

Research Article

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The Specific Immunological Biomarkers Used In the Screening of Rheumatic Diseases from 2004 to 2020 at the Immunity Biology Center of the Pasteur Institut of Cote D'Ivoire

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ABSTRACT

Background: to study the epidemiological evolution of rheumatic diseases and to assess the advantages and disadvantages of the methods for assaying rheumatic biomarkers.

Patients and Methods: the study population consisted of 844 patients who came to the Pasteur Institute in Côte d'Ivoire from 2004 to June 2020 for the assay of rheumatic biomarkers. The parameters assayed were Rheumatoid Factor (RF) and Citrullinated Antipeptide Antibodies (Anti CCP). The RF assay was performed using two techniques: agglutination (RF latex, RF Waaler-Rose) and ELISA (CHORUS trio). The anti CCP assay was carried out by the ELISA technique (CHORUS trio).

Results: among the 844 patients received, 144 had a positive result. Women made up the majority on the one hand of all patients (71%) and on the other hand of positive patients (77%). The most numerous patients were those aged between 41 and 60 years in both the total population and among the positive patients. The most common reasons for testing were rheumatoid arthritis and workup. The agglutination tests were used since 2004 for the determination of the RF from 2019 the RF was determined by ELISA chain. During this year 2019 there was a new more specific biomarker, the anti CCP assayed by ELISA.

Conclusion: RF remains a key factor in rheumatic diseases. However, when combined with anti CCP, they make it possible to confirm the diagnosis with more specificity.

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Introduction

Rheumatic diseases are a group of diseases that affect the joints, connective tissue, bones, blood vessels and muscles. They particularly affect the function of the musculoskeletal system, resulting in limitations to movement and pain [1]. They are of metabolic or degenerative origin. In the European Economic Community (EEC) 55-75 million Europeans suffer from rheumatic diseases [2]. In sub-Saharan Africa, few studies have been conducted on rheumatic diseases in adults. In Gabon, Nzenzé et al. reported 18% of rheumatoid arthritis in a series of 57 observations [3]. In Togo, Mijiyawa et al. estimated it at 3.5% in a series of 843 observations [4]. In Côte d'Ivoire, the data on this subject are partial. There are more than one hundred pathologies considered as rheumatic diseases. There are four main categories: inflammatory rheumatism, degenerative rheumatism, periarticular rheumatism

and bone rheumatism. The diagnosis of rheumatic diseases is based on clinical, imaging and biological findings. The biological workup is a major player in early diagnosis and prognosis assessment [5]. Indeed, radiological abnormalities may be delayed by several months compared to the clinical course [6]. However, biological markers have an early appearance. At the Institut Pasteur de Côte d'Ivoire, precisely at the immunity biology unit, the rheumatoid factor is a key parameter in the diagnosis of rheumatic diseases. The techniques for the determination of this biomarker have evolved in our laboratory. Since 2005, manual agglutination tests were used. However, as of October 2019, automated tests (ELISA) will appear. Also, although being an important biomarker, the rheumatoid factor is since 2019 associated with a more specific parameter the anti citrullinated protein antibody (anti CCP). The objective of this work is to study the epidemiological evolution of rheumatic diseases with the new methods of determination of rheumatic biomarkers.

Methods

Patients

Inclusion criteria: All patients (844) received for rheumatic biomarker testing. Non-inclusion criteria: No non-inclusion criteria were considered.

Methods

A retrospective study was conducted from 2004 to June 2020 at the Immunity Biology Unit of the Institut Pasteur de Côte d'Ivoire (IPCI). Paraclinical data were collected using the test request form and the test result collection register. Rheumatoid factor was determined by manual methods (RF Waaler-Rose and RF Latex). The latex test is a passive agglutination technique between IgM class rheumatoid factor present in serum and hemoglobins bound to the latex particle support. The latex test has been reported to be positive from dilution 1/80 [7, 8]. The RF Waaler-Rose test is a passive hemagglutination technique using sensitized sheep red blood cells coated with rabbit anti-sheep red blood cell IgM. It requires a control with non-sensitized red blood cells to avoid false positives due to heteroantibodies. The RF Waaler-Rose reaction has been considered positive from dilution 1/64 [7, 8]. The determination of autoantibodies to cyclic citrullinated peptide (anti CCP) and the quantification of rheumatoid factor was done by ELISA using CHORUS. ELISA is an enzyme-linked immunosorbent assay that allows the visualization of an antigen-antibody reaction by means of a colored reaction produced by the action on a substrate of an enzyme previously attached to an antibody. Rheumatoid factor and anti-CCP were considered positive when they had a value greater than 20 IU/ml [7, 9].

Results

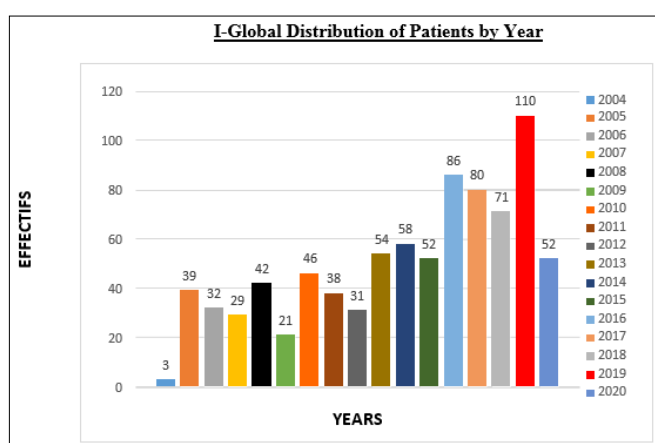


Figure 1: Number of Patients Received For Research of Rheumatic Disease from 2004 To 2020

The number of patients using the Pasteur Institute of Côte d'Ivoire for rheumatic biomarker testing has increased over the past 4 years. The total number of patients from 2004 to June 2020 was 844

II- Global Distribution of Patients According To Epidemiological Parameters

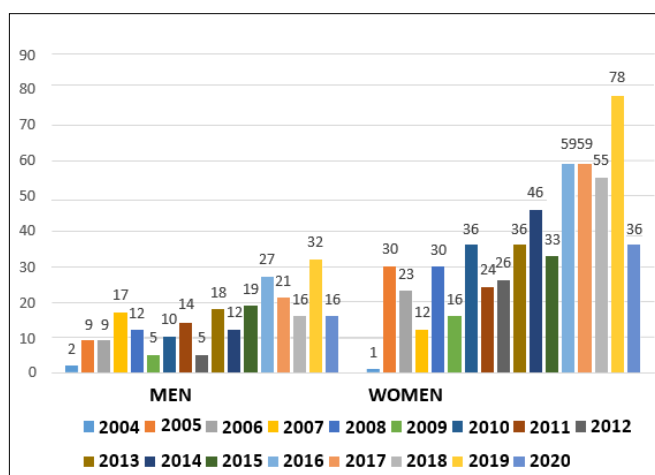


Figure 2: Distribution of patients by sex and year

Women constituted the majority of patients received for immunological testing. Approximately 71% of the patients were female, for a sex ratio of 2.45.

Table 1: Distribution of Patients by Age Group

	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	TOTAL
0-20	0	4	1	0	3	2	6	3	1	4	1	4	10	4	10	8	4	65
21-40	0	15	7	6	19	6	16	11	8	18	23	13	31	29	27	36	15	280
41-60	0	16	20	19	16	10	18	22	21	26	24	24	30	24	23	48	24	365
61 &	3	4	4	4	4	3	6	2	1	6	10	11	15	23	11	18	9	134
Total	4	39	32	29	42	21	46	38	31	54	58	52	86	80	71	110	52	844

The patients who were between 41 and 60 years old were the most numerous 365 people or 43.24%. When crossing the age and gender of the patients, women who were older than 40 years were the most numerous about 32.34%.

Table 2: Distribution of patient by clinical information and sex

	INFLAMMATORY SYMPTOMS	RHEUMATOID ARTHRITIS	ARTHRITIS	HEALTH CHECK	ANGINE	KISTE	ANEMIA	ASTHMA	HEPATHOPATHY	ENTEROPATHY	TOTAL
MEN	18	119	19	74	01	02	05	03	01	02	244
WOMEN	71	262	29	200	06	05	09	06	04	08	600
TOTAL	89	381	48	274	07	07	14	09	05	10	844

In the distribution of patients according to gender and clinical information, women were in the majority. Here RA and workup were also the primary reasons for requesting tests. In the distribution of patients, rheumatoid arthritis and workup were the primary reasons for testing.

III- The Results of the Global Seropositivity Tests

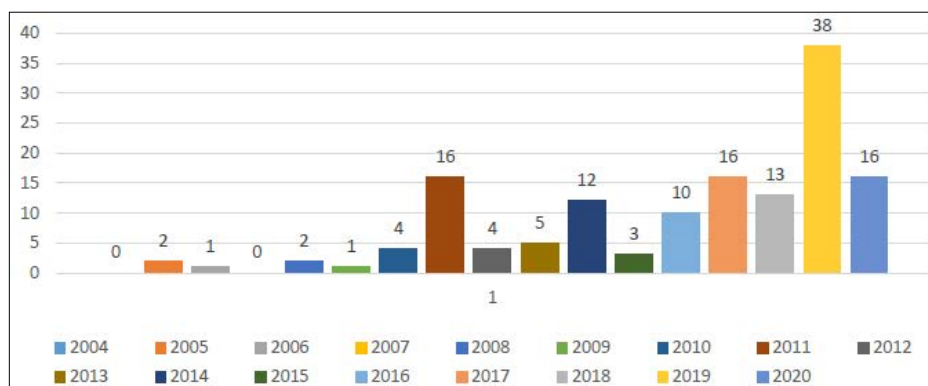


Figure 3: Number of Patients with To Positive Result from 2004 To 2020

The patients with positive results were 144 and constituted about 19% of all patients.

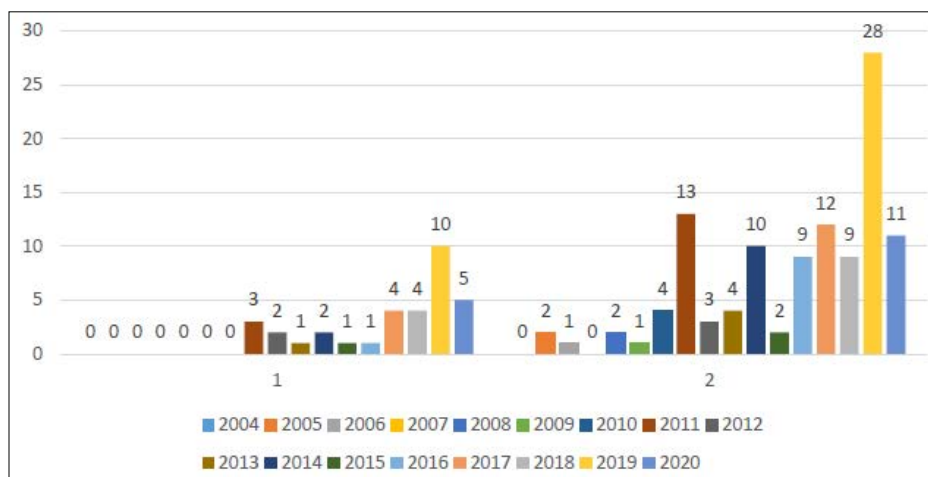


Figure 4: Distribution of positive result by sex

Of the 144 positive patients, women constituted the majority (77%) of positive patients.

Table 3: Distribution of Patient with To Positive Result by Clinical Information

	INFLAMMATORY SYMPTOMS	RHEUMATOID ARTHRITIS	ARTHRITIS	HEALTH CHECK	ANGINE	KISTE	ANEMIA	ASTHMA	HEPATHOPATHY	ENTEROPATHY	TOTAL
MEN	5	10	04	14	00	00	00	00	00	00	33
WOMEN	6	39	11	51	00	00	00	00	00	00	111
TOTAL	11	49	15	65	00	00	00	00	00	00	144

RA and health check were the main clinical information for requesting analysis

IV-Results of the Different Specific Biomarkers
Table 4: Number of Biomarkers Carried Out From 2004 To 2020

	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	TOTAL
RF-Latex	00	05	00	00	00	00	00	00	00	00	38	52	86	79	71	78	0	409
RF-WR	03	36	32	29	42	21	42	38	32	52	52	52	86	79	71	00	0	667
AntiCCP	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	7	7	14
RF Trio	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	26	45	71
Total	03	41	32	29	42	21	42	38	32	52	90	104	172	158	142	111	52	1161

Agglutination tests (RF latex and RF Waaler-Rose) have been used since 2004 for the diagnosis of rheumatic conditions. The ELISA technique begin in 2019.

Discuss

This study shows that the number of patients listing in Pasteur Institute of Côte d'Ivoire for biomarker determination of rheumatic diseases was increasing. Patients with a positive result represented 17%. Women constituted the majority of both the total and positive patient population. This may be explained by the fact that women are more prone to rheumatic diseases than men, and this is particularly true as age increases [10, 12]. The age group most affected was that between 41 and 60 years. It should be noted that the menopause favors the occurrence of these pathologies due to the decrease in hormones such as estrogen, which weakens the bones and joints [13]. In this study, various clinical information was observed but the most recurrent were in decreasing order Rheumatoid Arthritis (RA), health check, inflammatory syndrome and arthritis. Among the patients with a positive result, we observed that the health check-up was the most requested reason for the analyses; this would mean that for a large part of the patients in this study, the discovery of rheumatic diseases was done in an accidental way. It should also be noted that the number of patients has almost doubled as of 2019 due to the addition of new more sensitive and specific tests, namely anti-CCP and RF measured by the ELISA method. The advantage of anti-CCP is that it appears early and precedes the onset of the disease and the appearance of rheumatoid factor by several years [6]. Regarding RF, it is important to note that the ELISA method offers better sensitivity and specificity and has been recommended since 2006 by the French National Authority for Health [5]. Anti-CCP and RF are the markers of choice for the diagnosis of RA, a common rheumatic disease [14]. Likewise, rheumatoid factor IgM and anti-CCP are currently two crucial serological tests for the diagnosis and prognosis of inflammatory arthritis. These two types of autoantibodies have been retained as important criteria by the American College of Rheumatology (ACR) and the European League of Rheumatology (EULAR) [6,11].

Conclusion: RF remains a key factor in rheumatic diseases. However, when combined with anti CCP, they make it possible to confirm the diagnosis with more specificity.

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