

# Cytokine Levels Higher In White Hypertensives

BY PATRICE WENDLING

CHICAGO — Plasma levels of the proinflammatory cytokines tumor necrosis factor- $\alpha$  and interleukin-6 were surprisingly higher in whites vs. blacks with hypertension in a pilot study of 46 patients.

Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) was 1.19 pg/mL in 14 white hypertensives, compared with 0.62 pg/mL in 12 black hypertensives.

Interleukin-6 (IL-6) levels were higher in whites at 1.31 pg/mL versus 0.79 pg/mL in blacks, Dr. Ralph Watson said at a meeting sponsored by the International Society on Hypertension in Blacks. The difference between groups did not reach statistical significance for either cytokine, likely because of small patient numbers.

The finding is surprising because inflammation is thought to be one of the driving forces behind high blood pressure and end-organ damage, both of which have been shown in several studies to be worse in black than in white hypertensives.

The few studies that have compared IL-6, TNF- $\alpha$ , or C-reactive protein levels in blacks and whites have found higher levels in blacks or no difference between races.

Dr. Keith Norris, ISHIB conference cochair and interim president of Charles Drew University in Los Angeles, called the data provocative and asked whether weight could be driving the finding. Dr. Watson said the white hypertensives were slightly heavier at a mean weight of 202 pounds than were the black patients at a mean weight of 193 pounds.

White hypertensives had a slightly lower mean blood pressure of 128/78 mm Hg vs. 134/85 mm Hg for black hypertensives. Members of both groups were aged 59 years, but were on a variety of different antihypertensive medication regimens that may have affected their IL-6 or TNF- $\alpha$  levels,

said Dr. Watson, director of the hypertension clinic at Michigan State University in East Lansing.

Notably, IL-6 levels were significantly higher in the 26 patients with hypertension than in the 20 normotensive patients (1.34 pg/mL vs. 0.60 pg/mL), as were TNF- $\alpha$  levels (1.06 pg/mL vs. 0.46 pg/mL). This finding confirms several previous studies showing increased levels of inflammatory cytokines in persons with prehypertension and hypertension.

Still, the relationship between inflammation and hypertension remains unclear, Dr. Watson said. IL-6 and TNF- $\alpha$  are produced and secreted mainly by activated tissue macrophages in response to injury or infection, and act on endothelial cells at the DNA transcription level. The inflammatory response, however, is also closely intertwined with the process of repair, which begins during the early phases of inflammation.

“Blacks have far more strokes, end-stage renal disease, and coronary artery disease as a result of their hypertension than whites, and the assumption has been that this is because of increased inflammation contributing to the damage,” Dr. Watson said in an interview. “The question now is whether a lack of inflammation repair of the endothelial damage caused by hypertension could be contributing to the elevated rates of end-organ damage we see in black hypertensives, and whether elevated levels of inflammatory markers in white hypertensives contribute to their lower rates of end-organ damage.”

Dr. Watson and colleagues plan to validate the findings in another 50 black and white hyper- and normotensive patients and to assess the effect of hypertensive medications on TNF- $\alpha$  and IL-6 levels in hypertensives.

The study was funded by a grant from the National Institutes of Health. The investigators disclosed no relevant conflicts of interest. ■

# Fitness Lowered Mortality in Impaired Renal Function

BY SHERRY BOSCHERT

SAN FRANCISCO — Increased levels of fitness attenuated a higher risk of death in women with impaired renal function in a 16-year study of 5,716 participants who were asymptomatic at baseline.

Estimates of glomerular filtration rate (GFR) and fitness should be added to use of traditional cardiovascular risk assessments to help stratify risk and prioritize intervention in selected patients, Dr. Martha Gulati said at the annual meeting of the American Society of Hypertension.

The study recruited community women in 1992 who had no known renal or heart disease and compared baseline urinalyses, estimated GFR, and estimated fitness as measured by metabolic equivalent units (METs) with all-cause mortality in 2008.

At baseline, 79% of the women had a GFR of less than 60 mL/minute per 1.73 m<sup>2</sup>, putting them at higher risk for chronic kidney disease and cardiovascular disease than women with a higher GFR. The mostly white cohort had a mean age of 53 years and a mean waist circumference of 33 inches. Fifteen percent were smokers, 45% had hypertension, and 5% had diabetes. Overall, at baseline “this was a relatively healthy cohort with a really good level of fitness,” based on a mean of 8 METs, said Dr. Gulati of Northwestern University, Chicago.

In an analysis that adjusted for the effects of traditional cardiovascular risk factors using the Framingham risk score,

a creatinine level greater than 1.4 mg/dL increased the risk of mortality by 80%, compared with lower creatinine levels. Every unit increase in GFR decreased mortality by 3%, Dr. Gulati reported.

When exercise capacity was added to the analysis, these variables remained significant predictors of risk. Compared with those who had a GFR below 45 mL/minute per 1.73 m<sup>2</sup>, the mortality risk was 37% lower in the 66% of the cohort who had a GFR of 45-59, and 46% lower in the 21% of the cohort with a GFR of at least 60. About 75% of the lowest-GFR group was alive 16 years later, compared with 91% in the intermediate-GFR group and 94% in the highest GFR group.

In each of the GFR subgroups, women with better baseline fitness were less likely to die. Mortality rates (per 1,000 person-years) in the lowest GFR group were 3.18 at the highest fitness levels (greater than 8 METs), 3.81 with intermediate fitness (5-8 METs), and 7.62 among the least fit (less than 5 METs).

In the intermediate GFR group, mortality rates were 0.98, 1.76, and 3.16 per 1,000 person-years in the highest, intermediate, and lowest fitness subgroups.

In the highest GFR group, mortality rates were 0.56, 1.18, and 1.68 per 1,000 person-years in the highest, intermediate, and lowest fitness subgroups.

Dr. Gulati disclosed that she has been a speaker for AstraZeneca and Fujisawa Healthcare and has received research funds from the latter. ■

# Terminal Digit Bias Analysis Can Serve as BP Quality Check

BY PATRICE WENDLING

CHICAGO — Terminal digit bias analysis can be used to gauge the accuracy of blood pressure measurements at primary care clinics, a new study suggests.

Terminal digit bias is the tendency of an observer to round off a measurement to a digit of his or her own choosing. It has been shown in several studies to cause significant discrepancies in BP measurements in both the clinical and research settings.

No clear guidelines have been established for what is an acceptable range of end-digit preference, especially for zero—the most common terminal digit recorded. One study proposed a “0” end-digit preference by BP observers of less than 25% as being “optimal,” less than 30% as “acceptable,” and less than 35% as “minimal standard” (J. Clin. Epidemiol. 1996;49:869-77).

In the current study, Dr. Ahmed Dalmar and associates measured the terminal digit preference of 2,202 blood pressure readings at an inner-city hospital before caregiver training and 2,154 readings 3 months after training, which in-

cluded a video on proper techniques.

Terminal digit bias for zero significantly decreased among systolic and diastolic BP measurements from 57% (a very minimal standard) before training to 16% (optimal) after training, Dr. Dalmar, a research scientist with Aurora Health Care in Milwaukee, reported in a poster at a meeting sponsored by the International Society on Hypertension in Blacks.

The use of 2, 4, 6, and 8 as the last digit significantly increased after training, although the terminal-digit bias remained in the optimal range post intervention for all of the digits except 2, which fell into the minimal standard range.

The goal was to decrease or eliminate the zero-digit bias, with the hope that subsequently the bias for other digits would be in the acceptable or optimal range, Dr. Dalmar said in an interview.

“Unfortunately this did not happen in our study and, yes, these digits are also prone to bias,” he said. “We think this happened because after training many providers tended to avoid zero.”

The researchers disclosed no conflicts of interest and received no funding for the study. ■

## DATA WATCH

### States With the Highest Rates of Adult Hypertension

	Percentage of Adult Hypertension	Ranking	
		Hypertension	Obesity
Mississippi	34.5%	1	1
Alabama	33.5%	2	2
West Virginia	33.2%	3	3
Tennessee	32.1%	4	4
Arkansas	31.5%	5	10
South Carolina	31.3%	6	5
Louisiana	30.9%	7	8
Oklahoma	30.7%	8	6
Kentucky	30.1%	9	7
North Carolina	29.8%	10	12

Source: Robert Wood Johnson Foundation, “F as in Fat: How Obesity Policies Are Failing in America 2009”