)	22 (48.88)	14 (53.84)	0.63
Diabetes mellitus (*f*)	6 (13.33)	3 (11.53)	1.00
Hypothyroidism (*f*)	13 (28.88)	4 (15.38)	0.084
Corticosteroids (*f*)	17 (37.77)	16 (61.53)	0.083
Metotrexate (*f*)	21 (29.57)	11 (24.44)	0.91
Leflunomide (*f*)	17 (23.94)	10 (22.22)	0.84
Anti-TNF (*f*)	19 (42.22)	14 (53.84)	0.46
Total cholesterol > 240 (*f*)	11 (24.44)	14 (53.84)	0.020
HDL < 35 (*f*)	7 (15.55)	1 (3.84)	0.24
LDL > 160 (*f*)	6 (13.33)	9 (34.61)	0.067
Triglycerides > 200 (*f*)	10 (22.22)	10 (38.46)	0.17
DAS-28 (±SD)	4.48 ± 1.28	5.13 ± 1.42	0.024
SF-36 P (±SD)	39.2 ± 12.92	27.12 ± 12.71	<0.0001
SF-36 M (±SD)	48.69 ± 9.35	34.19 ± 10.50	<0.0001
SF-36 T (±SD)	42.55 ± 8.13	29.35 ± 7.37	<0.0001

anti-TNF, anti-tumor necrosis factor; HDL, high density lipoprotein; LDL, low density lipoprotein; DAS-28, diseases activity score in 28 joints; SF-36 P, short-form health survey (physical domain); SF-36 M, short-form health survey (mental domain); SF-36 T, short-form health survey (total score).

As for disease activity through DAS-28, 4/71 (5.63%) patients were found in a state of remission, 5/71 (7.04%) with mild disease activity, 29/71 (40.84%) with moderate disease activity and 33/71 (46.47%) patients with severe disease activity.

SF-36 was the questionnaire used to evaluate the quality of life of patients with RA. The results indicated that the mean values were 34.68 ± 13.05 for Physical Health Dimension and 43.33 ± 15.28 for Mental Health Dimension, with a mean total SF-36 score of 36.68 ± 13.35.

Regarding physical disability of patients (HAQ), the results were 45/71 (63.38%) with a mild level of disability, 21/71 (29.57%) for a moderate condition and 5/71 (7.04%) for a severe condition. Statistical significance was noted for total cholesterol ($p = 0.020$), DAS-28 ($p = 0.024$) and for physical domain ($p < 0.0001$), mental domain ($p < 0.0001$) and total ($p < 0$, 0001) SF-36, as shown in Table 3. Of these patients, 37.78% (17/54) were taking CS in HAQ > 1 group and 61.54% (16/26) in HAQ ≤ 1 group ($p = 0.084$).

Table 4 shows the results of the analysis of cholesterol levels and its fractions in patients not taking CS in relation to HAQ > 1.

Statistically significant differences were found in TC > 240 ($p = 0.019$), HAQ ≤ 1 (5/28 = 21.42%), HAQ > 1 (6/10 = 60%) and SF-36 ($p = 0.013$) variables. The results of these biochemical parameters for patients in treatment with CS were not presented, because the treatment with CS is associated with a higher prevalence of risk factors.

When the results of lipid levels for CS users *versus* not users were compared, we did not find statistical differences in total cholesterol ($p = 0.20$) or SF-36 ($p = 0.094$); but for triglyceride

Table 4 – Analysis of cholesterol level and its fractions, disease activity index and quality of life in patients without use of CS in relation to HAQ > 1.

	HAQ ≤ 1 (28)	HAQ > 1 (10)	p
Total cholesterol > 240 (f)	5 (17.86)	6 (60)	0.019
HDL < 35 (f)	5 (17.86)	0 (0)	0.96
LDL > 160 (f)	3 (10.71)	4 (40)	0.60
Triglycerides > 200 (f)	5 (17.86)	2 (20)	0.61
DAS-28 (±SD)	4.5 ± 1.48	5.29 ± 0.89	0.089
SF-36 (±SD)	43.39 ± 12.10	31.30 ± 13.81	0.013

HDL, high-density lipoprotein; LDL, low-density lipoprotein; DAS-28, disease activity score in 28 joints; SF-36, short-form health survey.

levels a statistical difference ($p = 0.025$) was noted, according to Table 5.

The higher prevalence of cardiovascular diseases, particularly coronary artery disease, is well established in RA. Regarding CS and dyslipidemias, admittedly CS treatment increase total cholesterol, LDL and triglyceride levels and reduce HDL; thus, in this study these variables were not analyzed in relation to the results of HAQ ≤ 1.0.

Discussion

Rheumatoid arthritis is a disease that affects both genders in a proportion of 3–4 women for every man.[11] In this study the gender ratio in our sample was 7:1, corroborating the results found by Boechat et al.,[12] who studied 350 non-indigenous patients in the state of Amazonas, and also emphasizes findings of European and American studies, who obtained a ratio of about 7:1.[13–15]

Presence of antibodies such as RF and anti-CCP are important prognostic markers for response to treatment. In this study it was observed that 12/71 (16.90%) patients were positive for ANA, a result that differs from a Japanese study, whose result was 39/104 (37.5%) ($p = 0.038$)[16] and from a European study that showed positivity for ANA in 16/36 (44%) patients ($p = 0.0045$).[17] Research of anti-MCV antibodies was positive in 48/71 (66.66%) patients–a result similar to the Norwegian study by Besada et al., who found positive cases in 57/75 (76%),[18] and to the European study by Sghiri et al., whose result was 74.1% of positivity for anti-MCV in 170 sera from RA patients.[19] As for anti-CCP, our results were similar to those found in studies in other Brazilian areas, for instance, Teixeira et al. and Silva et al., with results of 24/38 (63.15%) and 68/100 (68%), respectively.[20,21] Our results were higher than those of a Colombian study, which showed 53/165 (33.1%) of reactive sera for anti-CCP ($p = 0.0084$).[22] The results of RF positivity have been controversial in Brazilian studies, ranging from 49.3 to 91%.[20,23,24] In a Korean study the incidence of reactive samples was 209/302 (69.2%),[25] a significantly higher positivity than that found in this study: 37/71 (52.11%) ($p = 0.0077$).

RA is a disease associated with lower life expectancy, when compared to the general population.[26] This fact is explained by the increase in prevalence as well as by a greater progression of cardiovascular diseases in these patients.[27] Genetic factors and classic risk factors associated with inflammation for these diseases contribute to an increase and greater severity of cardiovascular diseases in RA.[28]

Current and former smoking are considered one of the few risk factors associated with RA with confirmation in epidemiological studies.[29,30] This risk factor was identified in 1/4 of the patients in this study, which indicates a higher proportion of smokers than that found by Mikuls et al.,[31] who identified smoking in 52/605 (8.52%) patients with RA ($p < 0.0001$).

As for BMI, results of a German study with 551 patients, which identified values of 26.7 ± 5.1, corroborate our results of 27.6 ± 4.94. Our results were similar to those of Myasoedova et al.,[32] who reported that 3/4 of patients with RA have BMI above the normal index.[33] In addition, the proportion of overweight and obese patients, as determined from BMI according to the criteria for the general population, may be underestimated, because it has been shown that, for a given amount of body fat, patients with RA have 2 pounds/m^2 less than normal controls. Therefore, BMI for these patients should be defined as 23 and 28 kg/m^2 for overweight and obesity, respectively.[34]

In relation to systemic hypertension, the results showed that 36/71 (50.70%) of RA patients had this disease, reinforcing the findings of Cunha et al., who reported systemic hypertension in 95/228 (41.66%) patients with RA.[35] Our results were similar to those found by Ferraz-Amaro et al., showing systemic hypertension in 36/101 (35.74%) of RA patients.[36]

As for thyroid disease, 16/71 (22.53%) of patients had hypothyroidism and 2/71 (2.82%) hyperthyroidism, results similar to those of Chan et al., who found 12/69 (17.4%) cases of hypothyroidism and 4/69 (5.8%) of hyperthyroidism in patients with RA.[37]

In a study by Park et al., diabetes was diagnosed in 27/302 (8.9%) patients,[25] while in the study by Giuseppe et al., the disease was diagnosed in 4/132 (3%) of patients.[38] In the present study, the diagnosis was confirmed in 9/71 (12.67%) patients, a finding similar to that in the first study, and significantly higher than in the second study ($p = 0.0035$), respectively.

The analyzed sample showed a higher prevalence of diabetic patients, 9/71 (12.67%), when compared to the study conducted in the state of Amazonas, Brazil, 4/142 (3%) ($p = 0.0030$).[12]

Table 5 – Comparison of lipid levels in patients with or without use of CS.

	With CS (n = 33)	Without CS (n = 38)	p
Total cholesterol > 240	12 (36.36)	12 (31.58)	0.20
HDL < 35	3 (9.09)	5 (13.16)	0.44
LDL > 160	7 (21.21)	8 (21.05)	0.61
Triglycerides > 200	14 (42.42)	7 (18.42)	0.025
HAQ	0.98 ± 0.72	0.73 ± 0.61	0.12
DAS-28	4.69 ± 1.14	4.74 ± 1.18	0.85
SF-36	34.85 ± 12.9	40.21 ± 13.41	0.094

HDL, high-density lipoprotein; LDL, low-density lipoprotein; HAQ, health assessment questionnaire; DAS-28, disease activity score in 28 joints; SF-36, short-form health survey.

As for quality of life, the results indicate that few patients achieved remission or mild disease activity, 4 and 5%, respectively, although only 5% of patients had HAQ associated with severe functional status.

The decreased quality of life in patients with less physical dysfunction was assessed by SF-36, admittedly a reliable and valid tool and able to measure important clinical features in RA patients. Its use has also been advocated during clinical follow-up of these patients, as SF-36 evaluates different areas, not just the physical domain.[39] In this study, besides the physical domain, the mental domain was also decreased in patients with high HAQ score. Mental health is an important topic, because depression is associated with poor treatment adherence and with increased morbidity and mortality.[40]

The presence of dyslipidemias in 36/71 (50.70%) patients showed a significantly higher frequency than that found by Park et al., where 58/302 (19.2%) of a Korean population with RA were dyslipidemic patients.[25]

Lipid disorders are one of the most important risk factors for cardiovascular disease and studies have shown that they are more prevalent in RA patients than in the general population.[41] In untreated patients with RA, Park et al. demonstrated that these patients present reduction in HDL cholesterol levels and that this change is related to C-reactive protein levels.[42] In untreated patients, total cholesterol and LDL reductions also occur.[41] Some authors also described that a decrease in inflammation coincides with an increase in serum levels of lipids.[13,43,44]

Despite the limitations of this study, of a cross-sectional nature, we found that total cholesterol levels are associated with higher physical dysfunction. The use of corticosteroids was more prevalent among patients with increased levels of triglycerides, but not among patients with high total cholesterol levels. Thus, Ferraz-Amaro et al. demonstrated decrease in the activity of cholesterol ester transfer protein (CETP) in RA patients who are undergoing treatment with CS, but showed no difference in lipid levels in patients who were undergoing treatment with *versus* without corticosteroids.[36] The function of this protein is complex and its relation to cardiovascular risk is not well understood.

The use of DMARDs can also induce increases in total cholesterol and in HDL and triglyceride fractions, especially methotrexate, leading to changes called "normalization" according to Saiki.[45] Regarding anti-TNF blockers, the published literature have shown increased rates of total cholesterol and also of all its fractions; however, Choy and Sattar reported that a meta-analysis is not possible, because the studies differ on the type of intervention and follow-up time.[41]

In this study, it was found that patients in RA treatment had lipid levels considered as a risk factor for cardiovascular disease.[46] However, there was no correlation between these levels and disease activity, as assessed by DAS-28, similar to Navarro Millán et al.'s results,[13] who also found no difference between patients treated with methotrexate monotherapy *versus* those treated with a combination therapy with anti-TNF blockers. However, the authors reported a significant increase in total cholesterol and in all its fractions in those patients assessed.

The patients in this study had been referred from the Basic Health Unit. It was observed that, before the treatment by a specialist, little was added to the diagnosis of systemic hypertension, diabetes and thyroid disease. These findings corroborate data from Desai et al., who showed that general practitioners were the professionals who treated risk factors for cardiovascular disease, not rheumatologists.[47] However, general practitioners identified more risk factors in the general population and in diabetics than in the RA population.

In this sense, the diagnosis of dyslipidemia has been underestimated, probably because RA association with cardiovascular risk and lipid abnormalities are not yet established in the literature and, therefore, this feature was not disseminated among general practitioners.[13] The recent published data shows evidence that dyslipidemias are present years before the onset of clinical symptoms of RA.[48] Park et al. reported that polymorphisms associated with LDL cholesterol (rs688 and rs4420638) are also related to RA susceptibility, severity and progression.[49]

Therefore we emphasize that the screening of several risk factors for cardiovascular disease indicates the need for pharmacological treatment and lifestyle changes, in order to achieve a better control of RA, so that these patients may improve their quality of life and decrease the risk for systemic complications.

Conclusion

From this study it was concluded that: (1) notwithstanding the therapeutic arsenal available to these patients, only a few have achieved remission or a state of mild disease activity; on the other hand, 5% were evolving to severe dysfunction. (2) A high prevalence of underdiagnosed dyslipidemia was observed in these patients. (3) Treatment with corticosteroids is associated with a higher prevalence of patients with hypertriglyceridemia. (4) Higher levels of total cholesterol are associated with more physical disability. (5) The quality of life is reduced in patients with major physical disability; however, this factor is not associated with the use, or not, of corticosteroids. (6) Follow-up of patients with RA is a complex task, due to the high risk for developing cardiovascular disease, thus requiring control not only of the disease activity, but also of traditional risk factors.

For future studies, it is suggested the establishment of more homogeneous groups to determine the influence of the disease and drug treatments used with respect to the presence of risk factors for cardiovascular disease in patients with RA.

Funding

Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), through Health Sciences Post-Graduation, Health Sciences School (FCS), UFGD.

Conflict of interests

The authors declare no conflict of interests.

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