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High sensitivity C-reactive protein distribution in the elderly: the Bambuí Cohort Study, Brazil

L.G.S. Assunção[1], S.M. Eloi-Santos[1,2], S.V. Peixoto[3,5], M.F. Lima-Costa[4,5] and P.G. Vidigal[1,2]

[1]Programa de Pós-Graduação em Patologia, Faculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brasil
[2]Departamento de Propedêutica Complementar, Faculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brasil
[3]Departamento de Enfermagem Aplicada, Escola de Enfermagem, Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brasil
[4]Departamento de Medicina Preventiva e Social, Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brasil
[5]Centro de Pesquisas René Rachou, Fundação Oswaldo Cruz, Belo Horizonte, MG, Brasil

Abstract

The measurement of the serum concentration of the acute-phase reactant C-reactive protein (CRP) provides a useful marker in clinical practice. However, the distribution of CRP is not available for all age and population groups. This study assessed the distribution of high sensitivity-CRP (hs-CRP) by gender and age in 1470 elderly individuals from a Brazilian community that participates in the Bambuí Cohort Study. Blood samples were collected after 12 h of fasting and serum samples were stored at -70°C. Measurements were made with a commercial hs-CRP immunonephelometric instrument. More than 50% of the results were above 3.0 mg/L for both genders. Mean hs-CRP was higher in women (3.62 ± 2.58 mg/L) than in men (3.03 ± 2.50 mg/L). This difference was observed for all ages, except for the over-80 age group. This is the first population-based study to describe hs-CRP values in Latin American elderly subjects. Our results indicate that significant gender differences exist in the distribution of hs-CRP, and suggest that gender-specific cut-off points for hs-CRP would be necessary for the prediction of cardiovascular risks.

Key words: C-reactive protein; Elderly; Epidemiology; Cardiovascular risk; Brazil

Introduction

Epidemiological surveys that estimate the prevalence of diseases and risk factors contribute to a general and particular analysis of the study population. Several studies have shown that high sensitivity C-reactive protein (hs-CRP) is of interest in predicting the risk of future cardiovascular disease (1,2). Determination of the distribution of hs-CRP in elderly people is also of interest for clinicians in screening for inflammatory diseases and monitoring the response to therapy. Although the available data indicate that gender-specific cut-off points for hs-CRP are not needed for the prediction of coronary heart disease risk, this question requires further studies using data from cohorts (1). Additionally, there are few data regarding hs-CRP values for the older population. We used data from the baseline of the Bambuí Cohort Study, Brazil, to evaluate the distribution of hs-CRP in elderly people from a Brazilian community (3). The Institutional Review Board approved the study and all subjects gave written informed consent to participate.

Correspondence: P.G. Vidigal, Departamento de Propedêutica Complementar, Faculdade de Medicina, UFMG, Av. Prof. Alfredo Balena, 190, Sala 403, 301030-100 Belo Horizonte, MG, Brasil. Fax: +55-31-3409-9782. E-mail: pedrovidigal@ufmg.br

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Material and Methods

The baseline survey of the Bambuí Cohort Study comprised residents of Bambuí city (Minas Gerais State, Brazil) aged 60 years or over. Of the 1742 residents, 1606 (92.2%) participated in the interview and 1496 (85.9%) were examined (blood sample, laboratory tests, physical measurements, and electrocardiogram) in the baseline cohort study. The subjects interviewed and examined were similar to the town population aged 60 years or more for all the characteristics evaluated: age, gender, number of residents in the household, marital status, family income, and education (3). Of the subjects examined, 1470 had their hs-CRP measured and were selected for this study; 26 (1.7%) were not tested because the amount of sample available was insufficient. Blood samples were collected after a 12-h fast and serum samples were stored at -70°C. Measurements were made by the hs-CRP immunonephelometric method, Dade-Behring N Latex hs-CRP particle-enhanced immunoassay on an automatic nephelometer (BNII™, Dade Behring, Germany) traceable to the international reference standard CRM 470 (4). Samples that showed results above the linearity of the test were automatically diluted and remeasured with the same hs-CRP assay. Pre-analytical factors related to blood collection were determined as previously described (5,6). The distribution was assessed by gender for all measured hs-CRP values. The goodness of fit test for normal distribution was evaluated using the Kolmogorov-Smirnov test. Serum level of hs-CRP was log-transformed to fit a less skewed distribution. The statistical analysis was carried out with the Stata software (7).

Results

A total of 188 of the individuals selected were excluded from the analysis because they had CRP values of 10 mg/L or higher. The CRP value (mean ± SD) was 23.8 ± 18 mg/L for this group. Thus, the study population consisted of 1286 subjects (501 men and 785 women). Mean age was 69.1 ± 7.2, 68.7 ± 7.2 for men and 69.2 ± 7.3 for women (P = 0.213). The distribution of hs-CRP values did not follow a symmetric bell-shaped curve and more than 50% of the results were above 3.0 mg/L for both genders. Table 1 shows the quartiles of hs-CRP values. Mean hs-CRP (log-transformed) was higher in women than in men for all ages, except for individuals older than 80 years (Table 2).

Discussion

This is the first population-based study to describe hs-CRP values in Latin American elderly subjects. Herbeth et al. (8), in France, used criteria similar to those of the present study and excluded values about 20 mg/L. We chose 10 mg/L to be the cut-off point, according to literature guidelines that indicate limits for persistently or inexplicably marked elevations in hs-CRP values (1,9). As the distribution of hs-CRP did not follow a symmetric bell-shaped curve, the values of the study population were divided into four equal-sized groups (quartiles). This log-Gaussian distribution is comparable to those observed in other younger and elderly populations (4,5,8,10,11).

A higher mean hs-CRP concentration was observed in all individuals studied compared to previous reports, including a Brazilian study (11-13). Results from the baseline survey of the Helsinki Ageing Study demonstrated association between aging and increase in hs-CRP concentration for elderly men and women (14). It has been suggested that this association is related to the increased production of interleukin-6 (IL-6) associated with aging. CRP levels are predominantly modulated by the hepatic effects of IL-6 (15,16). Differences in the results obtained in different studies may reflect the sociodemographic composition of the studied populations, sample size, and criteria for the selection of participants.

Women were found to have higher hs-CRP levels than men for all ages. The lack of difference in the over-80 group can be explained by the low number of individuals. Our results agree with those of Araujo et al. (11) who evaluated 684 healthy Brazilian individuals, aged 14-74 years, and with previous reports from other countries (5,10,17). Other investigators have not observed significant gender differences (4,18,19). Higher hs-CRP values in women may be related to hormone replacement, although the women in our cohort were not undergoing hormone therapy (8). In our study, body mass index and waist circumference were independently correlated with hs-CRP in men and women. In addition, these measures correlated positively with hs-CRP both in men and women (data not shown). The relationship between hs-CRP levels and measurements of obesity may be explained by the finding that adipose tissue releases IL-6 *in vivo*, being implicated as a major source of circulating IL-6 (20).

Many clinical and laboratory variables appear to influence the concentration of hs-CRP according to gender (11-14). Our study shows that significant gender differences in hs-CRP distribution exist in the elderly population and suggests that gender-specific cut-off points for hs-CRP should be clinically used in assessing the risk of future cardiovascular events.

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Table 1. Distribution of serum hs-CRP concentration (mg/L) according to gender.

	Males (N = 501)	Females (N = 785)	Total (N = 1286)
First quartile	0.17-1.01	0.16-1.48	0.16-1.26
Second quartile	1.01-2.22	1.48-2.98	1.26-2.73
Third quartile	2.22-4.33	2.98-5.35	2.73-5.04
Fourth quartile	4.33-10.0	5.35-10.0	5.04-10.0
Mean ± SD	3.03 ± 2.50	3.62 ± 2.58	3.39 ± 2.56

N = number of subjects.

Table 2. Serum concentration of hs-CRP (log-transformed) according to gender and age.

Age (years)	Males		Females		P
	N	Mean ± SD	N	Mean ± SD	
60-69	306	0.7 ± 0.9	465	1.0 ± 0.9	<0.001
70-79	145	0.7 ± 1.0	237	0.9 ± 0.9	0.022
80+	50	0.8 ± 1.0	83	0.8 ± 0.9	0.877
Total	501	0.7 ± 0.9	785	1.0 ± 0.9	<0.001

N = number of subjects. The Student *t*-test was used for statistical analysis.