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Population Distribution Of High Sensitivity C-Reactive Protein Values in Aboriginal Australians: A Comparison With Other Populations

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Abstract

Objectives: To examine the distribution of C-reactive protein (CRP) values in Aboriginal Australians and its relation to age and gender. Methods: High sensitivity CRP levels were measured in 954 Aboriginal participants aged 5–74 years. Fractional polynomial regressions were used to explore the relationship between CRP and age.

Results: CRP values changed with age and reached its lowest level around 10 years and then increased with age. Geometric means of CRP were 7.3 (95% confidence interval (CI): 6.6, 8.1) and 4.1 (95% CI: 3.7, 4.6) for female and male adults, respectively. Adjusting for age, the ratio of female to male CRP concentrations was 1.67 (95% CI: 1.45, 1.99) for adults, and 1.09 (95% CI: 0.84, 1.42) for children 5 to 19 years.

Conclusions: CRP changes with age. Females have higher CRP values than males. CRP values in Aboriginal people are substantially higher than other populations.

Keywords: Inflammation; C-reactive protein; Aboriginal health; Cardiovascular risk factors

Introduction

High sensitivity C-reactive protein (CRP) has emerged as a powerful risk marker for cardiovascular disease [1–5], although the magnitude of its effect is still debatable [6,7]. Recent studies have suggested that it might also affect the process of atherothrombosis [8–10]. The distribution of CRP level varies significantly among race/ethnic groups [9,11]. Aboriginal Australians experience a higher cardiovascular mortality rate [12] as well as higher CRP levels [13]. The increased risk in coronary heart disease in this population cannot be fully explained by the increased prevalence rates of traditional risk factors [14]. The population distribution of CRP in the Aboriginal population has not been described in detail. Understanding the distribution of CRP concentration can be useful for establishing the magnitude of Aboriginal people at increased risk for cardiovascular disease and for assessing potential contributions of CRP to cardiovascular disease risk. Most studies only describe the distribution of CRP in adult populations. In this study, we aimed to describe the distribution of CRP for Aboriginal people from 5 to 74 years of age in a remote community and to compare CRP values with those reported from other populations.

Methods

From 1992 to 1995, a community-wide chronic disease screening program was conducted in a remote island community in the Northern Territory of Australia. The program included 1365 participants aged 5 to 74 years. Serum samples were collected during the baseline survey and stored at -70°C until used for analysis. Nine hundred and fifty-four (954) serum samples were

retrieved and sent to a commercial laboratory for high sensitivity CRP testing in 2005. All samples were analyzed for high sensitivity CRP using the immunoturbidimetric CRP assay on a Hitachi 917 analyzer (Roche Diagnostics Australia) with a detection limit of 0.03 mg/L. The assay's analytical range was from 0.1 to 20 mg/L. Samples with values greater than 20 mg/L were measured using diluted samples. The imprecision of the assay is less than 5%.

TABLE 1.
Geometric means (95% CI) and median (interquartile range) of CRP in Aboriginal people

Age (years)	**Number**		**Geometric mean (95% CI)**			**Median (IQR)**	
	Female	**Male**	**Female**	**Male**	***P***	**Female**	**Male**
5–9	21	38	1.9 (1.0, 3.5)	1.4 (1.0, 2.0)	0.37	1.8 (1.1, 3.3)	1.1 (0.7, 3.0)
10–14	49	85	1.7 (1.2, 2.4)	1.9 (1.5, 2.4)	0.63	1.6 (0.8, 3.6)	1.9 (1.0, 3.6)
15–19	45	70	2.8 (2.0, 3.7)	2.3 (1.7, 3.0)	0.33	3.0 (1.1, 4.5)	2.0 (1.2, 5.0)
20–24	55	81	5.4 (4.1, 7.1)	3.7 (2.9, 4.7)	0.039	5.2 (2.8, 13.0)	3.4 (2.0, 6.1)
25–29	58	75	6.2 (4.7, 8.2)	3.3 (2.6, 4.2)	0.0007	8.5 (2.9, 13.0)	3.5 (1.6, 6.8)
30–34	51	58	7.3 (5.4, 10.0)	4.4 (3.3, 6.0)	0.02	7.8 (3.4, 15.2)	4.1 (1.8, 9.8)
35–39	35	46	7.7 (5.9, 10.1)	3.9 (2.9, 5.4)	0.0025	8.6 (4.0, 16.1)	3.3 (1.9, 6.1)
40–44	45	21	9.4 (7.3, 12.0)	5.8 (3.2, 10.5)	0.071	8.2 (5.7, 16.3)	4.0 (2.7, 6.9)
45–49	26	15	8.6 (6.0, 12.3)	3.9 (2.8, 5.6)	0.0053	9.4 (4.8, 14.4)	3.6 (2.8, 6.5)
50–54	18	17	11.5 (7.4,17.7)	5.8 (3.9, 8.4)	0.017	12.8 (6.9, 23.8)	6.5 (3.4, 8.3)
55–74	29	16	7.3 (5.1, 10.2)	7.2 (3.9, 13.4)	0.98	6.8 (4.1, 11.9)	5.2 (4.0, 12.7)
Total	432	522	5.2 (4.7,5.9)	3.1 (2.8,3.4)	< 0.0001	6.1 (2.5,12.3)	3.0 (1.5,6.1)

Statistical analysis

The CRP values have a distribution that is highly skewed. Therefore, CRP values were logarithmically transformed, and the results were expressed as back-transformed geometric means for age- and sex-specific groups. To be comparable with some published data, age- and sex-specific medians and interquartile ranges (IQR) were also calculated. T tests were used to examine the differences between males and females in CRP geometric means. Linear regressions with the logarithmic transformed values as dependent variables were used to test the gender difference adjusting for age. Fractional polynomial regressions were used to express the nonlinear relationship between CRP and age. The CRP cut-off points of up to 1, from 1 to 2.9, and from 3 to 10 and >10 g/ L were used to categorize people into the following four groups: low risk, intermediate risk, high risk and possible acute phase response groups [4,15]. Numbers and proportions of people according to CRP categories were calculated. All analyses were performed using Stata version 8.2 [16].

The project was approved by the Behavioral and Social Science Ethical Review Committee of the University of Queensland, the Human Research Ethics Committee of the

Northern Territory Department of Health and Community Services and Menzies School of Health Research and the Community Health Board.

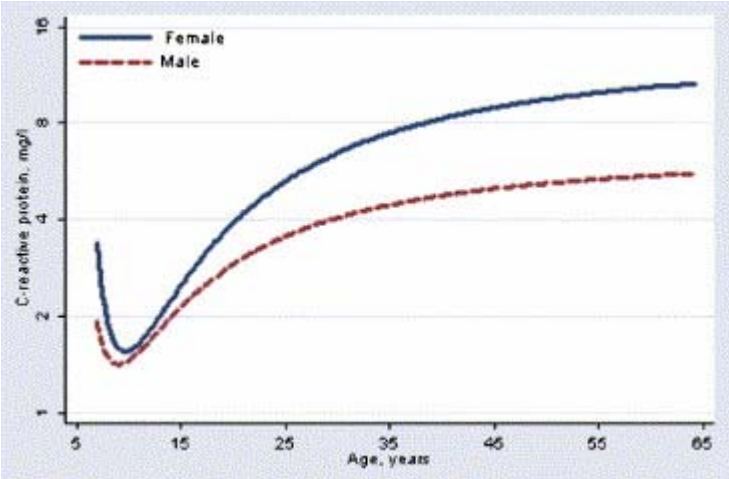

Fig. 1. CRP and age by sex in Aboriginal people.

TABLE 2.
Numbers (%) of participants by CRP categories

hs-CRP groups	**Age < 20 years**		**Age 20–74 years**	
	Female	**Male**	**Female**	**Male**
Low risk < 1 mg/L	31 (27.0)	50 (25.9)	11 (3.5)	24 (7.3)
Moderate risk 1–3 mg/L	40 (34.8)	80 (41.5)	47 (14.8)	105 (31.9)
High risk 3–9.9 mg/L	33 (28.7)	54 (28.0)	135 (42.6)	142 (43.2)
Possible acute phase response, 10+ mg/L	11 (9.6)	9 (4.7)	124 (39.1)	58 (17.6)

The characteristics of the study participants have been reported elsewhere [17]. The high sensitivity CRP values in the study sample ranged from 0.1 to 220.2 mg/L. There was a significant trend to higher CRP values with increasing age in both males and females. Females had higher CRP geometric mean and median values in all age groups than their male counterparts. Such differences were statistically significant for adults aged 20 to 54 years, as shown in Table 1. Geometric means of CRP were 7.3 (95% CI: 6.6, 8.1) and 4.1 (95% CI: 3.7, 4.6) for female and male adults, respectively. The female to male CRP ratio was 1.67 (95% confidence interval: 1.45, 1.99) in participants 20 years or older and 1.09 (95% CI: 0.84, 1.42) for people younger than 20 years. Fig. 1 shows that CRP values decreased with age among children before 10 years of age and increased with age after.

Only a small proportion of adults, 3.5% of women and 7.3% of men, were in the low risk category (CRP< 1 mg/L). Over 60% adult men and 80% women had CRP values greater than 3 mg/l. About 43% were in the high cardiovascular risk category (CRP 3–10 mg/L) (Table 2). Compared with published data in other populations, Aboriginal people had higher CRP concentrations. Fig. 2 shows the median concentrations of all CRP values from study

participants and those study participants who had CRP< 10 mg/L in comparison with the published data from countries such as Germany [18], Japan [19], Thailand [20], UK [18] and USA [21,22]. The median CRP values in Aboriginal Australians were substantially higher than those in other populations reported in the literature. Even though we excluded the participants with CRPz10 mg/L, the median CRP values in Aboriginal people remained higher in all age and sex groups.

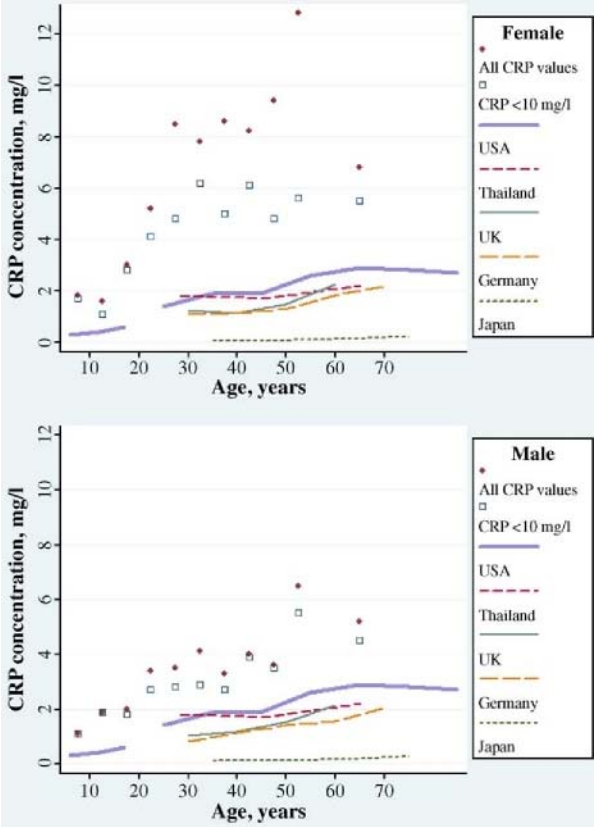

Fig. 2. CRP concentrations in Aboriginal people in comparison with published data in other populations. *Data from other populations derived from the following references: Japan [19], Germany [18], UK [18], Thailand [20], USA children and USA adults [21,22]. Data from Thailand and USA are for both sexes combined.

Discussion

The data in this study indicate that the CRP concentration in Aboriginal people increased with age after 10 years of age. Female adults had significantly higher concentrations than their male counterparts. Compared with other reported populations mainly from developed countries, Aboriginal Australians had substantially higher CRP levels in all age and sex groups. As in other populations, the distribution of CRP is right skewed with a log-normal distribution in Aboriginal people. It has also been reported in some populations that females have higher CRP levels than males. Woloshin and Schwartz used the data from the United States National Health and Nutrition Examination Survey (NHANES), showing that the levels of CRP were higher among women than among men [22]. Data from Ausburg (Germany) also showed that females had higher CRP levels [18]. Albert et al. reported that median CRP levels were significantly higher among women (2.9 mg/L) than among men (1.5 mg/L) in a multicenter study [23]. One interpretation of thegender difference was the use of hormone replacement therapy (HRT) [18,23]. In our study, the lack of data on HRT use limited our ability to assess its impact on our findings. Since elevated CRP levels among females were observed in all age groups, the elevated CRP in females was unlikely due to the use of HRT. In the Ten Towns

Children's Study of 699 10- to 11-year-old children in the United Kingdom, girls had significantly higher CRP levels than boys [24]. On the contrary, in a study in the Japanese population, CRP levels are significantly higher among men than among women [19,25]. No gender differences were found in several other populations [18,20,26–29]. The causes of higher CRP levels in Aboriginal women remain to be determined. Due to crowding, hot weather, humidity, insect bites, scabies infestations and poor hygiene, skin infections and other infections are common in Aboriginal children [30,31].

Racial/Ethnic differences in the distribution of CRP have been investigated in previous studies [11,32]. In the United States, black women had significantly higher and Asian women had lower CRP levels than their white and Hispanic counter-parts [11]. However, Ford et al. found that CRP concentrations did not differ among four ethnic groups in American men [29]. In the United Kingdom, higher CRP concentrations among South Asians were reported than among their white counterparts [33,34]. Compared with published data, Aboriginal people in the remote regions had higher CRP levels. The high CRP level in Aboriginal people has been reported in other studies with relatively small samples by McDonald et al. [13] and Rowley et al. [35]. McDonald et al. also found that females had a higher CRP level (geometric mean=8.0 mg/L) than males (6.4 mg/L). We found that Aboriginal people had elevated CRP levels in all age and sex groups.

In the US adult population, 6% of men and 13% women have CRP levels greater than 10 mg/L, while in this study population, 39.1% men and 17.6% women have such high CRP levels, indicating that acute and chronic infections or other disorders characterized by acute inflammation are far more prevalent in Aboriginal people.

Aboriginal people have a higher risk of coronary heart disease than the general Australian population. The risk of coronary heart disease is significantly underestimated using the Framingham function with traditional risk factors [14]. McDonald et al. report that CRP concentrations increase with the number of cardiovascular risk factors, carotid intima-media thickness and albuminuria [13]. The results from a clinical trial by Ridker et al. supports that reducing the levels of CRP in particular may have a role in altering the atherothrombotic process [36]. It needs to be confirmed that the elevated CVD risk in Aboriginal people is partly attributable to the high CRP values. Understanding the independent contribution of the CRP levels to the development of cardiovascular disease in this population has important clinical and public health implications.

Efforts have been made to describe CRP changing patterns with age in other populations [18–20,22,29], but few studies have examined both children and adults in the same population. The pathogenesis of cardiovascular disease often starts in childhood. Little is known about the contribution of inflammation in childhood to the development of cardiovascular disease in adult life. The CRP levels in Aboriginal children are much higher than those reported for children in the United Kingdom (0.15 g/L) [24] and the United States (0.5 g/L) [21]. This indicates the seriousness of infections and inflammatory conditions in Aboriginal children. Preventing the chronic and repeated infections early in life may be important in reducing cardiovascular disease in adulthood. CRP concentrations have been reported among children in the developing countries [37,38]. Compared to the median CRP for children aged 2 to 15 years from Bolivia (0.73 mg/L) [37], Aboriginal children in this study have much higher CRP concentrations.

CRP is a nonspecific marker of inflammation. Many diseases can cause the elevation of CRP. This study described the distribution of CRP in the general Aboriginal population in a remote community. We did not exclude participants with various health problems. However, excluding those with CRPz10 mg/L, the remaining participants still had higher CRP levels than other populations. Since the study participants were from a single remote community in the Northern Territory, the findings may not apply to the Aboriginal people living in urban areas or other Australian groups. Although it has been determined that 2 or 3 tests are needed to confirm patients' cardiovascular risk [39], the participants in this study only obtained a single test.

As the role of inflammation in cardiovascular disease has become appreciated by the medical community, the use of CRP measurements has increased. However, guidelines addressing the role of CRP testing in primary and secondary prevention of cardiovascular disease for different racial groups have not been developed. Our data could be useful to researchers, clinicians and policy makers. Whether the racial differences in CRP distribution are responsible for racial discrepancies in cardiovascular risk remains to be assessed.

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