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# LIPID ABNORMALITIES IN BLACK AFRICAN SUBJECTS WITH RHEUMATOID ARTHRITIS: CASE STUDY AMONGST A SENEGALESE POPULATION.


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**ABSTRACT** This study aimed at determining the lipid profile amongst a population of Black Africans with rheumatoid arthritis. This was a prospective study on a cohort of 49 polyarthritis patients. All of them were submitted to a biological test including lipid parameters.

We noticed a high prevalence of dyslipidemia (63.3%) in polyarthritic patients. Dyslipidemia was correlated with advanced age and presence of hypertension. The increase in total cholesterol was predominant (53.06%) followed by the increase in LDL cholesterol (28.57%). The increase in total cholesterol was significantly correlated with age ($p = 0.005$ $r = 0.395$), PAS ($p=0.005$), PAD ($p=0.005$) and PAM ($p=0.003$). The decrease in HDL cholesterol was the least frequent (2.04%) with an average of 1.62 mmol L. The atherogenic risk was low CT/ HDL = 3.45 and LDL/ HDL = 1.86. No link was found between the age of the disease, inflammatory syndrome, treatment (corticosteroid therapy and immunotherapy) and lipid abnormalities.

Dyslipidemia is common in Black Africans with polyarthritis having a very high HDL cholesterol level, resulting in a low atherogenicity index.


**KEYWORDS** : Rheumatoid arthritis, Lipid abnormalities, Atherogenic risk, Black Africans

**Introduction:**

Rheumatoid arthritis (RA) is a systemic, inflammatory, auto-immune and non-organ specific disease [1]. It is the most common form of chronic inflammatory rheumatism with a prevalence of 0.32% in the French population [2]. In Senegal, like in most Sub-Saharan countries, its prevalence is still unknown. RA is progressively causing bone structural damage, with a risk of deformity and destruction of the joints in the short term. This leads to severe disability and impaired quality of life [3]. Beyond these consequences that compromise quality of life, RA is associated with a reduction in life expectancy by five to ten years [4-6]. This excess mortality is primarily related to an increase in cardiovascular disease. Surprisingly, RA is ranked among cardiovascular risk factors like diabetes [2]. A meta-analysis shows more than 59% increase in cardiovascular mortality for coronary deaths and 52% in deaths related to stroke among patients with RA [7,8]. This risk factor can be explained by different reasons: late diagnosis of RA, inflammatory syndrome, positivity of auto-antibodies (FR, anti-CCP antibodies that have a prognostic effect), the least prevention of cardiovascular diseases and especially an increased risk of atherogenesis through a very atherogenic lipid profile [9]. However, the lipid profile fluctuates over time [10]. Before the onset of the disease, there appears a disturbance of lipid parameters (increase of total cholesterol (CT) and triglycerides) even though the inflammation is not marked (normal CRP) [11]. Plasma HDL-C (HDL-C) plasma levels are generally lower compared to control subjects of same sex and similar age [9,12]. On the other hand, data from the literature are contradictory from one study to another. This discrepancy can be explained by the difference in study populations and especially the methodology adopted by the various authors. The aim of this work is therefore to determine the prevalence and nature of lipid abnormalities among Black African patients with rheumatoid arthritis.

**Patients and Methods:**

This is a prospective, transversal and analytical study carried out from June to October 2016 in the Laboratory of Medical Biochemistry and Molecular Biology at the faculty of medicine of Cheikh Anta DIOP University in Dakar.

The study involved 49 patients aged 18 and above, with rheumatoid arthritis. They were followed up at the Department of Rheumatology of Aristide Le Dantec University Hospital in Dakar, Senegal. The diagnosis of RA was made in accordance with the 2012 ACR-EULAR criteria [13]. The recruited subjects were all briefed on the interest of this study, and gave their written consent. All parameters deemed necessary within this study were reported in a single medical examination. Subjects with RA were excluded but associated with another condition (pregnancy, other connective diseases). Sociodemographic data as well as information on the

disease history were reported using a questionnaire.
For each patient included, the weight and size were registered. The Body Mass Index (BMI) was calculated using the Quetelet formula (BMI = Weight / (height)$^2$).

Systolic (PAS) and diastolic(PAD)High blood pressures were measured after at least 10 min of rest. High blood pressure (HBP) was defined based on the 2007 ESH/ESC recommendations for the management of hypertension.
The average blood pressure (ABP) was determined using the following formula: PAM = (PAS + 2 * PAD) / 3.

All patients were submitted to a biological test including plasma glucose at empty stomach, C-reactive protein (CRP), and lipid balance (Total Cholesterol (TC), HDL-C Cholesterol (HDL-C), LDL cholesterol (LDL-C) and triglycerides (TG)). Serum and plasma obtained after centrifugation in patients at empty stomach for 12 hours, were aliquoted and stored at -20 ° C.

Total cholesterol, HDL-C, triglycerides and blood glucose were enzymatically assayed with Biosystem® reagents. The CRP was determined by immunoturbidimetry. The A25 BioSytem® multiparametric analyzer was used to perform quality control serum (Level I and Level II) analyzes at the beginning and at the end of each series of analysis. The LDL-C level was deduced using the formula of Friedwald Fredricksen. We also calculated the following ratios: CT/HDL (normal <4.85) and LDL / HDL (normal <3.55) to estimate the index atherogenicity.

The presence of rheumatoid factor and citrullinated citric antipeptides (anti-CCP) was investigated in the patient's file. Treatment modalities were based on prednisone 5 mg or 10 mg per day and methotrexate 10 mg or 15 mg per week.

For statistical analysis, we used the SPSS software version 18 and Epi Info 3.5.4. Sociodemographic data were expressed in percentage. Khi$^2$ independence tests allowed to test statistical associations between socio-demographic data. Bivariate, multivariate analyzes and correlation tests were performed to find associations between the different variables. The results of the tests are considered significant when p <0.05.

**Results:**

Forty-nine patients with RA were included in this study. The age average was 42.33 ± 12.46 with extremes of 18 and 69. Subjects aged above 40 were more likely to participate (53.1%). Female predominance was (87.8%) and the sex ratio was 0.14. Personal health history was predominantly hypertensive (24.48%, n = 12). Dyslipidemia was already present in 4 patients (8.16%. These patients were already under cholesterol-lowering therapy). FRCV data are summarized in Table I.

**Table I: Distribution of FRCVs amongst the population.**

| Variables | Numbers | Percentage (%) |
|---|---|---|
| Sedentary lifestyle | | |
| Yes | 44 | 89,8 |
| No | 5 | 10,2 |
| Alcoholism | | |
| No | 49 | 100 |
| Smoking | | |
| No | 49 | 100 |
| | | |
| HTA | | |
| Yes | 37 | 75,5 |
| No | 12 | 24,5 |
| Diabetes | | |
| Yes | 1 | 2,0 |
| No | 48 | 98,0 |
| BMI | | |
| <25 | 32 | 65,3 |
| 25 – 30 | 12 | 24,5 |
| ≥ 30 | 5 | 10,2 |
| **Dyslipidemia** | | |
| Yes | 31 | 63,3 |
| No | 18 | 36,7 |

Of the 49 subjects included, 14 (28.57%) had a family history of rheumatism and 24 (49%) had positive CRP (> 6 mg/l). Citrullinated citric anti-peptide antibodies (anti-CCP) was found in all subjects who were subject to the assay (83.67%, n = 43). Rheumatoid factor was present in 67.34% (n = 33) of the subjects. The average duration of the disease was 55.88 ± 64.82 months (6 - 360 months). All the subjects were under corticosteroid therapy of which 85.71% (n = 42) were under 10 mg prednisone. Methotrexate-based immunotherapy was initiated in 41 patients (83.67%) of which 73.5% were under 15 mg. The average duration of corticosteroid therapy was 18.69 ± 22.87 months (2 - 156 months) whereas it was 18.68 ± 24.61 months (1 - 156 months) for methotrexate.

The average and standard deviation of the quantitative variables are described in Table II as follows.

**Table II : Average values of quantitative variables**

| Variables | Average and standard deviation | Extremes |
|---|---|---|
| Age (years) | 42,33 ± 12,46 | 18 – 69 |
| BMI (kg/m$^2$) | 23,59 ± 5,15 | 15,36 – 37,10 |
| PAS (mm Hg) | 122,04 ± 19,26 | 90 – 170 |
| PAD (mm Hg) | 82,24 ± 11,41 | 70 – 100 |
| PAM (mm Hg) | 95,51 ± 13,29 | 76,67 – 123,33 |
| Blood glucose (mmol / l) | 5,11 ± 2,05 | 3,61 – 18,54 |
| CRP (mg / l) | 13,73 ± 16,72 | 0,16 – 80,99 |
| Cholesterol Total (mmol / l) | 5,43 ± 1,01 | 3,47 – 8,36 |
| HDL-C (mmol / l) | 1,62 ± 0,34 | 0,78 – 2,59 |
| Triglycerides (mmol / l) | 0,96 ± 0,55 | 0,41 – 3,82 |
| LDL-C (mmol / l) | 3,03 ± 0,78 | 1,55 – 5,23 |
| TC / HDL-C | 3,45 ± 0,9 | 2,29 – 7,21 |
| LDL-C / HDL-C | 1,86 ± 0,24 | 1,05 – 2,37 |
| Duration pathology (months) | 55,88 ± 64,83 | 6 – 360 |
| Duration Corticotherapy (months) | 18,69 ± 22,87 | 2 – 156 |
| Immunotherapy duration (months) | 18,68 ± 24,61 | 1 – 156 |

The prevalence of dyslipidemia was 63.27% (n = 31). FIG. 1 illustrates the distribution of lipid profile. It is also noted that 27 new cases of dyslipidemias were diagnosed in the targeted population. This represents a rate of 55.10%.

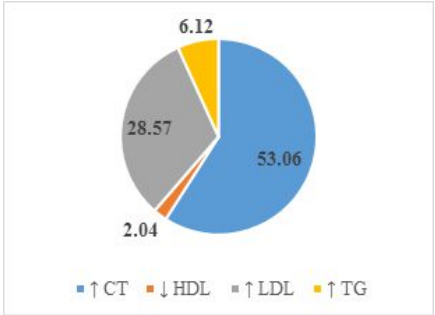


**Figure 1: Distribution of lipid abnormalities in the study population**

The bivariate analysis which results are presented in Table III, helped establish a statistical link between the age range above 40 (p = 0.03), hypertension (p = 0.01) and dyslipidemia.

**Table III: Population characteristics according to dyslipidemia**

| Variables | Modalities | Dyslipidemia | | P | OR (IC) |
|---|---|---|---|---|---|
| | | Yes (%) | No (%) | | |
| Sex | **Female** | 28 (65,1) | 15 (34,9) | 0,38 | 0,53 (0,10 - 2,99) |
| | **Male** | 3 (50,0) | 3 (50,0) | | |
| Age | **< 40 years** | 11 (47,8) | 12 (52,2) | 0,03 | 3,63 (1,07-12,38) |
| | **≥ 40 years** | 20 (76,93) | 6 (23,1) | | |
| APH | **No** | 22 (59,5) | 15 (40,5) | 0,27 | 2,045 (0,47-8,83) |
| | **Yes** | 9 (75,0) | 3 (25,0) | | |
| sedentary | **Yes** | 28 (63,6) | 16 (36,4) | 0,61 | 0,86 (0,13-5,68) |
| | **No** | 3 (60,0) | 2 (40,0) | | |
| CRP | **< 6 mg/l** | 14 (56,0) | 11 (44,0) | 1,15 | 1,91 (0,58-6,23) |
| | **≥ 6 mg/l** | 17 (70,8) | 7 (29,2) | | |
| Rheumatoid factor | **Negative** | 9 (56,3) | 7 (43,8) | 0,5 | 1,56 (0,46-5,29) |
| | **Positive** | 22 (66,7) | 11 (33,3) | | |
| HTAa | **No** | 11 (91,7) | 1 (8,3) | 0,01 | 0,11 (0,01-0,91) |
| | **Oui** | 20 (54,1) | 17 (45,9) | | |
| Obesity | **No** | 26 (59,1) | 18 (40,9) | 0,09 | - |
| | **Oui** | 5 (100,0) | 0 | | |
| Duration of pathology | **< 120 months** | 23 (65,7) | 12 (34,3) | 0,32 | 0,7 (0,20-2,47) |
| | **≥ 120 months** | 8 (57,1) | 6 (42,9) | | |
| Corticosteroid duration | **< 24 months** | 23 (67,6) | 11 (32,4) | 0,92 | 0,54 (0,16-1,89) |
| | **≥ 24 months** | 8 (53,3) | 7 (46,7) | | |
| immunotherapy | **Yes** | 26 (63,4) | 15 (36,6) | 0,63 | 1,04 (0,22-5,00) |
| | **No** | 5 (62,5) | 3 (37,5) | | |
| Immunotherapy time | **< 24 months** | 20 (66,7) | 10 (33,3) | 0,36 | 0,6 (0,15-2,45) |
| | **≥ 24 months** | 6 (54,5) | 5 (45,5) | | |
| Corticosteroid dosage | **5 mg** | 5 (71,4) | 2 (28,6) | 0,48 | 0,65 (0,11-3,75) |
| | **10 mg** | 26 (61,9) | 16 (38,1) | | |
| Immunotherapy | **10 mg** | 4 (80,0) | 1 (20,0) | 0,39 | 0,39 (0,04-8,89) |
| | **15 mg** | 26 (63,4) | 14 (38,9) | | |

HBPPH: High Blood Pressure Personal History; HBP: high blood pressure; CRP: C-Reactive Protein; OR: Odds ratio; IC: confidence interval.

[a] statistically significant relationship

The correlation study between lipid profile and independent factors was helpful within the identification of a positive correlation between total cholesterol, age (p = 0.005 and r = 0.395), BMI (p = 0.048 and r = 0.284), PAD (p = 0.005 and r = 0.398), PAD (p = 0.005 and r = 0.395) and PAM (p = 0.003 and r = 0.419). Triglyceridemia was positively correlated with the duration of the pathology (p = 0.020 r = 0.333).

**Table IV: Characteristics of the population according to the lipid profile**

| Variables | CT | HDL-C | LDL-C | TG | CT/HDL | LDL/HDL |
|---|---|---|---|---|---|---|
| Age | p = 0,005 r = 0,395 | NS | NS | NS | p = 0,047 r = 0,285 | NS |
| BMI | NS | NS | NS | NS | NS | NS |
| NOT | p = 0,005 r = 0,398 | NS | NS | NS | NS | NS |
| PAD | p = 0,005 r = 0,395 | NS | NS | NS | NS | NS |
| WFP | p = 0,003 r = 0,419 | NS | NS | NS | NS | NS |
| Blood Sugar | NS | NS | NS | NS | NS | NS |
| CRP | NS | NS | NS | NS | NS | NS |
| Duration | NS | NS | NS | p = 0,020 r = 0,333 | NS | NS |
| Pathology | NS | NS | NS | NS | NS | NS |
| Corticosteroid duration | NS | NS | NS | NS | NS | NS |

BMI: Body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; ABP: Average Blood pressure; CRP: C-reactive protein; NS: not significant.

A logistic regression for dyslipidemia allowed us to reach the results highlighted in Table V. Concerning the linear regression for total cholesterol, only the PAM had a statistically significant link (p <0.0001)

**Table V: Regression analysis of age and hypertension as a function of dyslipidemia**

| Variables | Modalities | ORaj (IC) |
|---|---|---|
| Age (years) | < 40 | 1 |
| | ≥ 40 | 0,230 (0,594-8,339) |
| HTA | Oui | 1 |
| | Non | 0,064 (0,017-1,498) |

HTA: high blood pressure; ORaj: odds ratio adjusted; IC: confidence interval.

**Discussion:**

Several studies have recently focused on the increased risk of cardiovascular events in RA, leading to excess mortality. Of the incriminated FRCVs, lipid-related troubles count among the main factors, especially in the genesis of the plaques of atheromas. The lipid profile is disturbed in RA with a deleterious side [9]. Assessment of lipid abnormalities in Senegalese PR found a high prevalence of dyslipidemia (63.26%) with a predominance of total hypercholesterolemia (53.06%) followed by hyper LDLemia (28.57%). Hypo-HDL was found only in one patient (2.04%). A study conducted between 2009 and 2010 in Senegalese PRs found a prevalence of 3.1% in 73 patients [14]. An increase in the frequency of dyslipidemia is noted in Senegalese PRs. A high prevalence in the Senegalese population was also found by Singwe-Ngandeu [15] in a study carried out in Cameroon (50%). 27 (55.10%) new cases of dyslipidemias were also diagnosed.

The study of an association between the presence of dyslipidemia and the factors studied correlated only with age (p = 0.03) and hypertension (p = 0.01). It appears that the occurrence of dyslipidemia is related to the presence of hypertension and advanced age in Senegalese PRs, although the link found does not allow us to identify which of dyslipidemia and HTA precedes the each other.

Analysis of lipid profile and other factors resulted in a positive correlation between TC and age (p = 0.005 and r = 0.395), PAS (p = 0.005 and r = 0.398), PAD = 0.005 and r = 0.395), PAM (p = 0.003 and r = 0.419), BMI (p = 0.048 and r = 0.284). Triglycerides were positively correlated with the duration of the disease (p = 0.020 and r = 0.333). These results show that, in addition to advanced age, an increase in blood pressure levels leads to an increase in total cholesterol, especially with an increase in PAM (p <0.0001).

These results show the importance of an overall PEC of all FRCVs in

RA, especially as 27 (55.1%) new cases of dyslipidemias were diagnosed and only half of the 12 (24.5%) patients with a history of hypertension had good control of blood pressure.

The average TC value (5.43 mmol / l) in our population was higher compared to other studies. Akrout et al. [9] found 4.5 mmol / l and explained this decrease by the low level of HDL-C (0.92 mmol / l). This increases the intracellular concentration of cholesterol and decreases its plasma concentration. Ruyssen et al found cholesterol at 4.86 mmol / l [16] in a meta-analysis of FRCVs associated with low-dose corticosteroids.

Several studies report a variation in triglyceridemia during RA. This can be increased [9,17] or lowered [18]. In our study, its mean value was normal and its increase was correlated with the age of the disease. In other studies, the age of the disease was related with LDL-C. Georgiadis et al. [17] found a correlation with the increase in LDL-C whereas the Cisternas study [18] fond a correlation with the decreased of LDL-C. We can therefore conclude that lipid profile, in addition to varying during the disease, also varies according to study populations. This could be explained by the involvement of environmental factors.

In rheumatoid arthritis, HDL-C is generally lowered [9,12]. In our study, the rate found was higher (1.63 mmol / l), compared to the average PR group (0.92 mmol / l) and even the control group (1.29 mmol / l) reported in the study of Akrout et al. [7]. In his meta-analysis, Ruyssen found a rate of 1.03 mmol / l [12]. The increase of this anti-atherogenic factor in our population results in a low atherogenicity index (CT / HDL = 3.45 and LDL / HDL = 1.85) in Senegalese PRs despite the prevalence of hypercholesterolemia and of hyperLDemia. In his case-control study, Akrout found the following values (CT / HDL = 5.32 and LDL / HDL = 3.57). The rate of CT / HDL was weakly correlated with age ($p = 0.047$ and $r = 0.285$) in our study. It appears that the PR of the African black subjects is less atherogenic. This low risk involves the use of a descriptive multicentric study with an intima media thickness (IME) measurement which is an excellent marker for the early onset of atherosclerosis.

In addition, there was no correlation between lipid profile, corticosteroid therapy, immunotherapy, and inflammation. Our results confirm the discrepancy in the involvement of inflammation in the occurrence of dyslipidemia in RA [9,19]. Although subjects with positive CRP had more dyslipidemia (70.8%, n = 17), there was no relationship between the two variables ($p = 1.15$). The study of Walberg [12] found that the increase in CRP was correlated with a decrease in protective factors (Apo A1 and HDL-C) whereas the study of Dursunoglu et al found a correlation with the increase in atherogenic factors [19]. Indeed, in RA the systemic inflammation could favor the endothelial dysfunction and the development of atheromatous plaques likely to increase CV risk [1,20]

PEC and RA with corticosteroids are likely to increase in the prevalence of CVD with cardiovascular excess mortality [21]. The increased risk of cardiovascular events associated with corticosteroid therapy has been demonstrated and depends on the posology [22]. In our study, patients under 10 mg of prednisone (85.7%, n = 42) had more dyslipidemia (53.06%, n = 26) without finding a link between the variables ($p = 0.48$). Dessein et al also found no link between dyslipidemia and corticosteroids [22].

The comparative study of Del Rincon on the effect of corticosteroid therapy in RA showed the presence of carotid plaques with hypercholesterolemia in patients with more than 16 mg of corticosteroid [23]. Other authors [24,25] have found an increase in HDL-C in patients with low-dose corticosteroids, whereas the study of Westhovens et al [26] reported a decrease in CT, LDL -C and triglycerides. Low-dose corticosteroids improve the structural lesions of RA and the lipid profile making it less atherogenic with an increase in HDL-C [27].

Methotrexate (MTX) reduces cardiovascular disease deaths by more than 70% compared to patients who were not on MTX [28]. In a retrospective study of 6707 patients with RA, Prodanowich et al [29] found 35% decrease in cardiovascular incidents in patients taking a low dose of MTX. Other authors have also found a decrease in the frequency of dyslipidemia and CV complications in patients with low-dose MTX [9,24]. MTX has demonstrated to be effective in reducing CV risk due probably to the long-term suppression of systemic inflammation [1]

In our study, no relationship was established between dyslipidemia and immunotherapy. Similarly, neither the duration nor the dosage of immunotherapy influences the occurrence of dyslipidemia in patients on methotrexate. However, a predominance of dyslipidemia (53.06%, n = 26) was found in patients under 15 mg of MTX.

## Conclusion:

Dyslipidemia is common in Senegalese RAs with a lower atherogenic risk, due to high HDL-C. However, the presence of another FRCV and advanced age seem to increase its prevalence. Therefore, a more global and better oriented management could significantly reduce the occurrence of cardiovascular complications by improving the lipid profile during the occurrence of RA in Black African subjects.

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