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Original article

Demographic and clinical features of patients with rheumatoid arthritis in Piauí, Brazil – evaluation of 98 patients☆

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ABSTRACT

Introduction: Brazilian epidemiological studies on rheumatoid arthritis are scarce, mainly in the northeast; thus many data currently available originate from the international literature.
Objectives: To describe demographic, clinical and serological characteristics of patients with rheumatoid arthritis (RA) followed-up by the same physician, in state of Piauí, Brazil.
Patients and methods: Data were collected between August 2010 and March 2013, in three health services of Piauí that provided health care in Rheumatology: a university-affiliated hospital, a public outpatient clinic and a private clinic.
Results: The numbers represent mean ± SD or percentage: 47.5 ± 11.03 years-old non-Caucasian woman, non-smoker (59.2%), low educational level, mean disease duration of 7.7 years ± 7.6, and major extra-articular manifestations were rheumatoid nodules (19.4%) and *sicca* syndrome (46.9%).
Conclusion: Features of rheumatoid arthritis obtained in this study are similar to those found in some national and international studies, but we observed higher female preponderance and illiteracy rate, in addition to a moderately severe erosive disease on average, with frequent *sicca* and other extra-articular manifestations.

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Características demográficas e clínicas de pacientes com artrite reumatoide no Piauí, Brasil – avaliação de 98 pacientes

Palavras-chave:
Artrite reumatoide
Epidemiologia
Nordeste brasileiro

R E S U M O

Introdução: São escassos os estudos epidemiológicos brasileiros sobre artrite reumatoide, sobretudo no Nordeste; assim, muitos dados atualmente disponíveis têm sua origem na literatura internacional.
Objetivos: Descrever as características demográficas, clínicas e sorológicas de pacientes com artrite reumatoide (AR) seguidos pelo mesmo médico no Estado do Piauí, Brasil.
Pacientes e métodos: Os dados foram coletados entre agosto de 2010 e março de 2013, em três serviços de saúde do Piauí com atendimento em reumatologia: um hospital universitário, uma clínica ambulatorial pública e uma clínica privada.
Resultados: Os números representam média ± DP ou percentual: 98 pacientes com 47.5 ± 11.03 anos de idade; não-brancos; predominância de mulheres; não fumantes (59.2%); baixo nível educacional; duração média da doença de 7.7 ± 7.6 anos; e as principais manifestações extra-articulares foram nódulos reumatoides (19.4%) e síndrome *sicca* (46.9%).
Conclusão: As características da artrite reumatoide obtidas neste estudo são similares àquelas encontradas em alguns estudos nacionais e internacionais, mas observamos maior preponderância de mulheres, um nível de analfabetismo maior e, na média, uma doença erosiva moderadamente grave com presença frequente de *sicca* e de outras manifestações extra-articulares.

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease manifesting itself in various extra-articular signs and progressive articular damage.[1] Clinical onset of this disease may be variable; it generally begins with symmetrical involvement of the small joints, pain, morning stiffness, and limitation of movement for more than 1 hour. Although the metacarpophalangeal (MCP) joints, the proximal interphalangeal (PIP) joints, the wrists, the metatarsophalangeal (MTP) joints and the knee joints are the most frequently involved joints, RA may also involve other ones.

Rheumatoid arthritis affects approximately 0.5%-1% of the population, and, although not directly life-threatening, it causes a reduction in the patient's quality of life and severe economic damages to society.[2] It is more prevalent in women (female/man ratio of 2:1), and its incidence increases with age.[3]

The incidence, severity, and outcome of the disease show variability between different ethnical-origin groups.[4–6] This variability is related to the socioeconomic level and the level of development of countries, as well as genetic and/or environmental factors. In underdeveloped countries, patients with RA are known to have a severe clinical course and a poor prognosis due to limited access to the physician, specialist, and/or drugs. Studies on RA demonstrated that different genetic and/or environmental factors could impact the disease in different ethnical groups. These studies suggest that RA patients, having different ethnic origin, may exhibit different manifestations and outcomes, which enables development of different targeted treatment modalities. In our country, there is limited data about incidence, clinical course, extra-articular symptoms, and outcomes of RA,[7,8] and there are few studies in Northeastern Brazil and no study in Piauí. To meet this necessity, the present study was designed to describe the demographic, clinical, and serological characteristics of patients with RA followed-up by a physician.

Material and methods

Ninety-eight patients (87 women, 11 men) with RA diagnosed according to the ACR classification criteria ACR,[9] between August 2010 and March 2013, were included in the study. The sample was chosen for convenience. Diagnosis, treatment and monitoring of all patients were performed by the same physician in a university-affiliated hospital, a public outpatient clinic and a private clinic. Clinical history and physical examination of all patients were evaluated by a single investigator. The following parameters were recorded in all patients during the first examination: demographic data, educational level, clinical findings, use of DMARDs, presence of extra-articular symptoms, presence of concomitant comorbid diseases, laboratory parameters (including complete blood count, rheumatoid factor [RF]) and radiological changes. Lung involvement was determined by high-resolution CT (HRCT). Erosive changes were detected on radiography by a rheumatologist and a radiologist together, and they used Sharp score.

Extra-articular symptoms were described as follows: (1) *sicca* symptoms were the presence of dry mouth and eyes, (2) pulmonary involvement was the presence of fibrosis, pleuritis, interstitial changes, and/or rheumatoid nodule, (3) vasculitis was the presence of mononeuritis multiplex, peripheral gangrene, deep ulcer, or histological evidence. Diagnosis of the rheumatoid nodules was

Table 1 – Demographics and disease characteristics of the 98 patients with rheumatoid arthritis in Piauí, Brazil.

M:F	11:87
Mean age (years)	47.5 ± 11.03
Age group (years)	
20-29	6 (6.12%)
30-39	16 (16.32%)
40-49	34 (34.69%)
50-59	32 (32.66%)
60-83	10 (10.21%)
Mean disease duration (years)	7.7 ± 7.6
Smoking	
Smoking (present)	14 (14.3%)
Smoking (past)	25 (25.5%)
Non-smoking	58 (59.2%)
Medication for RA	
Prednisone	30 (30.6%)
Methotrexate	39 (39.8%)
Antimalarial	30 (30.6%)
Leflunomid	14 (14.3%)
Anti-TNF-α	03 (3.06%)

described as the presence of subcutaneous nodules >5 mm on extensor surfaces of extremities. Normal ranges of laboratory parameters were described as follows: anemia (hemoglobin < 11 g/dL), RF (normal <5 by nephelometry method).

Informed consent was obtained. This study was approved by the Committee on Ethics and Research of Universidade Federal do Piauí and has not conflict of interest.

Statistical analysis

Data were inserted into Excel 2007 (Microsoft) sheets and managed to provide the epidemiological profile through description and simple mathematical calculations, such as percentage and arithmetic mean. Data was presented as mean, SD and range for continuous variable, and percentages for discrete variables.

Results

Of the 98 patients followed-up by the rheumatology clinic and enrolled in the study, 87 were female, and 11 were male. The mean age of patients was 47.5 years (ranging from 22 to 83 years), and mean duration of the disease was 7.7 years. Thirty-one (31.6%) live in urban area and 67 (68.4%) in rural. Thirty-five (35.7%) patients had respiratory symptoms, 14.3% were current smokers, 59.2% were non-smokers, and 25.5% had smoked in past (Table 1).

Data on education level are show in Table 2.

Six patients (6.1%) had diabetes mellitus. During the 3-year follow-up, two patients died (one due to cerebral hemorrhage, the other due to heart attack).

Thirty patients (30.6%) were taking oral steroids; 39 (39.8%) were taking methotrexate (MTX); 30, hydroxychloroquine (30.6%); 14, (14.3%) leflunomid; and 3 anti-TNF-α (3.06%). Drug history was difficult to analyze, since the patients had taken a mean of 4 ± 1.3 second-line drugs for RA at the time of assessment.

Table 2 – Educational level of patients in Piauí, Brazil.

Classification	n	%
Illiteracy/incomplete elementary education	49	50.0%
Complete elementary education	13	13.3%
Incomplete secondary education	8	8.2%
Complete secondary education	15	15.2%
Complete higher education	13	13.3%

The *sicca* symptom (46.9%) was the most common extra-articular involvement, and all patients fullfilled Sjögren's syndrome classification criteria, followed by pulmonary involvement (39.8%), vasculitis (5.1%), and the Raynaud's phenomenon (3.1%). Nineteen patients had rheumatoid nodules (19.4%).

Thirty-one patients (31.6%) were detected to have anemia, 86.7% of the patients had positive RF, and 61 patients (62.2%) had erosion (Table 3).

Sixty-three patients had no respiratory symptoms. Among those with respiratory symptoms, cough (n = 21%-21.4%) was the most common, followed by dyspnea (n = 19%-19.4%), and chest pain (n = 12%-12.2%) (Table 3). Findings on HRCT were rheumatoid nodule (12%), fibrosis (32%), pleuritis (5%), and interstitial changes (1%).

Discussion

Epidemiological studies on RA are mostly limited to developed countries, and the incidence of RA in developing countries is unknown.

The study investigated demographic, clinical, and serological data of Brazilian patients with RA born in Piauí and followed-up by a rheumatologist. It was observed that patients with RA have a similar clinical course and

Table 3 – Clinical and serological features of patients with RA in Piauí, Brazil.

Main Features	Frequency (%)
Sicca symptoms	46.9
Rheumatoid nodules	19.4
Respiratory symptoms	
Dyspnea	19.4
Chest pain	12.2
Sputum production	10.2
Dry cough	11.2
HRCT	39.8
Lung involvement	
Vasculitis	5.1
Raynaud phenomenon	3.1
Anemia	31.6
Erosion	62.2
Rheumatoid factor	86.7

HRCT, High resolution CT.

Table 4 – Comparison of the main features between patients with RA in different studies.

Features	Badsha *et al.*[17] n = 100	Al-Salem *et al.*[16] n = 100	Calgüneri *et al.*[13] n = 526	Kobak S[1] n = 165	Present study n = 98
Female	87	89	453	125	87
Age (years)	42.2	39.1	48	52.5	47.5
RF positivity (%)	73	62	68.3	90.3	86.7
Erosions (%)	55.2	42	N	55.8	62.2
Sicca s/m (%)	28	14	11.4	40.6	46.9
R. nodules (%)	4	9	18.1	3.6	19.4
Lung involvement (%)	n	7	4.8	6.6	39.8

RF, rheumatoid factor; *Sicca* s/m, *sicca* syndrome/manifestations; R. nodules, rheumatoid nodules.

prognosis compared with the patients from other ethnic origin (Table 4).

It is notable that the ratio female:male ratio of 8:1 in this study was much higher than that reported in Western populations, but closer to some studies in developing countries. This female preponderance may be more related to access clinical or demographic factors or hormones. Table 5

The level of education of patients is consistent with the results found in Piauí population, and with the literature showing that the disease is the most prevalent one in people with low education levels.

The pattern of involvement observed in our patients was similar to Caucasian and American patterns reported previously. The incidence of erosion was reported to be higher in our patients relative to Greek RA patients (29%).[10]

The most common extra-articular pattern, *sicca* complex (46.9%), was similar to that observed in the Greek RA patients.[10] The study carried out in São Paulo has reported concomitance of that syndrome in 28% of the sample.[11] It is the most common ocular manifestation. Secondary Sjögren's syndrome is diagnosed according to the European criteria modified by the American-European Consensus Group for Sjögren's syndrome in 2002.[12]

Sicca manifestations were observed in ophthalmologic exam.

In Turkey, Calgüneri *et al.* evaluated extra-articular findings of 526 RA patients followed-up by a single center.[13] The most common extra-articular findings, including rheumatoid nodules (18.1%) and *sicca* symptoms (11.4%), were similar to those observed in some Mediterranean countries. In another trial conducted in Turkey,[14] in that 562 patients with RA were evaluaed, eye involvement (8%) and subcutaneous nodules (7.5%) were reported as the most common extra-articular findings, and the rate of comorbid diseases was reported as 35.8%.

Positive RF rates detected in our patients were similar to the results reported in the literature. Positive RF rates are 65%, 62%, and 60% in English, Malaysian and Kuwaiti patients, respectively.[15,16]

The institution has resources for determining anti-CCP, as well as the number of swollen joints and DAS-28, and a measure of synthesis deficiency cannot be included in the study.

Interestingly, the incidence of rheumatoid nodules was only 19.4% in our patients, which is quite different from the rate reported in the literature (30%). Calagüneri *et al.* reported a similar incidence of rheumatoid nodules demonstrated in Turkish patients (18.1%).[13] Our values do not coincide with that reported in the study carried out in São Paulo (29%).[11]

Type 2 diabetes mellitus was described in 6.1% of the patients, a value similar to that of the general population (7.6%; range, 5%-10%).[18]

Pulmonary manifestations were 39.8%, and that frequency was greater than that reported in other studies (10%-20%). A study carried out in São Paulo has reported a 15% frequency. Pulmonary manifestations are believed to appear within the first five years after the diagnosis of RA. Although pulmonary infections and/or pulmonary toxicity due to drugs

Table 5 – Comparison of the main features between patients with RA in different studies in Brazil.

Features	David *et al.*[7] n = 38	Louzada Junior *et al.*[11] n = 1381	Mota *et al.*[21] n = 65	Vaz *et al.*[22] n = 19	Present study n = 98
Female	32	1184	56	15	87
Age (years)			46	50	47.5
RF positivity (%)	68.4	71		68	86.7
Erosions (%)	18.4				62.2
Sicca s/m (%)		28	13.8		46.9
R. nodules (%)	13.2	29	15.4	21	19.4
Lung involvement (%)		15	3.07		39.8

are frequent complications, pulmonary disease directly associated with RA is more common. Although cardiovascular diseases are responsible for most deaths related to RA, pulmonary complications are common and directly responsible for 10%-20% of the deaths directly attributed to RA.[19]

All patients have received at least one of the DMARDs. The first choice of therapy was methotrexate (39.8%) and antimalarial (30.6%). However, only 14.3% of our patients have received leflunomide, because the general health insurance system in our country restricts usage of the drug. Only three patients (3.06%) having persistent active disease refractory to conventional DMARD treatment have received anti-TNF-α therapy. This rate is 40%, and 54% for USA and France, respectively.[20]

Less than 40% of patients are receiving methotrexate. The inadequate treatment could have influenced the outcome of the disease.

A variety of clinical presentations of RA observed in different populations and reported in the literature may be associated with genetic and environmental factors. In our country, there is a problematic situation resulting from the small number of rheumatology centers available. Usually, patients present to clinics at a late stage of the disease. The socioeconomic level, noncompliance with treatment, and the failure to attend the control visits are the factors that have an impact on morbidity and mortality.

RA is a heterogeneous disease. It may exhibit different clinical presentation in different populations. Since our trial includes data from RA patients followed-up by a single center, it cannot be representative of the whole population of Piauí. To demonstrate the role of genetic and environmental factors, multicenter studies with a large patient sample that includes the immune system and the HLA typing are required.

Conclusion

We can conclude that, in comparison with patients from Western countries and other Brazilian studies, our RA patients were characterized by a similar age at onset, but a higher female preponderance, a higher illiteracy rate, and, on average, a moderately severe erosive disease with frequent *sicca* and other extra-articular manifestations.

Conflicts of interest

The authors declare no conflicts of interest.

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