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Interleukin 6 and Bone Erosions in Rheumatoid Arthritis in an African Hospital

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Abstract

Introduction: Rheumatoid arthritis (RA) is a chronic, erosive and deforming inflammatory rheumatic disease. In the era of biotherapies and the arrival of biosimilars in sub-Saharan Africa, the objective of this study was to describe plasma IL-6 variations in RA patients at Cité Verte District Hospital (Cameroon). **Material and Methods:** Descriptive and analytical cross-sectional study from December 1, 2021 to May 31, 2022. We included patients over 18 years old suffering from RA (ACR/EULAR 2010). Patients with an infection were not included. The data collected were age, sex, smoking status, family history, disease duration, disease activity by DAS28, CRP, rheumatoid factor, and plasma level of IL-6. Bone erosion was sought on radiography and ultrasound. **Result:** We included 31 patients, 25 of whom were women (80.6%). The mean age was 47.27 ± 17.97 years. Disease activity was predominantly moderate (32.3%) and severe (32.3%). Mean IL-6 level was 15.29 ± 2.36 pg/ml (extremes: 11.26 pg/ml and 20.15 pg/ml). IL-6 levels were higher in patients with a history of smoking. Similarly, IL-6 levels were higher in patients with mildly active RA in remission than in moderately and severely active RA. Mean IL-6 levels were significantly higher in patients with erosive RA (16.3 pg/ml VS 14.6 pg/ml). **Conclusion:** IL-6 levels were significantly elevated in men, weaned smokers and patients with bone erosions.

Keywords

Rheumatoid Arthritis, Interleukin 6, Bone Erosion-DAS28, Sub-Saharan Africa

1. Introduction

Rheumatoid arthritis (RA) is a chronic, non-organ-specific autoimmune disease

characterized by joint and extra-articular involvement. It is the most common chronic inflammatory rheumatic disease [1]. In Africa, prevalence varies between 0.1% and 0.9% depending on the region [1] [2]. The pathophysiology of RA involves a complex network of various cytokines (IL-1, IL-6, TNFα, IL-17) and cells that trigger the proliferation of synovial cells and damage cartilage and bone [3]. Smoking is a preventable risk factor for RA. The increased risk due to smoking is dependent on the amount of smoking and genotype [4]. The specificity of ACPA increases in the years just before the onset of RA and is higher in patients who have smoked compared to patients who have never smoked [5]. Biotherapies targeting these cytokines in the treatment of RA are rarely used in sub-Saharan Africa [6] where RA is often diagnosed in the erosive and deforming phase. In the era of biotherapies and the arrival of biosimilars in sub-Saharan Africa, the objective of this study was to describe plasma variations in Il-6 in RA patients at Cité Verte District Hospital (Cameroon).

2. Patients and Methods

This was a descriptive and analytical cross-sectional study in the rheumatology department of Cité Verte District Hospital between December 1, 2021, and May 31, 2022. We included patients over 18 years of age with rheumatoid arthritis according to ACR/EULAR 2010 criteria [7]. Patients with infections were not included. Qualitative and quantitative data were collected: socio-demographic data (age, sex); and clinical and paraclinical data (smoking, family history, disease duration, disease activity, CRP, rheumatoid factor, IL-6 levels. Latex CRP was positive if > 6 mg/L. Rheumatoid factor was determined by latex and Waaler-Rose reaction. IL-6 was assayed using an automated sandwich ELISA. Radiographic bone erosion was assessed using the SHARP/van der HEIJDE evaluation method and the Simple Erosion Narrowing Score (SENS) [8]. Bone erosion on osteoarticular ultrasound was assessed according to the criteria of the Outcome Measures in Rheumatology (OMERACT) group [9]. Disease activity was assessed by DAS28. Statistical analyses were performed using SPSS 28.0.1.1 software. Comparisons between two groups were made using Pearson's (or Spearman's) test for continuous variables, Student's (or Wilcoxon's) t-test between a continuous and a qualitative variable, and Chi2 test (or Fisher's exact method) for qualitative variables. The significance threshold was set at 5%.

The study was conducted with the approval of the Institutional Ethics Committee of the Faculty of Medicine and Pharmaceutical Sciences of Douala (Cameroon). Patient consent was required after an explanation of the study procedure and objective.

2.1. Data Analysis

The results were analysed using Microsoft Excel 2019 and Epi Info 7.2.3.1. Qualitative variables were summarised by frequency and percentage, and quantitative variables by mean and standard deviation (SD). Comparisons were made by

using the Pearson correlation test. All tests were two-tailed; the significance level was set at 5%.

2.2. Ethical Considerations

Informed consent was obtained from the patients and the research protocol was accepted by the ethics committee of the Ignace Deen national hospital in Conakry.

3. Results

We collected 31 patients with RA, 25 of whom were women. Mean age was 47.3 ± 17.9 years. Mean disease duration was 6.5 ± 6.2 years. Disease activity was predominantly moderate (32.3%) and severe (32.3%) (**Table 1**, **Figure 1**).

The mean interleukin-6 level was 15.13 pg/ml, with patients aged between 40 and 60 having the highest mean Il-6 level (15.97 ± 2.33 pg/ml) compared with younger patients aged between 18 and 21 (14.01 ± 0.79 pg/ml) (**Table 2**).

IL-6 levels were higher in patients with a history of smoking. Similarly, IL-6 levels were higher in patients with mildly active RA in remission than in moderately and severely active RA (**Table 3**).

Bone erosion was present in 12 patients (38.7%). Mean IL-6 levels were significantly higher in this group (16.3 pg/mL) compared with patients without bone erosion (14.6 pg/mL) (**Table 4**).

4. Discussion

We conducted a cross-sectional study of plasma IL-6 levels according to RA characteristics. The small sample size of this cohort was related to the level of attendance at this district hospital which is a limitation of the study, as well as the absence of non-smoking control patients. However, we described the variations of IL-6 in RA. Elevated mean IL-6 levels in patients followed for RA corroborated chronic inflammatory disease data [11] [12]. IL-6 levels were highest in patients aged 40 to 60, followed by those aged 60 and over, as described in the literature. [13] [14].

The elevation of this IL-6 level in patients with a history of smoking differed from the data of Aldaham *et al.* where IL-6 levels were lower in weaned smokers (0.86 ± 0.13 VS 0.44 ± 0.14) [15]. This is because, on one hand, tobacco has the ability to potentiate rheumatoid arthritis through ACPA [5], while on the other hand, cigarette smoking alone is able to have direct effects on immune cells, inducing chronic inflammation depending on the dose, the type of cigarette and the duration of exposure [16]; this can explain why stopping smoking or reducing exposure helps to improve the chronic inflammation induced by it. Mean IL-6 was high in patients with low activity Unlike the data of Cheng *et al.* [14], where IL-6 levels were higher in patients with severe activity; Some studies showed no significant correlation between IL-6 levels and DAS 28; according to Meguid *et al.*, IL-6 was correlated with pain, SR and anti-PCC but not with

Table 1. Socio-demographic, clinical and therapeutic characteristics of 31 rheumatoid arthritis patients.

	Frequency (%)	Means
Woman	25 (80.6)	
Age (years)		47.3 ± 17.9
Active smoking	6 (19)	
Duration of illness (years)		6.5 ± 6.2
1st degree family history of rheumatoid arthritis	14 (45)	
C-Reactive Protein		7.8 ± 1.1
Positive rheumatoid factors	21 (67.7)	
Anticorps anti-cyclic citrullinated peptide	19 (63.1)	
Disease activity score 28		4.3 ± 1.8
Disease activity		
Remission	9 (29)	
Mild	2 (6.5)	
Moderate	10 (32.3)	
Severe	10 (32.3)	

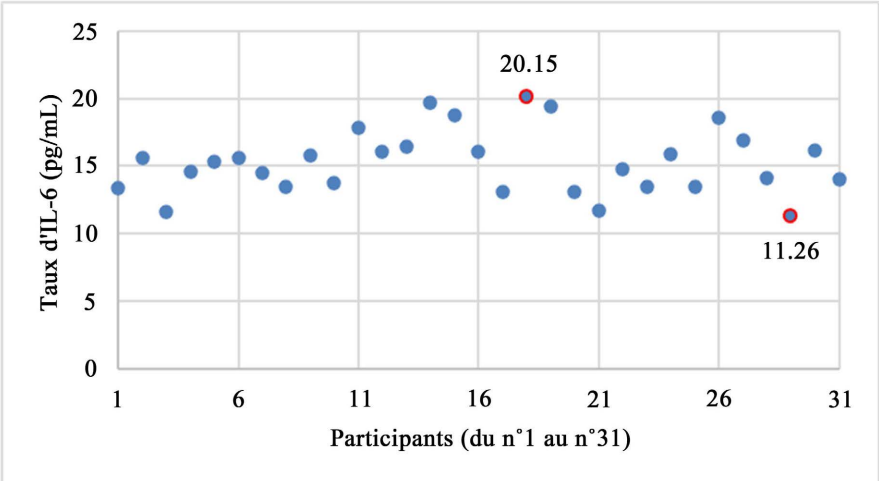

Figure 1. Variation in IL-6 levels in 31 RA patients (normal interleukin 6 values ranged from 0.01 to 11.5 pg/mL [10]).

Table 2. Plasma IL-6 levels according to age group.

Age (years)	Frequency	Mean IL-6 level (pg/ml)
[18 - 21[	02	14.01 ± 0.79
[21 - 40[	10	15.38 ± 2.93
[40 - 60[	09	15.97 ± 2.33
[60 - 80]	10	14.85 ± 2.02

Table 3. IL-6 levels according to sex, history and activity of rheumatoid arthritis.

Characteristics		Mean IL-6 level (pg/ml)	p-value
Sex	Female	15.08 ± 2.34	0.3
	Male	16.21 ± 2.46	
Smoking history (former smoker)	Yes	14.75 ± 1.86	0.006*
	No	17.59 ± 2.16	
History of rheumatoid arthritis in parents	Yes	15.13 ± 2.66	0.67
	No	15.50 ± 2.17	
Disease activity	Remission	15.63 ± 2.12	0.02*
	Mild	19.77 ± 0.54	
	Moderate	14.66 ± 2.18	
	Severe	14.74 ± 2.14	

Table 4. IL-6 levels in patients according to the presence of bone erosion.

Bone erosion	Frequency	Mean IL-6 level (pg/ml)	p-value
No	19	14.66 ± 1.90	**0.05**
Yes	12	16.30 ± 2.76	

DAS28 [17]. Concentrations of cytokines from the IL-6 family can be measured in both serum and synovium from RA patients, but these cytokines are mainly involved in the local reaction, which explains why IL-6 is not always positively correlated with disease activity at the systemic level [18].

The elevation of IL-6 in patients with bone erosion was previously reported by Yasushi *et al.* showing that an IL-6 level of 7.6 pg/ml or more was predictive of radiographic progression at one year. IL-6 is involved in bone destruction in RA [19] [20].

5. Conclusion

IL-6 levels were significantly elevated in men, weaned smokers and patients with bone erosions. In the era of biotherapies and similar biologics, this study shows that anti-IL-6s have a place in the therapeutic arsenal for rheumatoid arthritis in sub-Saharan Africa.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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