

# The Spectrum of Rheumatoid Arthritis in Patients Attending Rheumatology Clinic in Nizwa Hospital-Oman

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## Abstract:

**Objectives:** To determine the spectrum and expression of rheumatoid arthritis (RA) in patients attending the rheumatology clinic in Nizwa hospital, Oman.

**Methods:** Subjects and methods: 66 patients fulfilling the American College of Rheumatology (ACR) criteria for the diagnosis of RA were included in the study. The patients were either attending for the first time or were already diagnosed and attending for follow up. The demographic, clinical, laboratory and radiological findings are reported.

**Results:** Of the 66 patients studied, 16 were males and 50 were females. The mean age of patients at onset was  $44.5 \pm 14.5$  years, and the females were younger than males at presentation. 38 (57.57%) were seropositive and two (3.03%) only had rheumatoid nodules. The majority of the patients were considered as class 1 or 2 according to the ACR functional classification. The commonest extra-articular manifestation was anaemia (27.27%) followed by keratoconjunctivitis sicca (24.42%). The upper limb joints were affected more than the lower limbs and the most commonly involved joint was the wrist (81%) followed by the metacarpophalangeal (MCP) (66.66%) joints, the knee

(57.57%), ankle (45.45%), elbow (42.42%), shoulder (42.42%), and the proximal interphalangeal (PIP) (36.36%) joints. The main associated diseases were hypertension (21%), ischemic heart disease (13.63%) and diabetes mellitus (9.03%). Systemic features were predominantly morning stiffness (84.5%) and fatigue (45.45%). Reported deaths were due to sepsis and cardiac arrhythmia. Thus 63 (95.45%) of the patients were on conventional disease modifying antirheumatic drugs.

**Conclusions:** Demographic characteristics were similar to those reported by others, the seropositivity rate and nodular form of the disease was less in the studied patients and the disease seemed milder than that reported in western countries.

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## Introduction

Rheumatoid arthritis (RA) is a common disease with a worldwide prevalence of approximately 1% with an annual incidence of about 3/10,000 adults. It is two to three times more common in women.<sup>1</sup> Its prevalence varies between different countries. The recorded prevalence earlier in Oman was 8.4 per 1000 adults, while a higher prevalence has been reported from the other surrounding countries.<sup>2,3,4</sup> Earlier studies also indicate that the disease has a milder course in the surrounding countries in comparison to western patients.<sup>3,5</sup> This observation was also reported from Africa and the blacks.<sup>6,7</sup>

RA is a chronic systemic inflammatory disease. It is mainly characterized by persistent synovitis of diarthrodial joints, often symmetrical in distribution, resulting in pain, stiffness, and loss of function.<sup>8</sup> It is a potentially crippling disease which shortens survival, but most importantly, it significantly compromises the quality of life in most affected patients. Although the primary target of this disease is the synovium, most patients have systemic features such as fatigue.<sup>9</sup>

RA is characterized by chronic synovial inflammation and

pannus formation involving small and large joints. However, numerous extra-articular manifestations occur, particularly in male patients who are anti-nuclear antibody (ANA) and rheumatoid factor (RF) positive.<sup>10</sup>

The onset of disease can occur at any age but peak incidence occurs within the fourth and fifth decades of life.<sup>11</sup>

The aim of this study is to determine the spectrum of RA in patients attending the rheumatology clinic in Nizwa Hospital, Oman.

## Methods

This is a descriptive retrospective study involving all newly diagnosed patients or patients already diagnosed and were attending for follow up in the rheumatology clinic in the newly constructed Nizwa Regional hospital since its inception in August 1998 till December 2008. All the studied patients who fulfilled the American College of Rheumatology (ACR) criteria for the diagnosis of RA.<sup>12</sup> The study was approved by the regional research and research ethics committee.

Of the 66 patients, 12 patients were inpatient and 54 were outpatients. They were all attending the rheumatology clinic after

being referred either by other sub-regional hospitals and health centres in the region or from other departments in the hospital. The catchments area (population) of the hospital is approximately 380,000.

The assessment of functional status of the patients was made according to the ACR 1991 revised criteria for the classification of global functional status in rheumatoid arthritis.<sup>13</sup>

The duration of the disease before presentation for the first time, the age of the patient at onset of the disease and duration of the disease were all considered in this study, as well as the demographic characteristics, clinical manifestations including extra-articular features, past or current associated medical illness, laboratory investigations, chest X-ray and joints radiological abnormalities and medications including disease slow acting modifying drugs given were all recorded.

Standard radiographs of the hands, feet, other affected joints and the chest were reviewed by the treating clinician (FAT), and by the available radiologist in the hospital if required. Pulmonary functions and high resolution computed tomography scan (HRCT) of the lungs was also taken for patients found to have suggestive clinical features, pulmonary function tests and/or features suggestive of interstitial lung disease on plain chest X-ray films.

The biochemical profile including renal function tests, liver function tests, and lipid profile were measured using Hitachi 912 (automated analyzer Boehringer Mannheim). While for

hematological parameters measurement, Cell-Dyn 3500 Abott was used. Hepatitis C and B screening was done performed Axsym Abott system (Microparticle Enzyme Immunoassay, test for the rheumatoid factor by Latex slide agglutination technique (Avitex RF) and ANA by indirect immunofluorescence technique.

## Results

This study included 66 patients included, 16 (24.24%) males (M) and 50 (75.75%) females (F), with a male to female ratio of 3.187:1. 12 (18.18%) patients were inpatients while 54(81.81%) were outpatients. The mean age at onset was  $44.5 \pm 14.5$  years, with a higher range in males ( $50.2 \pm 16.6$  years) compared to females ( $41.06 \pm 16.99$  years). One female was divorced, 10 females were single and the remaining male and female patients were married.

The average duration of the disease at onset was  $9.21 \pm 7.00$  months while the average for disease duration on inclusion in the study was 2.5 years. The onset of the disease was acute in 22 (33.33%) patients and insidious in 44 (66.66%) patients. Moreover, 30 (57.57%) patients were positive for rheumatoid factor (RA F).

Table 1 shows the demographic data and functional classification of the patients in comparison with other studies. 3.03% of the patients had rheumatoid nodules which is double that of the Nigerian but less than that of the South African patients. The majority of the studied patients were considered to be class 1 or 2 according to the ACR functional classification which indicates a milder form of the disease.

**Table 1:** Demographic data and Classification of Patients

Parameter	Nizwa, Oman (N=66)	South Africa <sup>14</sup> (N=52)	Nigeria <sup>7</sup> (N= 71)	Scotland <sup>15</sup> (N=282)
Mean age (years)	44.5	44.6	Mode 21-30	50.5
Mean duration of RA (years)	2.5	8.2	1.7	7.0
Female : Male ratio	3.187:1	3.7:1	0.9:1	2.7:1
Rheumatoid nodules %	3.03	25	1.4	NR†
Functional classification %	ACR Criteria <sup>13</sup>	ARA Criteria <sup>16</sup>		
1	34.83	23	6	0
2	45.45	48	28	35
3	12.12	23	44	43
4	7.57	6	22	23

†NR: not reported \*ACR: American College of Rheumatology ‡ARA: American Rheumatism Association

Arthritis, morning stiffness, extra-articular features and fatigue were among the predominant clinical manifestations. (Table 2). The most common extra-articular manifestation was anaemia (27.27%) followed by keratoconjunctivitis sicca which was found in 24.42% of the study patients, (Table 5). Skin

atrophy was observed in 37.87% of the patients and this may be disease, treatment or age related phenomenon or a combination of all factors. (Table 3). The main associated co-morbidities were hypertension (21%), ischemic heart disease (IHD) (13.63%) and diabetes mellitus (9.03%) as shown in Table 4.

**Table 2:** Clinical data of Patients

Parameter	Number of cases (%)
Arthritis	66(100%)
Duration of morning stiffness (mean) minutes (55.5 ± 32.66)	56(84.5%)
Rheumatoid nodules	2(3.03%)
Raynauds phenomenon	3(4.54%)
Hair fall	6(9.09%)
Fever	4(6.06%)
Fatigue	30(45.45%)
Family history of rheumatoid arthritis	1(1.5%)
Extra-articular features	52(78.78%)

**Table 3:** Details of the extra-articular features of Patients

Parameter	Number(%) of cases	
<b>Extra-articular features</b>	52(78.78%)	
Cutaneous	Erythematous rash	2(3.03%)
	Skin atrophy	25(37.87%)
	Pleural effusion	1(1.5%)
Respiratory	Interstitial lung disease	2(3.03%)
	Pleurisy	1(1.5%)
Cardiovascular	Pericardial effusion	1(1.5%)
	Heart block	1(1.5%)
Gastrointestinal	Hepatitis	6(9.09%)
	Symptomatic gastritis (proved endoscopically)	2(3.03%)
	Symptomatic peptic ulcer (proved endoscopically)	2(3.03%)
	Symptomatic oesophagitis (proved endoscopically)	2(1.5%)
Nervous system	Symptomatic entrapment neuropathy (proved by NC)†	3(4.54%)
	Symptomatic peripheral neuropathy (proved by NC study)†	2(3.03%)
	Small muscles wasting	8(12.12%)
Ophthalmological	Keratoconjunctivitis	16(24.42%)
	Scleritis	1(1.5%)
Lymph node enlargement	Axillary & cervical lymph node (2 patients), In one due to non-Hodgkin's lymphoma, while it was reactive in the second one. A third patient had a reactive axillary lymphadenopathy histopathologically	3(4.54%)

†NC study: Nerve conduction study

The upper limb joints were affected more than the lower limbs, the most commonly involved joint was the wrist (81%) followed by the Metacarpo-phalangeal (MCP) joints (66.66%), the knee (57.57%), ankle (45.45%), elbow (42.42%), shoulder (42.42%), and the proximal interphalangeal (PIP) joints (36.36%). While the

predominant joint deformity was the ulnar deviation. (Figs. 1,2)

Table 5 elaborates in details the laboratory abnormalities found in this study. Acute reactant parameters were raised in more than 90% of the patients, and 27.27% were anaemic.

The radiological abnormalities of the joints were predominantly osteopenia seen in 74.24% of the patients, followed by decreased

joint space, osteoarthritic changes and erosive changes was seen in 16.66% of the patients. (Table 6)

**Table 4:** Associated diseases present along with Rheumatoid Arthritis

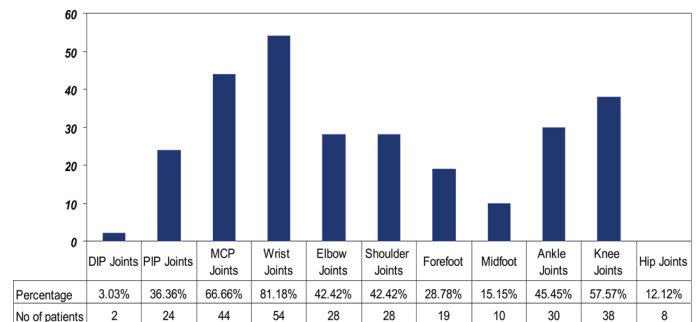
Associated diseases	Number (%) of cases
Hypertension	14(21.21%)
Ischemic heart disease	9(13.63%)
Diabetes mellitus	6(9.09%)
Bronchial asthma	2(3.03%)
Non Hodgkin Lymphoma	1(1.5%)
COPD	1(1.5%)
Rheumatic heart disease	2(3.03%)
Dementia	1(1.5%)
Parkinsonism	1(1.5%)
Dilated cardiomyopathy	1(1.5%)
Hypothyroism	2(3.03%)
Spondylolesthesis	1(1.5%)
Pulmonary stenosis	1(1.5%)

On the other hand, 95.45% (63) of the patients were on conventional slow acting anti rheumatic drug/ drugs, 48 (72.7%) were on methotrexate in addition to other medications, and 35(53%) of the patients were on steroids. Five deaths were reported among the among the studied patients, the cause for death was attributed to septicemia and septic shock in three patients and cardiac arrhythmia in two patients.

**Table 5:** laboratory abnormalities found in the study

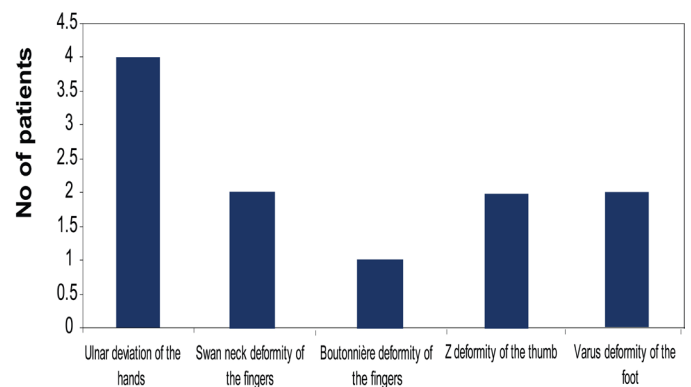
Test	Result	Number of Patients	Percent
Erythrocyte sedimentation rate (mm/1 <sup>st</sup> hour)	78.16±32.92	63	95.45
C-reactive protein (mg/dl)	80.59±70.4	61	92.42
Low haemoglobin (Hgb <11 gm/dl)	9.4±1.023	18	27.27
Red blood cells parameters			
	Hypochromic microcytic	12	18.18
	Normochromic normocytic	4	6.06
	Hypochromic normocytic	2	3.03
(High white cells count (>11,000 K/ul)	Mean = 12.72	5	7.57
(High platelets count (> 400 K/ul)	472±65	11	16.66
(Raised liver enzymes (IU/l	† AST > 32 , ALT > 31	6	9.09
(Low albumin (gm/dl	3.4 >	5	7.57
(Raised globulin (gm/dl	4.1 <	30	45.45
(Raised fasting cholesterol (mmol/l	6.46±0.71	15	22.72
(Rheumatoid factor (positive or negative	Positive	38	57.57
(Anti-nuclear antibody (positive/negative	Positive	12	18.18
(HBsAg (positive or negative	Positive	2	3.03

† AST: Aspartate transaminase, ALT: Alanine transaminase



DIP: distal interphalangeal joints, PIP: proximal interphalangeal joints, MCP: metacarpo-phalangeal joints

**Figure 1:** Frequency of upper and lower limb joints involvement



**Figure 2:** Frequency of joints deformities observed

**Table 6:** Radiological abnormalities in our Patients

Radiological examination	Result	No. of Patients	Percent
Chest X-ray	Cardiomegally	6	90.9
	Interstitial lung disease	2	3.03
	Emphysema	1	1.5
HRCT chest scan	Interstitial lung disease	2	3.03
	Osteopenia	49	74.24
	Soft tissue shadow	6	9.09
Joints X ray	Decreased joint space	17	25.75
	Erosions	11	16.66
	Osteoarthritic changes	16	24.24

### Discussion

In this study, the mean age of patients at onset was  $44.5 \pm 14.5$  years, with a higher range in men ( $50.2 \pm 16.6$  years) compared to females ( $41.06 \pm 16.99$  years). Females were more commonly affected (F:M=3.187:1). This is consistent with other studies.<sup>3,5,14,15</sup> The onset of the disease was insidious in 66.66% of patients which is also similar to what has been previously reported in other studies.<sup>17</sup> The average duration of the disease at onset was  $9.21 \pm 7.00$  months while the average for disease duration on inclusion in the study was 2.5 years.

38 (57.57%) patients were positive for rheumatoid factor (RA F), this is slightly low in comparison with previous results.<sup>7,17</sup> However, these results are consistent with the findings of Kuwaiti patients.<sup>5</sup> The prevalence of positive ANA is similar to what has been reported earlier.<sup>14,18</sup> The presence of rheumatoid nodules (3.03%) was fairly low in this study, but is comparable to that found in Nigeria,<sup>7</sup> but lower than in other studies.<sup>14,17</sup> This finding and the low rate of seropositivity for rheumatoid factor may explain the milder nature of the disease in the studied patients.

The results of the ARA/ACR functional classification in different countries including the studied patients as well as studies from Scotland and Africa are not comparable because all the patients in the Scotland series, 70% from the Nigerian study, 13% from a South African study, and 18.18% of patients from this study were inpatient at the time of inclusion.<sup>7,14,15</sup>

The main associated diseases were hypertension (21%), Ischemic heart disease (IHD) (13.63%) and diabetes mellitus (9.03%) which is more or less similar to what has been reported nationally in the Omani population. Morning stiffness ( $55.5 \pm 25.6$  minutes) was recorded in 56 patients and fatigue in 30 patients.

The commonest extra-articular manifestation was skin atrophy seen in 25 patients (37.87%) and this may be disease, treatment or age related phenomenon or a combination of all factors, followed

by anaemia which was observed in 27.27% of the patients. Keratoconjunctivitis sicca was seen in 24.42% of the patients and its prevalence was similar to observations among Caucasians and surrounding countries.<sup>19,5</sup> Wasting of the small muscle of the hands was seen in 12.12% of the patients. It was also observed that the fasting cholesterol was raised in (22.72%) of our patients and taking into consideration the increased risk for coronary artery disease in patients with RA there is a need to develop identification and intervention strategies for acute coronary syndrome (ACS) specific to this high risk group of patients.<sup>20</sup>

The upper limb joints were affected more than the lower limbs, hence the most commonly involved joint was the wrist followed by the MCP joints, the knee, ankle, elbow, shoulder, and the PIP joints, other joints were involved less frequently, these findings are consistent with those of other studies.<sup>4,5,14</sup>

The deformities were mild and infrequently encountered, ulnar deviation was seen in four patients (6.06%), swan neck deformity of the fingers and varus deformity of the feet were seen observed in two patients (3.03%), while Boutonnière deformity was seen in only one patient (1.5%).

The chest X-ray showed cardiomegally in six patients, five patients had an underlying ischemic heart disease and one was hypertensive. On the other hand, two patients had interstitial lung disease which was confirmed by HRCT chest and pulmonary function tests and one patient had emphysematous changes.

The commonest radiological abnormality in the joints form standard plain radiograph was juxta-articular osteopenia which was observed in 72.24% of patients followed by decrease in joints space which was seen in 25.75% and osteoarthritis which was observed in 24.24% of the patients. Erosions were seen in only 16.66% of the patients. Joints affected with erosive changes were wrists, metacarpophalangeal joints, knees, ankles, and metatarsophalangeal joints in decreasing frequency. This pattern is consistent with earlier findings, however the radiological damage was lower in frequency and severity in the current study.<sup>21,22</sup>

Five deaths were reported among the studied patients, three were as a result of septic shock, two were on immune suppression, and the third one was elderly and bedridden with bed sores but was not on immunosuppression. Cardiac arrhythmia was the cause in the other two cases. This is consistent with an earlier report among the common etiologies of death in patients with rheumatoid arthritis.<sup>23</sup>

## Conclusion

Overall, a national study of patients with rheumatoid arthritis will definitely elaborate more on the spectrum of rheumatoid disease, the size of the problem in different regions, its articular pattern, extra-articular manifestations, laboratory and radiological manifestations, outcome and complications. This may help to have a national plan toward a comprehensive uniform management to help the patients.

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