RESEARCH GROUP IN CARDIOVASCULAR DISEASES

MICROALBUMINURIA IS NOT ASSOCIATED WITH ENDOTHELIAL DYSFUNCTION IN OBESE AND OVERWEIGHT WOMEN, BUT IS STRONGLY CORRELATED WITH FASTING GLYCEMIA

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Abstract
This study aimed to evaluate the association between endothelial dysfunction and microalbuminuria levels in overweight and obese women. **Methods:** This cross-sectional study analyzed secondary data of patients with BMI ≥ 25 Kg/m^2 who had microalbuminuria and endothelial function test already performed and inserted into the survey database. The endothelial function was evaluated by reactive hyperemia test (endothelium-dependent vasodilation). **Results:** This study included 41 women aged of 53 ± 11 years, BMI of 32.56 ± 5.06 Kg/m^2, WC of 100.36 ± 23.21 cm. There was no correlation between microalbuminuria and endothelial function. A multivariate logistic regression analysis identified glucose fasting ($\beta = 0.804$; $p < 0,00,1$) and HDL ($\beta = -0.309$; $p = 0.048$) levels as independent predictors of microalbuminuria. **Conclusion:** Microalbuminuria is not useful as a marker of subclinical atherosclerosis in this population, however can be associated to glucose fasting and HDL levels.

Keywords: Obesity; Endothelial dysfunction; Microalbuminuria; Atherosclerosis; Flow-mediated dilation.

INTRODUCTION

The increasing prevalence of atherosclerotic diseases has been an interesting study issue, nowadays.[1] In the 90's, endothelial function test was created to identify subclinical atherosclerosis by evaluating the flow mediated vasodilatation (FMD), which is endothelium dependent.[2] In the other hand, microalbuminuria (mALB) is a precocious marker of renal vascular harm, an independent marker of cardiovascular disease and has been correlated with generalized vascular compromise.[3-11] This study aimed to evaluate the association between mALB and endothelial function in women with overweight/obesity, as well as the correlation between mALB and anthropometric and metabolic variables.

METHODS

This cross-sectional study included overweight or obesity women treated in an outpatient basis by a multidisciplinary team. These patients had mALB levels and endothelial function evaluated already made and entered into the database of a "clinical and epidemiological aspects of obesity" survey, in progress.

After signing the informed consent form, patients were evaluated by interview and physical examination that included measures of body mass index (BMI), waist circumference (WC) and blood pressure (BP).

Microalbuminuria dosage was performed in an isolated sample of the first morning urine to avoid diurnal variations. The normal range was 30-199 mg/dL. Fasting glucose and lipids were measured with 12-hour fast.

Endothelial function (EF) assessment was performed by an echocardiographist physician by high-resolution ultrasound VIVID 3. After 30 minutes rest, the subjects had been lying in supine position for 10 min in a stable-temperature room and then was performed a baseline measurement of brachial artery diameter (BAD) in a longitudinal section (2 – 15 cm above the elbow). Reactive hyperemia was induced by occluding arterial blood using a sphygmomanometer, positioned on the forearm and insufflated to 50 mmHg above the systolic pressure. After 5 min, the cuff was released. Arterial flow velocity was measured by a pulsed Doppler signal at a 60-degree angle to the vessel, during the resting scan and for 15 s after the cuff deflated. The artery was scanned for 30 s before and 120 s after cuff release.[12,13] Every patient had at least 4-hour fast.

All the exams were recorded and analyzed by the same physician who performed the exam and blinded to the patient's mALB levels. The BAD was measured from the anterior to posterior wall, with reference to the line between media

and adventitia layers ("M line"). The mean diameter was calculated from measurements of three cardiac cycles coincident with the R wave on the electrocardiogram. Diameter changes were derived as percentage changes relative to the first scan. Flow-mediated dilation (FMD); mean flow velocity during reactive hyperemia (FMV); and absolute change in flow-mediated dilation (ΔFMD) were considered predictive variables of EF.

The statistical analysis was performed using a SPSS version 14. Variables were expressed by mean ± sd or by median and interquartile in dependence on of their distribution. Comparisons between means or medians were performed by Student's T test for independent samples or Wilcoxon-Mann-Whitney test. Correlations were performed by Spearman test or by multivariate logistic regression analysis stepwise method.

RESULTS

Forty-seven patients met the criteria of having mALB and EF test in the database. Six patients were excluded because their EF test had a quality of images unsuitable for analysis. Table 1 shows the clinical and demographic characteristics of 41 women aged of 53±11 years; non-smoker; predominantly non-white; BMI of 32.56±5.06 Kg/m^2 and WC of 100.36±23.21cm.

Table 1 – Clinical and Demographic Characteristics of Population (n = 41)

Age (years)	53.27 ± 11.63
Ethinicity[a]	
White, *n* (%)	4 (10.0%)
Non-White, *n* (%)	36 (90.0%)
BMI[a] (Kg/m^2)	32.56 ± 5.06
WC[a], mean ± SD, (cm)	100.36 ± 23.21
SBP[a] (mmHg)	134.88 ± 20.28
DBP[a] (mmHg)	86.20 ± 10.36
mALB[c], median/Interquartile range	3.95/2.7
FMV (cm/s),	56.33 ± 24.45
FMD (%)	8.56%± 5.07%
ΔFMD[c]	0.302 ± 0.173
Fasting Glucose (mg/dL)[c]	112.56 ± 41.46
Total Cholesterol(mg/dl)[c]	202.18 ± 37.53
Triglycerides (mg/d)[d]	128.78 ± 65.58

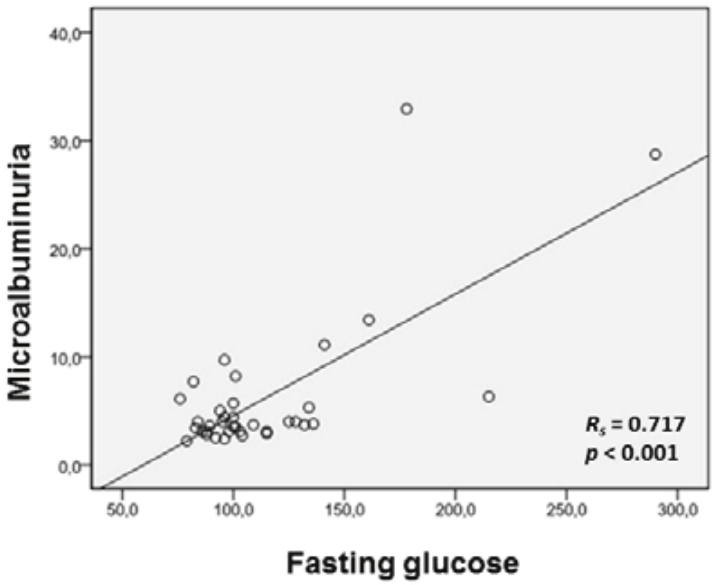
LDL[d]	130.61 ± 32.76
HDL[d]	46.65 ± 11.63

N, n: Sample number; BMI: Body mass index; WC: waist circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; mALB: Microalmuminuria; FMV: Flow-mediated mean velocity in reactive hiperemia; FMD: Flow--mediated vasodilation; ΔFMD: Absolute difference between arterial basal diameter and arterial diameter after reactive hiperemia; LDL: Low-density lipoprotein; HDL: High-density lipoprotein. [a]N = 40; [b]N=35, [c]N=38,[d]N=37.

There was no correlation between mALB and: FMD (r_s = 0.183/p = 0.27), ΔFMD (r_s = – 0.11/p = 0.52). Although, when the groups were dichotomized by the median of mALB (4mg/dl), the group over the median had higher FMD (10.85 ± 5.28% vs 7.22 ± 4.78%; p=0.04) and ΔFMD (0.36 ± 0.17 vs 0.24 ± 0.15; p=0.04).

No correlation was also observed between mALB and lipid profile: Total Cholesterol (p = 0.893); triglycerides (p = 0.687); LDL (p = 0.667); HDL (p = 0.931). In the other hand, mALB was inversely correlated with waist circumference (r_s = -0.39; p = 0.015) and positively with fasting glucose (r_s = 0.717; p < 0.001) (Figure 1).

Figure 1- Correlation Between Microalbuminuria and Fasting Glucose



In order to test the power of the associations found in the univariate analysis, a multivariate linear regression with stepwise method was used. Only fasting glucose (beta = 0.804, p <0.001) and HDL (beta = -0.309, p = 0.048) were independent predictors of microalbuminuria

DISCUSSION

The population of our study was exclusively female, non-smoker, mostly obese with abdominal adiposity. The mALB median was 3.95 mg/dL, value within the normal range. The prevalence of increased mALB has large variability between different studies, ranging from 5% to 40%.[6, 14, 15, 16, 17, 18] Interestingly, although the average value of mALB is within normal parameters and may reflect a population with slightly altered glucose (112.56 mg/dL ± 41.46 dL), glucose was the best marker of elevated microalbuminuria.

Impaired FMD is a marker of endothelial dysfunction and could indicate subclinical atherosclerosis.[2] In this study, endothelial function was lightly impaired (FMD = 8.56% ± 5.07%), which may represent an initial vascular harm.[19, 20] However, no correlation was observed between EF and microalbuminuria.

In contrast, Ladeia et al in a cross-sectional study that included 18 type 1 diabetic patients and 14 control subjects showed a negative correlation between mALB and FMD.[12] It is important to emphasize that our sample shows normal levels of microalbuminuria and no significant impairment of endothelial function. Even when mALB were dichotomized, we observed a positive association with FMD, fact without a biological plausibility, this association not remained after multivariate regression.

It is noteworthy that multivariate linear regression for Microalbuminuria included other variables imbricated in the genesis of vascular aggression (TC, TG, LDL, HDL, BP, fasting glucose). However, only a fasting glucose and HDL were independently correlated with microalbuminuria. Unlike us, other authors demonstrated higher levels of mALB on the hypertensive group when compared to non-hypertensive group.[20-23]

The strong correlation between mALB and fasting glucose ($r_s = 0.717$; $p < 0.001$) is consistent with what is suggested by literature, which associate mALB in diabetic and pre-diabetic subjects to a high cardiovascular risk condition, including those subjects with an impaired endothelial function.[2,24-26]

Therefore, in obese women, microalbuminuria was not useful as a marker of subclinical atherosclerosis. This finding opens the possibility for two propositions: 1) mALB is definitely not associated with endothelial function; 2) the study population did not have a level of mALB sufficient to harm endothelial function. On the other hand, although not the main subject of our study, there was a correlation of average impact between HDL and microalbuminuria. This association is relatively new, and may represent a further step in understanding the initial vascular aggression.

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