

# Clinical Features of Rheumatoid Arthritis in a Sub-Saharan African Population: A 308 Study Cases in Senegal

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## ABSTRACT

**Background:** Rheumatoid arthritis, formerly rare in sub-Saharan Africa, is becoming increasingly reported. The objective study determines the epidemiological, clinical and biological features of rheumatoid arthritis at diagnosis.

**Methods:** A cross-sectional study conducted at the Rheumatology outpatient department of Aristide Le Dantec Teaching Hospital of Dakar in Senegal.

**Results:** Three hundred eight patients with rheumatoid arthritis according, to American College of Rheumatology 1987 criteria, were included: 273 women and 35 men (ratio of 7:8). Median age was 41 years (Q1: 31; Q3: 53 years); predominant age group was 30-40 years. Ninety-three percent resided in urban areas and 7% in rural areas. Family history of chronic inflammatory arthritis was reported by 35.1% of patients. Thirty-nine percent of patients initially consulted a traditional healer. On admission, the median Disease Activity Score 28 was 6.5 (Q1: 5.5; Q3: 7.3). Rheumatoid arthritis was very active in 81.1% and a positive factor in 84% of patients. Cyclic citrullinated peptide antibodies assessed in 116 patients; 95 reported positive (81.9%). Of 169 patients, at least one extra-articular manifestation was presented; the most common, anemia and sicca syndrome.

**Conclusion:** Rheumatoid arthritis was characterized by an important delay in diagnosis, a polyarticular presentation, and a high positivity of immunological markers. Extra-articular manifestations included mainly anemia and sicca syndrome. Early management and a better understanding of rheumatoid arthritis in sub-Saharan Africa are required.

## Keywords

Rheumatoid arthritis, Sub-Saharan African, Senegal

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## INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease of connective tissue, affecting mostly the synovial joints. It can be associated with disabling joint destruction and extra-articular manifestations that can affect survival rates. Rheumatoid arthritis (RA) affects all populations, although its prevalence varies from one region to another: it is estimated at approximately 0.5 to 1% in developed countries<sup>[1]</sup>. Formerly speculated as rare in sub-Saharan Africa region due to the lack of specialist, thus recently, becoming increasingly described<sup>[2,3]</sup>. Though, RA was previously presumed relatively benign in sub-Saharan Africa<sup>[2]</sup>; however, recent data suggest a greater severity. In fact, in a previous study on 100 patients, it showed RA activity very high at the time of diagnosis in Senegal<sup>[4]</sup>.

The objective of this study was to determine the epidemiological, clinical, biological and immunological features of RA at diagnosis in a sub-Saharan African population.

## PATIENTS AND METHODS

This cross-sectional cohort study was conducted at the rheumatology outpatient department of the Medical Clinic I at the Aristide Le Dantec Teaching Hospital of Dakar in Senegal from October 2005 to December 2012, in accordance with the ethical principles of the Declaration of Helsinki. The Ethics Committee of the Medical School of Dakar approved the study.

All patients with RA according to the criteria from the American College of Rheumatology (modified in 1987) were included in the study<sup>[5]</sup>. For all patients, the following data were collected: Demographic data (age, gender, place of residence), clinical data (diagnostic delay, articular index, synovial index, number of awakenings at night, duration of morning stiffness, and extra-articular signs) and biological parameters (blood count, erythrocyte

sedimentation rate, C reactive protein, rheumatoid factors, cyclic citrullinated peptide antibodies). Disease activity at diagnosis was assessed with the Disease Activity Score 28 (DAS28, Web Version 4.05) test.

The lab norms for variables was: ESR < 15 mm in first hour; CRP < 6 mg/l; hemoglobin [12-16 g/dl]; RF < 8 IU; anti-CCP < 25 IU.

Quantitative variables were reported as median (1<sup>st</sup> quartile, 3<sup>rd</sup> quartile) because of their non-normal distribution, and reported as a percentage for each modality of the variable.

## RESULTS

A total of 308 patients with RA were included in the study. The main baseline characteristics of the patients are summarized in Table 1. The population included 273 women and 35 men, for a sex ratio of 7:8 (W/M). The median age was 41 years (Q1: 31; Q3: 53 years). The predominant age group was 30-40 years, followed by 40-50 years (Fig. 1).

Ninety-three percent of the study population resided in urban areas, and 7% resided in rural areas. A family history of chronic inflammatory arthritis was reported by 35.1% of patients. Thirty-nine percent of patients had initially consulted a traditional healer. On admission, the median DAS28 was 6.5 (Q1: 5.5; Q3: 7.3). RA was very active in 81.1% of patients, with a DAS28 > 5.1. The median number of painful joints was 27, with a median duration of morning stiffness of two hours. Hand deformities were generally symmetrical (Fig. 2).

Rheumatoid factors were positive in 84% of patients. Cyclic citrullinated peptide antibodies were assessed in 116 patients and were positive in 95 of them (81.9%). The extra-articular manifestations reported are summarized in Table 2. A total of 169 patients presented at least one extra-

**TABLE 1.**  
Main characteristics of the RA study population at diagnosis.

Variables at the Time of Diagnosis	Percentage (%) or Median (Q1;Q3)
Evolution of symptoms before diagnosis (in months)	46 (24;90)
Number of painful articulations	27 (16;30)
Number of synovitis	3 (1;10)
Duration of morning stiffness (in hours)	2 (1;3)
Positive CRP (> 6 mg/l)	90.2%
High ESR (>15 mm in first hour)	85.9%
Positive rheumatoid factors (> 8 IU)	84.0%
Positive anti-cyclic citrullinated peptide antibodies (>25 IU)	95/116 (81.9%)
DAS28	6.5 (5.5;7.3)
RA in remission <sup>a</sup>	0.7%
Mild activity <sup>b</sup>	1.3%
Moderate activity <sup>c</sup>	16.9%
Very active <sup>d</sup>	81.1%

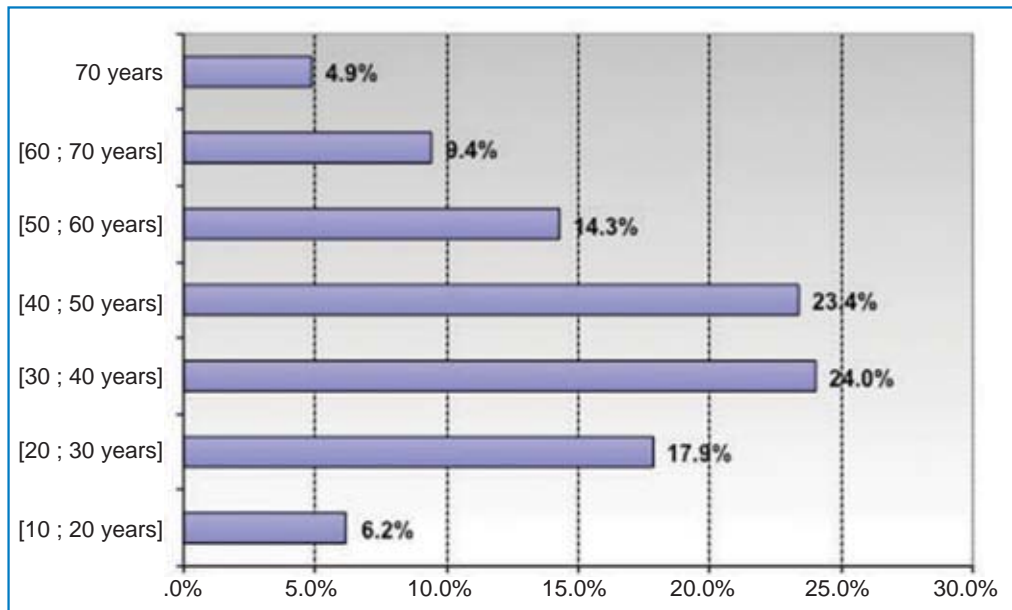
DAS: Disease Activity Score with 28 joints count

<sup>a</sup>DAS ≤ 2.6;

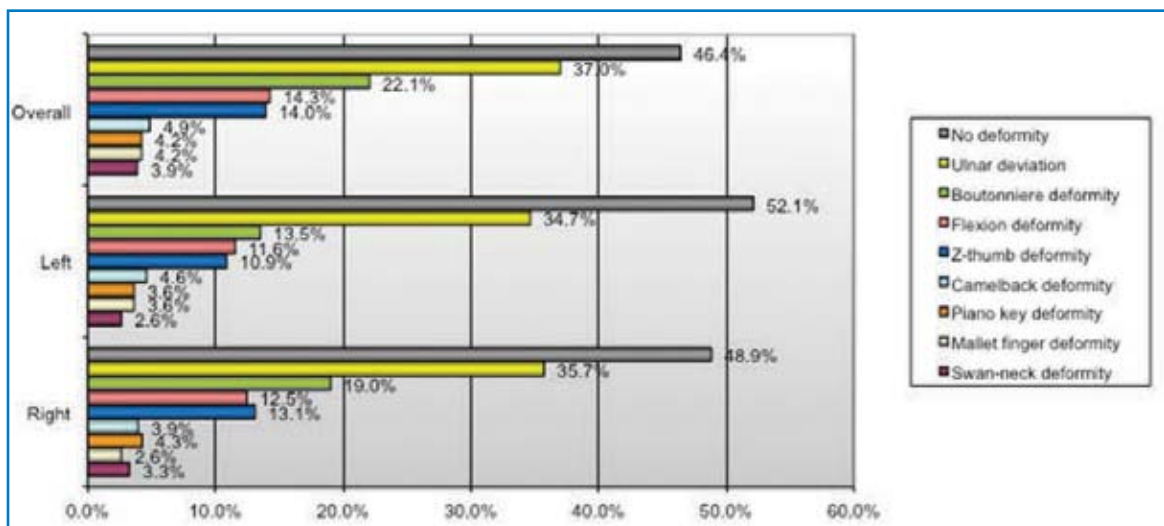
<sup>b</sup>2.6 < DAS ≤ 3.2

<sup>c</sup>3.2 < DAS ≤ 5.1

<sup>d</sup>5.1 < DAS



**FIGURE 1.**  
 Age distribution of the study population (by 10-year ranges).



**FIGURE 2.**  
 Hand deformities distribution at time of diagnosis. "Overall" represents both left and right hand deformities.

articular manifestation, the most common being anemia and sicca syndrome.

Tables 3 and 4 show the effect of sex and age at the beginning of the symptomatology. Women were significantly more affected in less than 60 years.

### DISCUSSION

Through the analysis of 308 cases, this study enables to assess the epidemiological, clinical, biochemical and immunological features of RA in a sub-Saharan African population, where there has been an insurrection in RA therapy in the past few years.

Rheumatoid arthritis (RA) remains poorly acknowledged by the medical staff in Senegal, which results in a significant delay in diagnosis. The median duration of

**TABLE 2.**  
 Extra-articular manifestations.

Variables	N (%)
Anemia	102/308 (33.1%)
Sicca syndrome	90/308 (29.2%)
Interstitial pneumonia	6/308 (2.0%)
Rheumatoid nodules	4/308 (1.3%)
Adenopathies	4/308 (1.3%)
Fever	2/308 (0.7%)
<b>Number of Extra-Articular Manifestations per Patient</b>	
0	139/308 (45.1%)
1	136/308 (44.2%)
2	27/308 (8.8%)
3	6/308 (1.9%)
At least 1 manifestation	169/308 (54.9%)

**TABLE 3.**  
Effect of the age at the beginning of symptomatology.

	Less than 60 years N = 270 (91%)	60 years or more N = 26 (9%)	p-value
<b>Sex</b>			p=0.005
<i>Women</i>	244/270 (90.4%)	18/26 (69.2%)	
<i>Men</i>	26/270 (9.6%)	8/26 (30.8%)	
			p=0.02
<i>Urban</i>	207/260 (79.6%)	15/25 (60.0%)	
<i>Rural</i>	53/260 (20.4%)	10/25 (40.0%)	
<b>Disease Activity Score 28</b>			p=0.10
Median (Q1; Q3)	6.6 (5.5; 7.3)	6.0 (5.3; 6.5)	
Min; Max	1.4; 9.7	2.7; 7.3	
<b>Duration of Evolution of Symptomatology (Month)</b>			p=0.45
Median (Q1; Q3)	47 (24; 92)	37 (28; 58)	
Min; Max	1; 382	9; 141	
<b>Positive Rheumatoid Factors (&gt; 8 IU)</b>	87%	60%	-
<b>Positive anti CCP Antibodies (&gt; 25 IU)</b>	83%	67%	-
			p=0.56
<b>Extra-Articular Signs</b>			
<i>No sign</i>	120/270 (44.4%)	10/26 (38.5%)	
<i>At least a sign</i>	150/270 (55.6%)	16/26 (61.5%)	

**TABLE 4.**  
Difference of the symptomatology men/women at the beginning of symptomatology.

	Women N = 273 (89%)	Men N = 35 (11%)	p-value
<b>Age (years)</b>			p=0.17
Median (Q1; Q3)	41 (30; 52)	42 (34; 68)	
Min; Max	16; 81	17; 80	
			p=0.42
<i>Urban</i>	78.9%	72.7%	
<i>Rural</i>	21.1%	27.3%	
<b>Disease Activity Score 28</b>			p=0.40
Median (Q1; Q3)	6.5 (5.5; 7.3)	6.5 (5.1; 7.1)	
Min; Max	1.4; 9.7	2.7; 7.7	
<b>Duration of Evolution of Symptomatology (Month)</b>			p=0.48
Median (Q1; Q3)	46 (25; 90)	44 (22; 84)	
Min; Max	1; 382	5; 260	
<b>Positive Rheumatoid Factors (&gt; 8 IU)</b>			p=0.72
Median (Q1; Q3)	32 (12; 160)	32 (12; 64)	
Min; Max	6; 1024	6; 512	
<b>Positive Anti CCP antibodies (&gt; 25 IU)</b>			p=0.88
Median (Q1; Q3)	100 (13; 340)	160 (10; 340)	
Min; Max	0; 340	2; 340	
<b>Extra-Articular Signs</b>			p=0.66
<i>Aucun signe</i>	122/273 (44.7%)	17/35 (48.6%)	
<i>Au moins un signe</i>	151/273 (55.3%)	18/35 (51.4%)	
Min; Max	0; 28	0; 28	

symptoms before diagnosis was 46 months in this study, which is a long time, but it is lower than the 54-month period previously reported in Senegal<sup>[4]</sup>. This significant delay in diagnosis was described in other African studies<sup>[2,6]</sup>. In Western studies, the delay in diagnosis is lower. In France it was estimated at 6 months<sup>[7]</sup>. Therefore, efforts

should be made to further reduce diagnostic delay periods. The increasingly common use of the ACR/EULAR 2010 criteria<sup>[8]</sup> should be allowed for an earlier diagnosis of RA.

A clear female predominance was found in our series. This female predominance in RA has been widely

reported in both African and Western studies, although it tends to decline with age. The role of hormonal factors is incriminated in this constation<sup>[1]</sup>.

The median age was 41 years (Q1: 31; Q3: 53). This result is comparable to data from other African studies<sup>[2,6]</sup>, and is well below the age of 55 years reported in Western countries<sup>[7,9]</sup>, and of 54 years reported in the African-American population<sup>[10]</sup>. We were unable to characterize the family history of chronic inflammatory arthritis, which is under genetic control during RA, and other systemic autoimmune diseases<sup>[11]</sup>. On admission, RA was active in 81.1% of patients, according to the DAS28. This could be due to the significant delay in diagnosis or an inappropriate initial therapy, especially because many patients first go to traditional healers<sup>[4]</sup>. Because of the limited number of physicians, particularly those who specialize in rheumatic diseases, access to traditional healers is easier for our patients. Moreover, the high number of patients with both positive rheumatoid factors and positive cyclic citrullinated peptide antibodies could help explained the severity of RA in our patients. Indeed, the presence of rheumatoid factors and cyclic citrullinated peptide antibodies is associated with a poor prognosis<sup>[12-13]</sup>. In addition, extra-articular manifestations, which are also considered poor prognostic factors, were detected in more than half of the patients. Among African-Americans, 38% of patients present extra-articular manifestations<sup>[3]</sup>. Our results contrast with previous data, which suggested that extra-articular manifestations were rare in the sub-Saharan African population<sup>[2,14]</sup>. Although, the interpretation of hospital studies should be done with caution as it includes a limited number of patients. However, rheumatoid nodules, which indicate severe RA, were found in only 1.3% of our patients, despite the high seropositivity for rheumatoid factors (84%) and cyclic citrullinated peptide antibodies (81.9%).

The present study presents some limitations. First, the recruitment of patients in a hospital setting could constitute a selection bias. A population-based study would be more appropriate, but the limited number of rheumatologists in Senegal makes this type of study difficult to perform. However, due to the number of RA cases included in this study (308 patients), this is one of the largest RA series described in sub-Saharan Africa. Second, a radiological assessment of lesions would have provided additional information for determining the rate of RA severity in Senegal. Nevertheless, in a previous study, we showed that radiological lesions are noted in 56% of patients at diagnosis, with a modified Sharp score of  $21.8 \pm 4.7$ <sup>[4]</sup>.

## CONCLUSIONS

In a Senegalese hospital setting, RA is characterized by an important delay in diagnosis, a polyarticular presentation, and a high number of extra-articular manifestations plus a high positivity of immunological markers. RA extra-articular manifestations include mainly anemia and sicca syndrome. Initial awareness and a better understanding of RA in sub-Saharan Africa are necessary for the early management of these patients.

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Submitted Date: 31 Mar. 2014

MS Approval Date: 29 Apr. 2014



## الأعراض السريرية للتهاب المفاصل الروماتويدي في سكان جنوب الصحراء الأفريقية، دراسة ٣٠٨ حالات من السنغال

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### المستخلص:

يُعتقد سابقاً أن إلتهاب المفاصل الروماتويدي كان نادراً في جنوب الصحراء الكبرى الإفريقية، ولكنه الآن أصبح يذكر على نحو متزايد والهدف من هذه الدراسة هو تحديد الملامح الوبائية والسريرية والبيولوجية لإلتهاب المفاصل الروماتويدي من أجل التشخيص والعلاج المبكر لهذا المرض.

وقد أجريت هذه الدراسة في قسم العيادات الخارجية للروماتيزم في مستشفى أريستيد لودانتك الجامعي في مدينة داكار في السنغال.

### النتائج:

شملت هذه الدراسة ثلاثمائة وثمانية أشخاص من المصابين بإلتهاب المفاصل الروماتويدي وفقاً لمعايير ١٩٨٧ للكلية الأمريكية لأمراض الروماتيزم، وهم ٢٧٣ مريضة و ٣٥ مريضاً، وكانت نسبة النساء إلى الرجال ٧،٨، و متوسط الأعمار ٤١ عاماً بين ٣١ و ٥٣ عاماً والفئة العمرية الغالبة ٣٠-٤٠ عاماً، يسكن منهم ٩٣٪ في المناطق الحضرية، و ٧٪ في المناطق الريفية وهناك ٣٥،١٪ من المرضى ظهر في عائلاتهم إلتهاب المفاصل، واستشار ٣٩٪ من المرضى معالماً تقليدياً، و كانت نسبة إلتهاب المفاصل الروماتويدي النشط جداً هي ٨١،١٪ والعامل الروماتويدي إيجابياً في ٨٤٪ من المرضى، كما كانت الأجسام المضادة البيبتيدية متواجدة في ٨١،٩٪ من ١١٦ مريضاً تم إجراء الفحص عليهم، وقد ظهر على الأقل عرض واحد من أعراض المرض خارج نطاق المفاصل في ١٦٩ مريضاً، وكانت أكثر الأعراض شيوعاً فقر الدم و متلازمة الجفاف.

### الاستنتاج:

توصلت هذه الدراسة إلى أن إعتلال المفاصل الروماتويدي يتم تشخيصه متأخراً في مراحل متقدمة من المرض، وأنه يصيب عدة مفاصل وأن التحليلات المخبرية عالية الإيجابية، كما تميزت الإصابات خارج نطاق المفاصل بفقر الدم و متلازمة الجفاف وخلصت هذه الدراسة إلى أن المعرفة الجيدة لإلتهاب المفاصل الروماتويدي في جنوب الصحراء الكبرى من إفريقيا هو مطلب ضروري للوصول إلى التشخيص والعلاج المبكر لهذا المرض.