

Research Article

An imbalance in serum concentrations of inflammatory and anti-inflammatory cytokines in hypertension  CrossMark

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**Abstract**

Hypertension is an important risk factor for cardiovascular disease and there is increasing evidence that inflammation and abnormal immune responses are involved in the pathogenesis of hypertension. However, the data on the association between specific cytokine concentrations and hypertension are inconsistent. We have evaluated the association between 12 cytokines/growth factors and the presence of different degrees of hypertension, comparing these concentrations to values in a healthy group of subjects. The concentrations of interleukin (IL)-1 $\alpha$ , -1 $\beta$ , -2, -4, -6, -8, -10, tumor necrosis factor (TNF- $\alpha$ ), interferon- $\gamma$  (IFN- $\gamma$ ), monocyte chemoattractant protein (MCP-1), epidermal growth factor, and vascular endothelial growth factor were measured in 155 hypertensive patients and 148 healthy subjects, using EV-3513 cytokine biochip arrays, a competitive chemiluminescence immunoassay. Univariate and multivariate analyses were used to evaluate the association of specific cytokines and growth factors with systolic blood pressure (SBP) and diastolic blood pressure (DBP). Hypertensive subjects had higher serum concentrations of IL-1 $\alpha$ , -2, -8, vascular endothelial growth factor, IFN- $\gamma$ , TNF- $\alpha$ , MCP-1, and epidermal growth factor; and lower concentrations of anti-inflammatory cytokine, IL-10 ( $P < .05$ ), compared with the healthy individuals. The serum concentrations of IL-4, -6, and -1 $\beta$  did not differ between the hypertensive subjects and control group. Univariate and multivariate analyses revealed that IL-1 $\alpha$  and IFN- $\gamma$  were independent predictors of a high SBP, while IFN- $\gamma$ , IL-1 $\alpha$ , TNF- $\alpha$ , and MCP-1 remained statistically significant for DBP after correction for age, gender, Body mass index, smoking, fasting blood glucose, and triglycerides. There was a significant association between the concentrations of several cytokines and hypertension. These associations may either be related to common underlying factors that cause hypertension and may

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also be proinflammatory or because these inflammatory cytokines might directly be involved in the etiology of hypertension. *J Am Soc Hypertens* 2014;8(9):614–623. © 2014 American Society of Hypertension. All rights reserved.

**Keywords:** Blood pressure; growth factors; inflammation.

## Introduction

Cardiovascular disease is now the most important cause of morbidity and mortality globally, and is usually due to atherosclerosis.<sup>1</sup> The prevalence of atherosclerosis has increased over past decades and is now a major cause of morbidity in developing countries. There is increasing evidence suggesting a key role of inflammation during all stages of atherogenesis.<sup>2</sup> Inflammatory cells, including activated macrophages and T lymphocytes, are present during all stages of atherosclerotic lesion development and contribute to the proinflammatory milieu that modulates the local inflammatory responses within the plaque.<sup>3–7</sup> Serum tumor necrosis factor (TNF)- $\alpha$  concentration has been shown to predict the severity of peripheral arterial disease.<sup>8</sup> Serum interleukin (IL)-2 concentrations are reported to be increased in patients with stable, but not unstable, angina.<sup>9,10</sup> There is also evidence that increased serum concentrations of IL-8 are associated with an increased risk of coronary artery disease in healthy subjects.<sup>11</sup> IL-10 is an anti-inflammatory cytokine with a potential protective

role that limits the local inflammatory response. IL-10 can regulate the production of proinflammatory cytokines derived from type 1 T-helper lymphocytes promoting a type 2 T-helper cell immune response that it is necessary in the modulation of the inflammatory process.<sup>12</sup>

Hypertension is strongly associated with cardiovascular mortality.<sup>13</sup> The prevalence of hypertension is also increasing globally<sup>14</sup> and within the Iranian population specifically.<sup>15</sup> Hypertension was defined by the World Health Organization as a blood pressure >140/90 mm Hg, and more recently by the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP-III) guidelines as >130/85 mm Hg.<sup>16,17</sup> Chronic inflammation may be an independent risk factor for the development of hypertension. Serum TNF- $\alpha$  and IL-6 concentrations have been reported to be associated with hypertension in otherwise healthy subjects.<sup>18</sup>

Previous studies have been inconsistent in their reports on the relationship between hypertension and serum cytokine concentrations. This may, in part, be related to other confounding factors including diet. In the present study, the association between serum cytokines concentration

**Table 1**  
Demographic and biochemical characteristics of subjects in each group

| Characteristics          | Healthy (N = 148)     | Hypertension (N = 155) | P Value |
|--------------------------|-----------------------|------------------------|---------|
| Age (year)               | 49.62 $\pm$ 12.31     | 50.29 $\pm$ 13.03      | .647    |
| Sex [n (%)]              |                       |                        |         |
| Male                     | 61 (41.2)             | 64 (41.3)              | .990    |
| Female                   | 87 (58.8)             | 91 (58.7)              |         |
| Smoking [n (%)]          |                       |                        |         |
| Yes                      | 25 (19.1)             | 43 (30.3)              | .085    |
| No                       | 93 (71)               | 84 (59.2)              |         |
| Former                   | 13 (9.9)              | 15 (10.5)              |         |
| Height (cm)              | 1.61 $\pm$ 0.07       | 1.60 $\pm$ 0.09        | .956    |
| Weight (kg)              | 70.12 $\pm$ 12.10     | 76.15 $\pm$ 14.04      | < .001  |
| BMI (kg/m <sup>2</sup> ) | 27.16 $\pm$ 4.73      | 29.51 $\pm$ 4.74       | < .001  |
| WC (cm)                  | 91.58 $\pm$ 11.45     | 98.54 $\pm$ 11.84      | < .001  |
| HC (cm)                  | 102.96 $\pm$ 8.99     | 106.68 $\pm$ 10.08     | .002    |
| ArmC (cm)                | 29.91 $\pm$ 5.07      | 31.75 $\pm$ 3.47       | < .001  |
| FBG (mg/dL)              | 83.55 $\pm$ 12.63     | 86.34 $\pm$ 10.48      | .040    |
| TC (mg/dL)               | 193.89 $\pm$ 35.80    | 195.33 $\pm$ 39.08     | .582    |
| TG (mg/dL)               | 117.00 (83.00–154.25) | 138.00 (100.00–186.50) | .002    |
| hsCRP (mg/dL)            | 2.42 (1.24–6.02)      | 2.55 (1.30–6.25)       | .434    |
| HDL-C (mg/dL)            | 44.02 $\pm$ 8.57      | 42.70 $\pm$ 9.30       | .962    |
| LDL-C (mg/dL)            | 123.55 $\pm$ 32.53    | 118 $\pm$ 31.79        | .396    |
| SBP (mm Hg)              | 111.70 $\pm$ 11.03    | 136.57 $\pm$ 13.57     | < .001  |
| DBP (mm Hg)              | 75.62 $\pm$ 6.92      | 88.95 $\pm$ 7.21       | < .001  |

ArmC, arm circumference; BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; HC, hip circumference; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; SD, standard deviation; TC, total cholesterol; TG, triglyceride; WC, waist circumference.

Values are expressed as mean  $\pm$  SD, median and IQR for normally and nonnormally distributed variables, respectively.

Bold values represent significant *P* value.

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