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Case Report

C Reactive Protein And Obesity In Type 2 Diabetes Mellitus Patients From The Dicariva Study

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Abstract

Obesity is a very prevalent condition in Type 2 Diabetes Mellitus (T2DM) patients. A low-degree inflammation is also prevalent in T2DM patients. However, the conjoint effect of obesity and elevated waist perimeter (WP) on C reactive protein (hs-CRP) has been scarcely reported. Present study aims analyzing the hs-CRP values in the Diabetes Cardiovascular RIsk of VAllecas (DICARIVA) study and to assess differences in central obesity prevalence in 650 T2DM patients presenting lower or ≥3 mg/L hs-CRP values. 42.9% of participants were obese while 32.9% presented high hs-CRP values. High WC and the conjoint presence of high BMI-high WP increased 29.5% and 55.6% respectively (both $P<0.0001$) hs-CRP values vs control patients. The probability of showing high hs-CRP in T2DM was 4.7-times higher in high WP-obese than in their control counterparts. Primary prevention should be addressed to avoid obesity and high WC in order to decrease inflammation and their deleterious effects in T2DM patients.

Key words: Type 2 Diabetes mellitus; obesity; waist perimeter; C Reactive protein.

Introduction

The term Diabesity has been created to clearly define the powerful link between Diabetes and Obesity [1]. Nonetheless, this linkage has limitations as gynoid vs android adipose tissue location implies relatively low cardiovascular risk and is not highly prevalent in Type 2 Diabetes Mellitus (T2DM) [2]. The adipose organ tissue can be considered a true endocrine organ able to secrete a variety of molecules, called generically adipocytokins, in response to multitude of physio and physiopathological process [3]. Those molecules modulate resistance to insulin, with direct action on insulin signaling pathway or indirectly by stimulating inflammatory pathways [4].

Inflammation is characterized by the presence of a series of cardinal signs, redness, sweat, etc., and changes in the concentrations of certain peptides and other susbtances known as acute-phase reactants [5]. These include CRP, whose high levels in blood have been linked to different obesity degrees [6]. Moreover, CRP elevated levels have been reported in T2DM. Having into account previous premises, we hypothesized that CRP values increase in T2DM patients mostly when central obesity is present. Thus, the aims of the paper were a) to analyses the values of CRP in a T2DM population affected from the conjoint effect of increased Body Mass Index (BMI) and waist perimeter (WP); b) to assess differences in prevalence of central obesity in T2DM presenting CRP values higher or lower than 3 mg/L.

Methods

An observational, epidemiological and cross-sectional study was conducted in T2DM patients from the Diabetes Cardiovascular RIsk of VAllecas (DICARIVA) study and diagnosed in the Diabetes and Cardiovascular risk office at the Endocrinology and Nutrition Service of the Infanta Leonor Universitary Hospital in Madrid, Spain. The study sample comprises 650 T2DM patients (304 men and 346 women) managed by endocrinologist from Vallecas area filed in the hospital endocrinology office. Written informed consent was obtained from all patients. Details of the selection made an inclusion criteria have been published elsewhere [7]. Taking into account that CRP values ≥10 mg/L are indicative of strong inflammation and not of low-degree inflammation [8], T2DM patients with CRP values ≥10 mg/L were not included in the

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present study. Thus, 650 T2DM patients from a total of 735 T2DM patients included in the DICARIVA study were studied.

Anthopometrical and Laboratory measurements

Height was obtained using a stadiometer (Holtain© LTD., Dyfed, UK) with patient barefoot and wearing light clothing. Body weight was obtained using an electronic weighing scale (SECA©alphaGmbH&Co., Igni, France). BMI was estimated using the formula body weight (kg)/height (meters) squared. WP was measured at the midpoint between the lowest rib and the iliac crest using a flexible non-stretch measuring tape (Holtain, Dyfed, UK).

Blood samples were collected from the antecubital vein after an overnight fast in the laboratory of the Infanta Leonor hospital. Serum was separated by centrifugation (Orto Arlesa 21; Madrid, Spain) at 3500 rpm for 20 minutes. *High sensitivity* c reactive protein levels were measured by immunoturbidimetry (Wiener Laboratory, Rosario, Argentina).

Two cut-off points to define obesity and its location were used. A BMI ≥30kg/m^2 for obesity diagnosis [9] and WC ≥84 cm in women and ≥94cm in men for defining cardiovascular risk according to the truncal obesity presence in European people [10]. The conjoint use of both markers allows us to get four T2DM groups 1) Low BMI and Low WC (BMI <30 kg/m^2 and WC<84 cm for women and < 94 cm for men); 2) Low BMI and High WC (BMI <30 kg/m^2 and WC ≥84 cm for women and ≥94 cm for men), 3) High BMI and Low WC (BMI ≥30 kg/m^2 and WC <84 cm for women and < 94 cm for men) and 4) High BMI and High WC BMI ≥30 kg/m^2 and WC ≥84 cm for women and ≥94 cm for men. Two different levels of hs-PCR, <3 mg/L and ≥3mg/L, were established [8]. Shapiro-Wilks and Kolmogorov-Smirnov tests were performed to assess normality distributions in all population and studied subgroups. As hs-CRP appeared non-normally distributed, a natural logarithm transformation for hs-CRP data was performed. Significant differences between groups were evaluated by ANOVA followed by the T2-Tamhame *post-hoc* test. The chi-square test was applied to assess differences in obesity prevalence between groups. Linear regression equations between BMI and WC were separately calculated for men and women to ascertain what WC (in cm) corresponds to a BMI of 30 kg/m^2. Statistical significance was set at P<0.05 using the SPSS version 22.0 and the SAS version 9.2 statistical software packages.

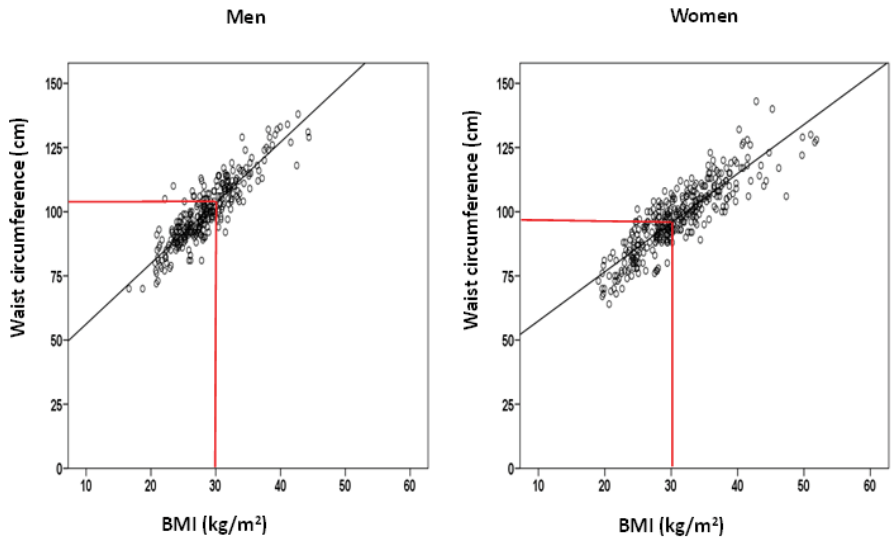

Figure 1: Foot note Linear adjustment between Waist circumference in cm (WC) and Body mass index in kg/m^2 (BMI) in men and women from the DICARIVA study. Men, n=304; WC= 32.59 +2.362*BMI; r^2=0.889; P<0.00001; Women, n=346; WC= 38.33 + 1.912 *BMI; r^2=0.872; P<0.0001.

Category[a]	Number	Mean ± SD	[95%CV]	ANOVA
Low BMI & Low WC	153	2.03 ± 0.32 [a]	[1.40, 2.66]	P<0.0001
Low BMI & High WC	218	2.44 ± 2.37 [b]	[2.12, 2.77]	
High BMI & High WC	279	3.16 ± 2.55 [c]	[2.86, 3.47]	

Table 1: C Reactive Protein values in Type 2 Diabetes Mellitus patients classified according to Body Mass Index (BMI) and Waist Circumference (WC) form the DICARIVA study. Values bearing differ letter were significantly different (p<0.0001) (a<b<c). [a]Low or High BMI, BMI <30 kg/m^2 or BMI ≥ 30 kg/m^2, respectively; [a]Low or High WC, WC <84 cm in women and <94 cm in men or WC 84 cm in women and ≥94 cm in men, respectively [9, 10].

		BMI-WC groups			Total	Chi- squared (*P*)
		Low BMI & Low WC (Group 1)	Low BMI & High WC (Group 2)	High BMI & High WC (Group 3)		
hs-RCP <3mg/L	Number	128	153	155	436	<0.0001
	% among BMI-WC groups	83.7%	70.2%	55.6%	67.1%	
hs-RCP ≥3mg/L	Number	25	65	124	214	
	% among BMI-WC groups	16.3%	29.8%	44.4%	32.9%	
Total	Number	153	218	279	650	
	% among BMI-WC groups	100%	100%	100%	100%	

Table 2 : Distribution of Type 2 Diabetes Mellitus patients presenting low or high hs-C reactive protein (hs-CRP) values and different degree of Body Mass Index (BMI) and Waist circumference (WC) .Values for low and high BMI or WC have been included in text and foot-note of Table 1.

Results

All patients showing BMI ≥30 kg/m^2 presented elevated WC; thus, only group 1, 2 and 4 were evaluated. **Figure 1** shows lineal adjustments between WC and BMI for men and women**.** The equation for men was (WC= 32.59 +2.362*BMI r^2 = 0.889; *P*<0.00001) and for women (WC= 38.331 + 1.912 *BMI r^2 = 0.872; *P*<0.0001)**. Table 1** shows that hs-CRP significantly differs among groups (*P*<0.0001) and progressively increased from group 1 to 4. T2DM with one (increased WC) and two factors (obesity and high WC) presented higher hs-CRP values (*P*<0.0001) that their non-obese with non-elevated WC counterparts. A significant lineal regression (r^2=0.9755; *P*<0.001) was found between number of factors (0, 1 and 2) and hs-CRP values; thus, each factor increased the serum value in 0.565 mg/L of hs-CRP.

Table 2 shows that 32.9% of T2DM patients had hs-CRP values ≥3 mg/L, and that there were significant differences (*P*<0.0001) in the prevalence of patients with none, one or two factors among T2DM showing low or high CRP values. Contingence tables shows that obesity distribution was also different (*P*<0.0001), and the probability to have high hs-CRP values was 4.7–times higher in T2DM with obesity and increased WC than in their control counterparts.

Discussion

The results from the DICARIVA study clearly suggest that obesity was highly prevalent among T2DM patient (42.9 %). This data agree with those of other studies [1, 11]. All T2DM showing BMI ≥30 kg/m^2 displayed increased WC; thus, only three categories were drawn. According to lineal regression adjustments a BMI of 30 kg/m^2 corresponds to 103.5 cm in men and to 95.8 cm in women. Concerns on the validity of BMI as a marker of BMI as been reported [11]. In fact 33.5% T2DM patients were non-obese but presented increased WC. The absence of normal WC among obese were probably conditioned by the cut-off points selected [10].

As expected hs-CRP levels progressively increased according to the presence of none, one or two (high BMI and high WC) factors selected related to obesity are its location. Thus, T2DM patients with two factors show CRP values 56% higher than people with 0 factors, suggesting that inflammation was highly prevalent in obese with increased WC. Increased hs-CRP values in obesity have been documented [5, 12]; however, much less information is derived from T2DM patients with augmented WC but do not diagnosed of obesity. Our results clearly suggest that the conjoint increase of BMI-WC negatively affect inflammation markers that in turn should increase insulin resistance and cardiovascular risk among those patients [3,13]. In fact, obese T2DM people with high levels of WC have 4.7 times higher probability of having CRP values ≥3 mg/L than non-obese T2DM patients with normal WC.

Based in this finding, primary prevention should be addressed to avoid WC and BMI increment in order to decrease inflammation and their deleterious effect in among T2DM patients.

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