

COMMENTED SUMMARIES FROM CURRENT MEDICAL LITERATURE

ZAP-70 EXPRESSION AS A SURROGATE FOR IMMUNOGLOBULIN-VARIABLE-REGION MUTATIONS IN CHRONIC LYMPHOCYTIC LEUKEMIA

Summary: The mutational status of immunoglobulin heavy-chain variable-region (Ig VH) genes in the leukemic cells of chronic lymphocytic leukemia (CLL) is an important prognostic factor in this disease. We investigated whether the expression of ZAP-70 by CLL cells correlated with the Ig VH mutational status, disease progression, and survival.

The expression of ZAP-70 was analyzed in T-cell and B-cell lines, and in the peripheral blood samples from 56 patients with CLL using flow-cytometry, western blotting, and immunohistochemistry. The results were correlated with the Ig VH mutational status and clinical outcome.

ZAP-70 was detected by flow-cytometric analysis in the cells of the T-cell lineage and in the leukemic cells from 32 of 56 patients with CLL. In all patients in whom at least 20% of the leukemic cells were positive for ZAP-70, Ig VH gene was nonmutated, whereas Ig VH mutations were found in 21 of 24 patients in whom less than 20% of the leukemic cells were positive for ZAP-70 ($p < 0.001$). Concordant results were obtained when ZAP-70 expression was assessed by immunohistochemistry or western blotting. The level of ZAP-70 expression did not change over time (median, 37 months) in sequential samples from 30 patients with CLL. Patients with Binet stage A CLL who had at least 20% ZAP-70-positive leukemic cells experienced more rapid progression and poorer survival than those with less than 20% ZAP-70-positive cells.

Among patients with CLL, the expression of ZAP-70, as detected by flow-cytometric analysis, correlated with Ig VH mutational status, disease progression, and survival.

Comment: Chronic lymphocytic leukemia (CLL) is one of the most common types of leukemia in the world. The disease is diagnosed with absolute lymphocytosis, noted in the peripheral blood. Prognostic factors include tumor burden and marrow function while factors such as old age, elevated thymidine kinase, uric acid, alkaline phosphatase, lactic dehydrogenase, large cell type, and rapid lymphocyte doubling time are considered the most important.

The staging system^{1, 2} of chronic lymphocytic leukemia (CLL) still cannot identify the stable or progressive forms of the disease. In the recent study of zeta-associated protein (ZAP-70) expression, significant advance has been made.

Immunoglobulin heavy-chain variable-region (Ig VH) genes in the leukemic cells of CLL were considered as an important prognostic factor in the disease.

It is well established that the expression of ZAP-70 by CLL cells is a reliable test for identifying Ig VH mutation, which will prognosticate the outcome of the CLL. It is reasonable to have this test available in our main diagnostic laboratories, so that the cost of the diagnosis of those with good prognosis would be significantly reduced.

Mansour Haghshenas MD, Professor of Medicine, Nemazi Hospital, Shiraz University of Medical Sciences, Shiraz, Iran.

Source: Crespo M, Bosch F, Villamor N, et al. ZAP-70 expression as a surrogate for immunoglobulin-variable-region mutations in chronic lymphocytic leukemia. *N Engl J Med.* 2003; **348**: 1764 – 75.

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2. Binet JL, Auquier A, Dighiero G, et al. A new prognostic classification of chronic lymphocytic leukemia derived from a multivariate survival analysis. *Cancer*. 1981; **48**: 198 – 206.

PREVALENCE OF METABOLIC SYNDROME IN AN URBAN POPULATION: TEHRAN LIPID AND GLUCOSE STUDY

Summary: The aim of the present investigation was to determine the prevalence of the metabolic syndrome among 10,368 adults (4,397 men and 5,971 women) aged 20 years or over participating in Tehran Lipid and Glucose Study. Metabolic syndrome was defined by the presence of three or more of the following components: abdominal obesity, hypertriglyceridemia, low high-density lipoprotein-cholesterol (HDL-C), high blood pressure, and high fasting blood glucose. The unadjusted prevalence of metabolic syndrome in the study population was 30.1% (29.2 – 31.0 with a confidence interval [CI] of 95%) and age-standardized prevalence was 33.7% (32.8 – 34.6 with a CI of 95%). The prevalence increased with age in both sexes. The metabolic syndrome was more common in women (42%) than in men (24%), ($p < 0.001$). Low HDL-C was the most common metabolic abnormality in both sexes. Except for high fasting plasma glucose (FPG), all abnormalities were more common in women than in men ($p < 0.001$). Most of those with metabolic syndrome (58%) had 3 components of the syndrome while 33% had 4 and 9% had 5 components. This report on the metabolic syndrome from Iran shows a high prevalence of this disorder. All efforts must be made for promoting healthy diets, physical activity, and blood pressure control.

Comment: The constellation of abdominal obesity, hypertension, type 2 diabetes, and dyslipidemia has been defined as metabolic syndrome.¹ Abdominal obesity is associated with resistance to the effects of insulin on peripheral glucose utilization; the associated hyperinsulinemia may then lead to hypertension and adverse metabolic consequences. Hypertriglyceridemia, low HDL-C, and fasting hyperglycemia are the metabolic consequences of this syndrome all of which accelerate the development of atherosclerosis. The strong association of metabolic syndrome with coronary heart disease (CHD), and cardiovascular mortality has been confirmed in several prospective trials.^{2,3} The metabolic syndrome has also been associated with nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH).⁴ Several recent studies have shown that elevated alanine aminotransferase (ALT) is associated with body mass index (BMI) and higher waist to hip ratios.^{5,6}

In this study, Azizi and his colleagues have assessed the prevalence of metabolic syndrome in Tehran. Using ATP III criteria,⁷ the study found that nearly one third of people in Tehran suffered from metabolic syndrome. Surprisingly, this prevalence was even higher than that reported in western world.⁸ Although genetic factors have a role in predisposing to metabolic syndrome,⁷ at least in part, the high prevalence of the syndrome in Tehran can be explained by dramatic lifestyle changes we have witnessed in Iran and especially in Tehran during the past three decades. In a recent survey of healthy blood donors in Tehran, 71% of the studied population were overweight (BMI ≥ 25) and 24% were obese (BMI ≥ 30).⁶ The high prevalence of metabolic syndrome in Tehran is in line with a recent mortality report of year 2000 from Iranian Ministry of Health. According to this report, cardiovascular diseases were the most common cause of mortality in Iran and cause 45% of all deaths in the country.⁹ Nonalcoholic fatty liver disease—another consequence of the metabolic syndrome—is also common in Tehran. According to a recently finished pathologic study (28), 34% and 2.1 % of individuals who died in accidents or due to trauma and underwent autopsy for forensic reasons in Tehran had evidence of NAFLD and NASH, respectively.¹⁰ In another study, NASH accounted for 88% of the causes of elevated serum ALT in healthy Iranian blood donors (Pourshamas et al unpublished data). The importance of metabolic syndrome is derived from the fact that while it greatly impacts the healthcare system, most of its components are modifiable through population-wide strategies for preventing and treating obesity.

There are many factors that push us to eat unhealthily and lead a sedentary life. Fast foods that are both cheap and energy dense with high fat content are very convenient today. These foods, offered now more than before in a variety of flavors, are very appealing compounded by the tremendous marketing advertisement in the media for food intake. Many people would make less money if we started eating less food, and the same would happen if we increased our physical activity. Entertainment is sedentary; we have all kinds of conveniences and communication tools which keep us sedentary and well outbalance our desire for health which is really telling us to be active and eat less. The best strategy is to consider a population-wide obesity prevention policy. These should be performed in large scale with government, industry,

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educational systems and community partnership. We need incentives for eating good food; cheaper vegetables and fruits, for example, may be far better than expensive and taxed, energy-dense foods that are detrimental to health. While we should try to make it harder to be sedentary, we should increase activity opportunities for people with parks, sidewalks, bike paths, etc. Our people should be encouraged to have healthier lifestyles to lower the relevant risk factors in the whole population through healthy diet, weight control, and increased physical activity.

Reza Malekzadeh MD, Mehdi Mohamadnejad MD, Digestive Disease Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran.

Source: Azizi F, Salehi P, Etemadi A, Zahedi-Asl S. Prevalence of metabolic syndrome in an urban population: Tehran Lipid and Glucose Study. *Diabetes Res Clin Pract.* 2003; **61**: 29 – 37.

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