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RESEARCH ARTICLE

POLYUNSATURATED FAT IS ASSOCIATED WITH SUBCLINICAL INFLAMMATION IN WOMEN WITH OVERWEIGHT

Djeyne Silveira Wagmacker, M.Sc[1,2,*], Amanda Silva Fraga[2], Lilian Brito Lima[1], Patrícia Sobreira Alves[1], Luzete Fernandes Santos[1], Jessica Layane Vilhena Ferreira[1], Jaqueline Barbosa Moreira[1], Jefferson Petto, M.D, PhD[1,2,3,4], Luiz Erlon Araujo Rodrigues, M.D, PhD[2] and Ana Marice Ladeia, M.D, PhD[2,5]

[1]College of Adventist Bahia, Bahia Brazil
[2]Bahian School of Medicine and Public Health, Science Development Foundation of Bahia, Salvador, BA, Brazil
[3]Social College of Bahia, Salvador, BA, Brazil
[4]Salvador University, Salvador, BA, Brazil
[5]Catholic University of Salvador, Salvador, BA, Brazil

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ABSTRACT

Introduction: The inflammation process is considered as a central factor with in the aspects that atherosclerosis. Several factors can affect the vascular inflammatory disease, such as dietary and metabolic patterns. **Objective:** to verify if there is an association between subclinical inflammation and dietary and metabolic factors in women with overweight. **Methods:** 66 women with overweight (BMI = 29±4,3kg/m^2), sedentary with the age of 24±4.1 years. Lipid profile, insulin and C-reactive protein (CRP) were dosed after fasting. The nutrition survey was made through the 24-hour recall. Subclinical inflammation defined by levels of CRP>3,0mg/L. It was utilized *t*-tests for independent samples, Spearman' rho, multivariate logistic regression, as significance level p<0,05. **Results:** Women with vascular inflammation present higher values of blood glucose levels85±8,1vs 83±7,9mg/dL (p=0,02) and BMI of32±5,6 vs 28±3,2kg/m^2 (p=0,02), reduced intakeofpolyunsaturatedfats6±5,2 vs 10±8,1% (p=0,03) andfibers13±5,0 vs 20±13,8g/day (p<0,01). After the analysis of logistic regression, remained as independent decisive factors: the BMI (OR=1,2, IC95% 1,1-1,5) and the total intake of polyunsaturated fat (OR=0,8 IC95% 0,7-0,8). **Conclusion:** In women with overweight, the total polyunsaturated fats in take is a protective factor, while increasing BMI is an independent predictor factor for the development of the subclinical inflammatory condition.

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INTRODUCTION

The inflammation process is considered a central factor within the aspects that determine atherosclerosis, both in relation to the development and to the progression. Several factors can affect the vascular inflammatory disease, including dietary and metabolic patterns (Francisco *et al*., 2006). The C-reactive protein (CRP) is the inflammatory marker of the acute phase more used in the clinical practice, participating actively in the pathogenesis of atherosclerosis, besides being a predictor of cardiovascular events (Francisco *et al*., 2006; Silva, 2012).

Corresponding author: **Djeyne Silveira Wagmacker, M.Sc,** College of Adventist Bahia, Bahia Brazil.

The hypertrophy or hyperplasia of the adipose tissue has been related to an increase of the CRP concentrations (Visser *et al*., 1999). Although considering the complexity of the physiological mechanisms involved with obesity, it is understood that adipocytes produce cytokines as Tumor Necrosis Factor alpha (TNF-α) and Interleukin 6 (IL-6). Once in the bloodstream, they stimulate the hepatocytes to produce acute phase proteins of inflammation, such as CRP. This protein can be increased in response to organic injuries even before appearing clinical manifestations of a concomitant cardiovascular disease (Brasil, 2007). The consumption of lipids also can be a control factor or an inflammatory stimulus (Lopez-Garcia *et al*., 2004; Niu *et al*., 2006). The polyunsaturated fats, for example, are considered precursors of eicosanoids and other anti-inflammatory mediators that could

avoid several pathological conditions, including cardiovascular diseases (De Roos *et al*., 2009). Nevertheless, until this moment, results about the actions of fatty acids in the inflammatory process are not yet conclusive (Saravanan *et al*., 2010). Thus, more studies are necessary in order to clarify the role of diet and other risk factors in the induced inflammatory response in individuals with cardiovascular risk. Therefore, the objective of this article is to verify if there is an association between subclinical inflammation and dietary and metabolic factors in women with overweight.

METHODS

Design and population study: Analytical observational study with participants from Clínica Escola of the Adventist University at Bahia, in the city of Cachoeira, BA, Brazil. The samples were collected between September 2015 and May 2016. All participants registered in the Physiotherapy service at Clínica Escola, who presented body mass index (BMI) above 24.9kg/m^{2}were invited to participate in the study. Sixty-six volunteers fulfilled the inclusion criteria, which were: age between 18 and 30 years, BMI>24.9kg/m^2 and being sedentary. The sedentary lifestyle was determinate based on the international physical activity questionnaire – long version (Matsudo *et al*., 2001). Were excluded individuals that presented cardiovascular disease, metabolic disorder, alcohol abuse or tobacco smoking history; use of hypolipidemic agents, corticosteroid, diuretic, beta-blockers, contraceptive pills, hypothyroidism, renal parenchymal disease or diabetes mellitus.

Instruments

Data collectionprotocol: The data collection protocol was divided into 4 parts: application of the standard questionnaire, physical examination, 24-hour recall, blood collection. The volunteers selected answered initially to the standard questionnaire and were subjected to a physical examination. The physical examination included body mass index and stature. It was calculated body mass index (BMI) from weight and height by Quetelet's equation: BMI=weight (kg)/ height²(m). The waist circumference was measured with an inelastic tape at the midpoint between the iliac crest and the lastrib . The hip was measured at the greatest circumference of the gluteus.

24-Hour Recall: The patients were evaluated in relation to their diet in the day before the exam through a 24-hour recall. The 24-hour recall was made through an interview realized in the moment of blood collection, in which the volunteers answered about what they had consumed in the day before the interview – concerning the three main meals and the snacks. The same examiner applied this instrument, and in order to facilitate the answers, cooking measures were used[10]. The quantitative assessment of the diet was executed with the software *avanutri revolution*. In order to analyze data, micronutrients consumption (vitamins and minerals), cholesterol, saturated, total monounsaturated and polyunsaturated fat, total dietary fiber were considered using SBC parameters (Fisberg, 2002).

Procedures

Blood collection and metabolic profile: The volunteers were subjected to blood collection after a 12 hours fasting. 5ml of blood in tubes with edta were collected and centrifuged at a speed of 3000 rotations/min for 10 minutes. The analysis of serum were made in the following way: the high-sensitivity CRP was made by nephelometry. Glycemic and fasting total cholesterol levels were made through dry slide method for blood glucose and dry for cholesterol. HDL cholesterol was measured by the cholesterol analysis method with an hdl *vitrus* kit. Triglycerides (TG) were analyzed by dry slide method and the LDL was calculated by friedwald equation (Sposito *et al*., 2007). The Homa-IR index of insulin resistance was calculated by the equation proposed by Matthews *et al*. (1985). The individuals were classified as presenting subclinical inflammation when with CRP>3,0mg/L (Ghiringhello *et al*., 2006).

Ethical aspects: The study was submitted to the Research Ethics Committee of the Adventist University at Bahia and was approved under the protocol34017514.5.0000.0042. The guidelines about research with humans of the resolution 466/2012 of the Brazilian National Health Council were observed during the whole study.

Statistical Analysis: The data were previously analyzed in relation to symmetry by kolmogorov- smirnov test. The C-reactive protein (CRP) did not present normality criteria. The results were expressed by mean ± standard deviation or medians, and interquartile interval according to variable distribution. The significance level was defined by the value of $p<0.05$. Spearman' rho was made between CRP and predictor metabolic and dietary factors. The variables that presented a statistical significance (blood sugar, insulin, HOMA, BMI, consumption of total polyunsaturated fats and fibers) were included in the logistic regression model. The calibration of the model was tested by Hosmer–Lemeshowtest and it was calibrated ($p= 0.07$). Data were analyzed using the software statistical package for the social science (spss) version 14.0.

RESULTS

It was included in the analysis 66 young women with age between 24 ± 3.6 years old, BMI of 29 ± 4.3Kg/m^2, with lipid profile and with no alterations in the metabolic profile. The clinical characteristics evaluated are described in Table 1.In Table 2, It is depicted the mean consumption of vitamins, minerals, total polyunsaturated fats and fibers in women with overweight. As described in table 3, women with vascular inflammation presented higher blood sugar values(85 ± 8,1 vs 83 ± 7,9mg/dl) ($p= 0.02$) and BMI (32 ± 5.6; 28 ± 3.2kg/m^2) ($p= 0.02$), less consumption of polyunsaturated fats(6 ± 5.2; 10 ± 8.1%) ($p= 0.03$), and fibers (13 ± 5.0 vs 20 ± 13.8g/day) ($p= 0.01$). There were not differences between HDL, LDL, total cholesterol and triglycerides values (Table 3). When the relation between metabolic and clinical aspects with CRP was analyzed, a positive correlation between CRP and HOMA ($r= 0.42$; $p= 0.01$), insulin and inverse with fibers was found. Association with other clinic-metabolic variables was not found (Graphics 1, 2 and 3). Multivariate logistic regression was made between CRP and the variables that presented a statistical significance in the univariate analysis (blood sugar, insulin, HOMA, BMI, polyunsaturated fats, and fibers). Remained as independent predictor variable for vascular inflammation the variables BMI ($OR= 1.27$; $IC= 1.079 – 1.505$) and consumption of total polyunsaturated fats ($OR= 0.870$; $IC = 0.768 – 0.987$), the last one presenting itself as a predictor factor (Table 4).

Table 1. Clinical and anthropometric characteristics of the sample (n=66).

VARIABLES	VALUES
Age (years)	24±3,6 *
Body Mass Index (kg/m^2)	29±4,3*
Triglyceride (mg/dL)	94±43,5*
Total cholesterol (mg/dL)	162±32,3*
High-densitylipoprotein (mg/dL)	49±10,2*
Low-densitylipoprotein (mg/dL)	94±28,2*
Blood Sugar (mg/dL)	84±8,4*
Insulin (mcIU/mL)	10±4,9*
HOMA	2,4±1,2*
C-reactive protein basal level (mg/L)	1,1 (0,2 - 3,9)#
Inflammation	n (%)
CRP > 3,0 (mg/L)	46 (72)
CRP ≤ 3,0 (mg/L)	18 (28)

*Mean ±SD #median (interquartileinterval).

Table 2. Dietary profile of women with alterations on body weight (n=66).

VARIABLES	VALUES
Vitamin A (RE/day)	262 (130 – 553)#
Vitamin D (mcg/day)	0,4 (0,1 - 1,1) #
Vitamin B1 (mg/day)	1±1,6*
Vitamin B2 (mg/day)	0,7±0,5*
Vitamin B5 (mg/day)	1,4 (0,9 - 2,2) #
Vitamin B6 (mg/day)	0,5 (0,3 – 1,2) #
Vitamin B12 (mg/day)	0,7 (0,1 – 1,8) #
Vitamin C (mg/day)	66 (18 – 213) #
Vitamin E (mg/day)	7,3 (2,8 – 15,2) #
Folic Acid (mcg/day)	60 (27 – 104) #
Calcium (mg/day)	346±262,5*
Phosphorus (mg/day)	604±314,5*
Iron (mg/day)	9,5 (6,7 – 13,8) #
Magnesium (mg/day)	124±69*
Zinc (mg/day)	4,6±3,5*
Selenium (mcg/day)	27 (13,9 – 56,6) #
Manganese (mg/day)	0,9 (0,6 – 1,6) #
Potassium (mg/day)	1119±620,6*
Sodium (mg/day)	2119±1400,7*
Cholesterol (mg/day)	156±152,5*
Saturated fat (%)	17±12,7*
Polyunsaturated fat (%)	8±7,4*
Monounsaturated fat (%)	10±7,3*
Fibers (g/dia)	17±12,3*

*Mean ±SD #median (interquartileinterval).

Table 3. Comparison of anthropometric, laboratory and dietaries aspects of the analyzed sample (n=66).

Variables	GVI Mean ±SD/ Median (IQR)	GWVI Mean ±SD/ Median (IQR)	P-value
Age (years)	24±2,9	24±3,9	0,93
BMI (Kg/m^2)	32±5,6	28±3,2	0,02*
Blood sugar (mg/dL)	84±8,1	83±7,9	0,02*
Insulin (mcIU/mL)	11±4,3	39±5,1	0,14
HOMA	2,7±1,2	2,2 ±1,2	0,11
Cholesterol (mg/dL)	154±26,9	163±33,6	0,29
Triglycerides (mg/dL)	96±40,9	92±45,5	0,71
HDL (mg/dL)	45,9 ±7,1	49,6±11,1	0,18
LDL (mg/dL)	88,4±24,7	95,1±29,1	0,39
Vitamin A (RE/day)	234 (115-625,7)	271 (150,2 – 564,8)	0,56
Vitamin D (mcg/day)	0,2(0,1 – 1,7)	0,4 (0,1 – 1,0)	0,11
Vitamin B1 (mg/day)	0,8 (0,4 - 1,2)	0,75 (0,5 – 1,3)	0,92
Vitamin B2 (mg/day)	0,7±0,6	0,6±0,3	0,52
Vitamin B5 (mg/day)	1,7 (0,8 – 3,3)	1,4 (0,9 – 2,1)	0,10
Vitamin B6 (mg/day)	0,4 (0,3 – 1,2)	0,6 (0,3 – 1,2)	0,60
Vitamin B12 (mg/day)	0,4 (0,0 – 2,1)	0,8 (0,2 – 1,6)	0,77
Vitamin C (mg/day)	47 (6,5 – 200,1)	87 (24,1 – 227,7)	0,97
Vitamin E (mg/day)	5 (2,5 – 8,8)	11 (2,9 – 16,2)	0,43
Folic Acid (mcg/day)	68±60,32	93±92,3	0,32
Calcium (mg/day)	392±321,7	328±242,4	0,39
Phosphoro (mg/day)	537±334,7	644±304,1	0,22
Iron (mg/day)	9,6 (6,4 – 11,3)	10,4 (6,7 – 15,3)	0,87
Magnesium (mg/day)	108±60,1	132±72,9	0,74
Selenium (mcg/day)	24 (13 – 55)	27 (14 – 58)	0,16
Sodium (mg/day)	2472±1698,2	2043±1246,2	0,27
Potassium (mg/day)	936±639,6	1216±604,5	0,10
Cholesterol (%)	95 (28 – 178)	126 (44 – 233)	0,53
Polyunsaturated fats (%)	6±5,2	10±8,1	0,03
Monounsaturated fats (%)	6,1 (4,0 – 12,9)	10,4 (6,1 – 14,6)	0,38
Fibers (g/dia)	12,7±5,0	19,76±13,8	<0,01

IQR – Inter quartile interval; GVI – Group with vascular inflammation; GWVI – Group without vascular inflammation

Table 4.Predictor variables of vascular inflammation of the sample (n=66).

	OR*	CI95%	P-value
Blood Sugar (mg/dL)	0,931	0,832 – 1,041	0,21
Insulin (mcIU/mL)	0,898	0,589-1,369	0,61
HOMA	2,421	0,363 – 16,164	0,36
BMI (Kg/m^2)	1,275	1,079 - 1,505	<0,01
Polyunsaturated fats (%)	0,870	0,768 – 0,987	0,03
Fibers (g/day)	0,936	0,850 – 1,032	0,18

*Odds Ration

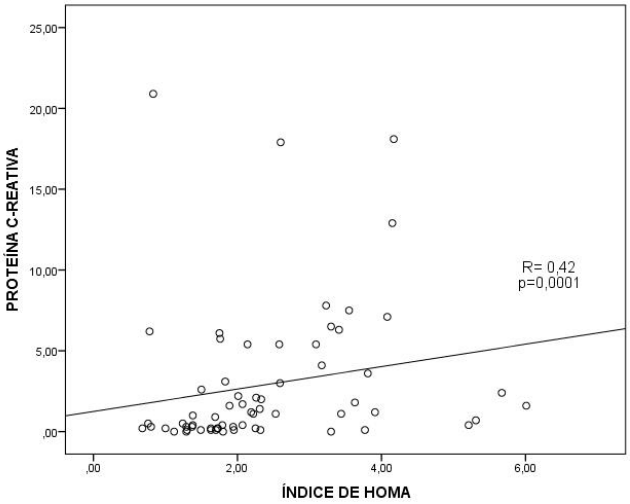

Figure 1. Correlation between C-reactive Protein and HOMA

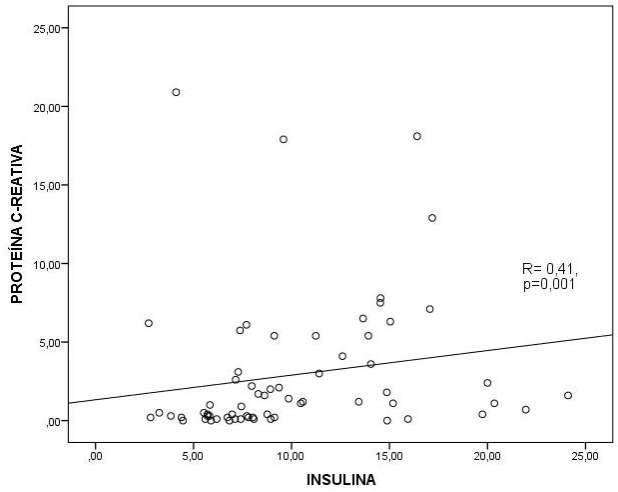

Figure 2. Correlation between C-reactive Protein and insulin

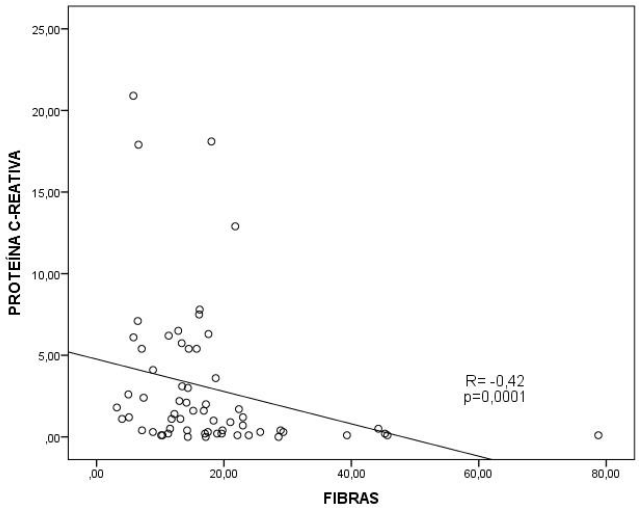

Figure 3. Correlation between C-reactive protein and Fibers

DISCUSSION

Based on the results of this research it is possible to observe that women with overweight who consume more polyunsaturated fats present a lower subclinical inflammatory profile. From this, some points will be presented and discussed. It is observed in the population studied unaltered dietary profile according to Dietary Reference Intake (DRI)[14] with vitamin deficiencies especially of vitamins A, D, B6, B12, C and E, as well as mineral deficiency of iron, zinc, and potassium, besides a high consumption of polyunsaturated fats and fibers. It is suggested that dietary pat terns marked by low in take of high-fiber foods, by an increase in the consumption of trans fat, and by consumption of foods with high glycemic index could be the responsible for an activation of the immune system, which leads to over production of proinflammatory mediators with concomitant reduction of anti-inflammatory mediators (Geraldo, 2008). Studies have demonstrated that excess of body weight is associated with high CRP values (Visser *et al*., 1999; Wu *et al*., 2010). In this study, it was possible to identify the subclinical inflammation in women with overweight, and, based on this value, they were characterized as with medium risk to cardiovascular disease (Amezcua-Guerra *et al*., 2007). It is known that the inflammatory condition can be the responsible for the development, progression, and outcome of the atherosclerotic process, which is considered a precursor of cardiovascular diseases (Hermann, 2001). Despite that, there are several inflammatory biomarkers; the CRP has been the biomarker of the inflammatory process most largely studied (Kinlay, 2006; Calabrò *et al*., 2009).

The groups with and without inflammation were compared and it was possible to observe those volunteers who presented subclinical vascular inflammation, that is, CRP higher than 3mg/L, had higher glycemic values and BMI. The increase of CRP related to BMI is based, among other aspects, in the fact that adipose cells produce pro inflammatory cytokine that stimulates the production of the CRP by the liver – which explains the association between obesity and CRP[21]. However, the elevation of plasma glucose affects the oxidative stress initiating the inflammatory response, which leads to the concomitant CRP increase (Monnier *et al*., 2006). It is also noticed a lower consumption of total polyunsaturated fats and fibers in the CRP group higher than 3mg/L. Different studies presented a relation between the consumption of fibers and an improvement of the inflammatory state, despite the consumption of fibers did not present itself as an independent variable to subclinical inflammation (Delzenne, 2005; Ajani *et al*., 2004). The mechanisms through which the consumption of fibers reduces the concentration of CRP were not yet clarified. However, it is considered the possibility that the fiber slows the absorption of blood sugar and the modulation of cytokine, attenuating hyperglycemic, oxidative stress and favouring the response of the intestinal flora with the production of the anti-inflammatory cytokine. Only the intake of polyunsaturated fats and BMI remained as determining variables for subclinical inflammation when logistic regression was made between variables that presented statistical significance in the univariate analysis. The relation between weight gain and the increase of inflammatory response is well explored in the literature[3,4]. However, the relation between inflammation and consumption of polyunsaturated fats such as alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) presents conflicting results and still needs confirmation about its real effects (Lopez-Garcia *et al*., 2004; Rallidis *et al*., 2003; Madsen *et al*., 2001; Chan *et al*., 2002). Besides the conflicting results, studies demonstrate that consumption of polyunsaturated fat is an important anti-inflammatory factor, which can act as a precursor of eicosanoids and other anti-inflammatory mediators, being able to improve several pathologic conditions including the cardiovascular (Lopez-Garcia *et al*., 2004; Niu *et al*., 2006). Rallidis and cols[25] observed a significant reduce in the CRP levels and IL-6 after ALA supplementation, whilelinolenic acid (LA) did not affect the concentrations of inflammatory markers. Although observational studies suggest an inverse correlation between fish consumption or fish oil with high polyunsaturated fat (EPA and DHA) and the levels of inflammatory biomarkers (Lopez-Garcia *et al*., 2004; Madsen *et al*., 2001), intervention studies did not confirm these effects (Chan *et al*., 2002).

Conclusion

According to results of this study, BMI and total intake of polyunsaturated are independent predictors of subclinical inflammation in women with an excess of body weight, the consumption of polyunsaturated fats being a protector mechanism, and the increase of BMI a trigger mechanism. The association with other variables, such as consumption of fibers, glycemic levels, insulin, HOMA suggests a multifactorial aspect in the genesis of the inflammatory response in women with overweight.

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Glossary of abbreviations

Alpha-linolenic acid	ALA
body mass index	BMI
C-reactive protein	CRP
Dietary Reference Intake	DRI
Docosahexaenoic acid	DHA
Eicosapentaenoic acid	EPA
Interleukin 6	IL-6
National Council for Scientific and Technological Development	(CNPQ)
Triglycerides	TG
Tumor Necrosis Factor alpha	TNF-α
Whilelinolenic acid	LA

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