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Original Research Article

**Prevalence of rheumatoid factors in malagasy blood donors****Randriamahazo Rakotomalala Toky<sup>1\*</sup>**, Lalarizo Rakoto Mahary<sup>2</sup>, Raherinaivo Anjatiana Annick<sup>1</sup>, Jaonaso Jean de la Croix<sup>2</sup>, Rasamindrakotroka Andry<sup>1</sup>, Randriamanantany Zely Arivelo<sup>2</sup><sup>1</sup>*Immunology Laboratory of Joseph Ravoahangy University Hospital Center Andrianavalona/University of Antananarivo (Madagascar)*<sup>2</sup>*National Center Blood Transfusion Antananarivo/University of Antananarivo (Madagascar)***Abstract****Introduction:** Rheumatoid factors are autoantibodies targeted against the Fc portion of IgG. These autoantibodies are found in various autoimmune diseases, particularly in rheumatoid arthritis; in multiple bacterial and viral infectious diseases; and also in healthy subject. In the range of investigations on autoimmune diseases in Madagascar, the current study evaluated the prevalence of rheumatoid factors in healthy Malagasy blood donors in 2016.**Material and Methods:** The study was a multicentric descriptive transversal study investigating the prevalence of rheumatoid factors in healthy blood donors from the CNTS Antananarivo and the CRTS Fianarantsoa using a latex agglutination test (Cypress Diagnostic ® RF Latex Agglutination, Belgium).**Results:** From the 375 included samples, 4 were positive for IgM rheumatoid factors, giving a global prevalence of 1.1%. Prevalence was 1.4% (4) and 0% (0) for the CNTS Antananarivo and the CRTS Fianarantsoa respectively. Among the positive samples, 2 samples had low titers, 1/1 and 1/2 respectively, and 2 samples had high titer (1/256).**Conclusion:** Prevalence of IgM-RF found in the current study is low. Exploration of other isotypes using ELISA assays may be interesting for the exploration of these antibodies. Although, study of the several factors influencing the production of RF in the Malagasy population is a matter of research. The current study opens new perspectives for the exploration of auto-immunity in Madagascar.**Keywords:** Rheumatoid factors, blood donor, prevalence, titer, Madagascar.**\*Correspondence Info:**Dr. Randriamahazo Rakotomalala Toky  
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University Hospital Center Andrianavalona**\*Article History:****Received:** 22/05/2019**Revised:** 28/06/2019**Accepted:** 28/06/2019**DOI:** <https://doi.org/10.7439/ijbar.v10i6.5188>**QR Code****How to cite:** Toky, R., Mahary, L., Annick, R., Croix, J., Andry, R., & Arivelo, R.. Prevalence of rheumatoid factors in malagasy blood donors. *International Journal of Biomedical and Advance Research* 2019; 10(6): e5188. Doi: 10.7439/ijbar.v10i6.5188 Available from: <https://ssjournals.com/index.php/ijbar/article/view/5188>Copyright (c) 2019 International Journal of Biomedical and Advance Research. This work is licensed under a [Creative Commons Attribution 4.0 International License](https://creativecommons.org/licenses/by/4.0/)**1. Introduction**

Rheumatoid factors (RF) are autoantibodies directed against the Fc fragment of IgG. They are highlighted both in pathology and in the healthy population. In pathology, they are present in various autoimmune diseases, in particular in rheumatoid arthritis (RA), but also in bacterial, viral and parasitic infections [1]. Interpretation of the presence of RF in the serum should be careful. Some people will be RF-positive, keep this serologic statue without any symptoms related to RA, while others will be symptomatic. The appearance of these autoantibodies prior to the onset of disease symptoms in RA is called: "Preclinical Rheumatoid Arthritis" [2].

In Madagascar, few studies about RF, mainly focused on patients with clinically manifest pathologies have been performed. This is the first study to determine the prevalence of RF in the healthy Malagasy people. The objectives of this study were to determine the prevalence of RF in Malagasy blood donors in two cities Antananarivo and Fianarantsoa in 2016 and determine the titers of the positive samples.

**2. Material and methods**

This is a prospective descriptive study on the seroprevalence of rheumatoid factors in blood donors at two

blood transfusion centers in the Malagasy territory: National Center of Blood Transfusion (NCBT) Antananarivo and Regional Center of Blood Transfusion (RCBT) Fianarantsoa. The samples were obtained from blood donations made at the two blood centers from July 1st to September 30th, 2016. This concern all blood donors, of any age, of any gender, of any geographical or ethnic origin, came for a regular blood donation (regular volunteer donor, new volunteer donor) or occasional donation (family donor) to NCBT Antananarivo or RCBT Fianarantsoa. We included all blood donors found to be "fit" after the medical screening stage of the donor according to the NCBT criteria from which a sample of blood was taken. We excluded "fit" donors with at least one of the signs in favor of rheumatoid arthritis such as chronic joint pain, fever, joint swelling, joint deformity, peripheral joint involvement. But also the signs related to systemic lupus erythematosus as erythematous-squamous lesions in butterfly wing, pruritus, dermatological lesion exaggerated by light, oral mucosal lesion and / or pharyngeal. Other signs such as chronic cough (3 months), antituberculous treatment, morbilliform trunk erythema, treatment with benzathine-benzylpenicilline treatment excluded patients. In addition to these criteria, we also excluded donors with a positive result for at least one of the routine screening serology (malaria, viral hepatitis B and C, HIV, syphilis).

The blood donor sample were collected in 5 ml dry tube and then tested for IgM-class RF by the Cypress Diagnostic® Latex Agglutination latex agglutination test (Belgium). According to the manufacturer's recommendations, the presence of agglutination visible at naked eye which stands for a titer ≥ 8 IU / mL was considered positive; for the titration of positive samples, the same method was applied using double serial dilutions samples in saline solution at 9 g / dL. The data was collected on Microsoft Office Excel 2013 and the statistical analysis of the data was performed with the R software. The threshold value of p is 5%. The Chi-square test was used to compare the percentages observed. The Student's *t* test was used to compare the averages. Steps were taken to maintain strict confidentiality when preparing the files. The study was performed with the agreement signed by the patient.

### 3. Results

During the study period, 500 samples were collected, 400 from the NCBT and 100 from the RCBT Fianarantsoa. Of these 500 samples, 125 were excluded including 123 for NCBT and 2 for RCBT Fianarantsoa. A total of 375 sera were collected, of which 282 (75.2%) were male and 93 (24.8%) were female. The sex ratio of the blood donors was 3.03. The average age of blood donors was 35.04 years, with extremes of 18 and 64 years. Of the

375 samples tested, 4 males coming from Antananarivo were IgM-RF positive giving an overall prevalence of 1.1% (4/375) (Table I). No RCBT person had a positive RF.

The difference found between the prevalence of RF observed at the two sites was not statistically significant (p: 0.12). Titers found for positive samples ranged from 8 to 2048 IU/ml. Two samples had low titer, 8 IU/ml and 16 IU/ml respectively. The other two samples had high titers at 2048 IU/ml. These samples were all from male donors (Table II). We found a significant correlation between the person had a positive RF (p: 0.02) and the values of the titles (p: 0.01). However, no correlation was found between gender and positivity (p: 0.14) (Table III).

**Table I: Seroprevalence of RF in sera**

	RCTB Fianarantsoa n = 98 (100%)	NCBT Antananarivo n = 277 (100%)
Positive	0% (0)	1,4% (4)
Negative	100% (98)	98,6% (273)

**Table II: Titers of positive samples**

Positive sample n : 4	Gender	Age (years)	Titers (UI/ml)
1	Male	27	2048
1	Male	46	2018
1	Male	45	16
1	Male	21	8

**Table III: p value according to the studied variables**

	Variables	p (<0.005)
RF positive	Age	0.02
	Gender	0.16
Titers	Age	0.01

### 4. Discussion

In industrialized countries, there are a higher proportion of potential female blood donors before the age of 25 (7.5%) than men (5.5%). Female blood donors accounted for 40% of donors in Austria, 49.7% in France, 50% in Norway and 55% in Great Britain [3]. In the present study, the majority of the samples studied were from males (75.2%) at both sites. It's similar to many studies in sub-Saharan Africa that report a male predominance, with a ratio of 5 men to one woman, this proportion even reaching 90% in a study done in Ghana [4].

The average age of the individuals included in this study was 35.04 years, [18-64]. The average age of positive individuals was 34.75 years. These data are connected with those of a Cameroonian study reported by *Atabongeng et al* in 2015 [5].

Regarding, the overall prevalence of RF in the general population also increases with age [6]. In the serum of young and middle-aged subjects the rate is approximately

4% [1]. In developed countries, *Taslyurt et al* found a prevalence of 2.8% in 941 individuals from the general population, prevalence of 12.0% middle-aged women (45 to 64 years) [7]. In regard of African continent, the general prevalence of RF is higher than that of developed countries, indeed, *Viatte et al.* found a prevalence of 16% in the African healthy population [8] but a little weaker in Cameroon (an overall prevalence of 5.4%) as reported by *Atabonkengin* 2015 [5]. Interestingly, it has been suggested that there is an association with high prevalence of chronic infections found in the populations studied. These include leprosy, Kalaazar disease, trypanosomiasis, malaria and pulmonary tuberculosis.

Among populations at risk represented by family members of a rheumatoid arthritis patient, a Swedish study conducted by *Ärlestig et al* (2011) found a prevalence of 14.0% among 157 members of the first-degree family of rheumatoid arthritis patients with a mean age of 54 years (37 to 71 years) [9]. For *Goeldner et al* (2010), the prevalence was 8% in 200 individuals from families of patients with rheumatoid arthritis (61% women, 39% men with a mean age of 36.7 years) [10].

Very few studies have investigated the prevalence of IgM-RFs positivity in blood donors. The present study found a low overall IgM-RF prevalence of 1.1%. Similar results in the Netherlands (2004), prevalence of 1.1% and in the United States, Litwin and Singer found a prevalence of 2% in control sera from former blood donors who subsequently developed RA [11]. Higher rates were found by *Li et al* (2011) with a prevalence of 21.5% in a total of 1018 blood donors [12].

Our results could be explained by the technique used, the Latex Fixation Test (LFT) is more specific 87 to 95% but have the lowest sensitivity 75% to 83.11% [13]. Studies in Africa (Nigeria, New Guinea) have shown the excess positivity of LFT. The use of better techniques such as (Enzyme Linked Immunosorbent Assay) ELISA methods allows quantitative measurements of the different RF isotypes and also avoids interpretation problems and is more standardized than agglutination tests [14].

About antibodies levels, it is recognized that a high titer of RF in healthy subjects is a predictor of arthritis [1]. The risk of developing RA in a healthy individual is correlated with RF, the higher the titers, the higher the risk. Many studies have shown that RFs are frequently present in serum several years before clinical manifestations. Individuals with high levels of RF are 26 times more likely to develop RA in the long term and an absolute 10-year risk of 32% [15]. In 2008, *Majka et al* found a prevalence of 57% in 243 sera from 83 former blood donors who later developed rheumatoid arthritis, with 47% RF-positive individuals on their first collected sample [16]. In 2004,

*Nielen et al* found a prevalence of 27.8% of former blood donors who subsequently developed rheumatoid arthritis [17]. In 2003, *Rantapaa-Dahlqvist et al* found a prevalence of 19.3% of 98 samples from former blood donors who subsequently developed rheumatoid arthritis [18]. In the present study, titers ranged from 8 to 2048 IU / mL, 2 individuals with high titers (2048 IU / mL). The determination of RF titers is also important in the pathogenesis of the disease and the determination of prognosis [19]. Other factors to be considered are gender, age, smoking, genetic and environmental factors, and the levels of other markers of RA, including Anticitrullinated Peptide Antibody (ACPA). The specificity of ACPAs for RA is high (90-95%) with sensitivity ranging from 40 to 60% [20]. ACPAs generally appear to be present in the serum of RF-positive patients with early RA. *Rantapää-Dahlqvist et al* had demonstrated that ACPA isotypes with IgG isotype frequently found well before the diagnosis of RA. They also demonstrated that immune responses to citrullinated peptides were restricted to a small number of targets in preclinical RP and increased as the diagnosis progressed [18]. The search for this serologic marker is very interesting in our study, unfortunately for lack of means it could not be done.

Our study rejoins the conclusions of many authors who suggest that the incidental detection of RF should lead to clinical vigilance and may be a reference to a rheumatologist. However, RF research tends to follow a clinical suspicion. These authors do not suggest "screening", which means that individuals, particularly young people, are only rarely detected as RF-positive.

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