Metabolic factors may play a role in risk for breast cancer

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Physiological changes associated with the metabolic syndrome may play a role in the risk of postmenopausal breast cancer, according to study results published in *Cancer Epidemiology, Biomarkers & Prevention*, a journal of the American Association for Cancer Research.

The metabolic syndrome, or insulin resistance syndrome, consists of a constellation of factors including abdominal obesity, high blood glucose levels, impaired glucose tolerance, abnormal lipid levels and high blood pressure.

Affecting roughly 47 million Americans, the metabolic syndrome is also associated with poor diet and lack of physical activity. It can also increase the risk for diabetes and heart disease.

The metabolic syndrome is characterized by elevated insulin levels, and in recent years scientists have proposed that insulin may contribute directly or indirectly to the development of breast cancer. Researchers suspect that the metabolic syndrome could influence the risk for breast cancer by affecting interrelated hormones, such as insulin, estrogen, cytokines and growth factors.

"This study suggests that having the metabolic syndrome itself or some of its components may increase a woman's risk of postmenopausal breast cancer. However, much more work is needed to understand the role of these metabolic factors and their interplay with better established breast cancer risk factors, such as reproductive and hormonal factors," said

researcher Geoffrey C. Kabat, Ph.D., senior epidemiologist in the department of epidemiology and population health at Albert Einstein College of Medicine, New York.

Studies to date have evaluated individual components of the metabolic syndrome and breast cancer, with inconsistent results, according to Kabat. For the first time, Kabat and colleagues assessed whether women who met the criteria of having the metabolic syndrome were at greater risk for postmenopausal breast cancer.

In this longitudinal study, the researchers used existing data from the Women's Health Initiative — a large, national study designed to assess major causes of chronic disease in women. Participants included postmenopausal women aged 50 to 79 years at enrollment who had repeated measurements of components of metabolic syndrome over an eight-year period. These included blood levels of glucose, HDL-cholesterol and triglycerides, as well as waist girth and blood pressure.

Results showed a modest positive association of having the metabolic syndrome as a whole, according to Kabat. Of the 4,888 women with baseline measurements who did not have diabetes, 165 incident cases of breast cancer were diagnosed during the follow-up period. Presence of the metabolic syndrome at baseline was not associated with breast cancer risk.

However, in analyses that made use of the repeated measurements, "women who had the metabolic syndrome during the three to five years prior to breast cancer diagnosis had roughly a doubling of risk," he said.

Findings also showed significant associations with elevated blood glucose levels, triglycerides and diastolic blood pressure. For diastolic blood pressure, the result was stronger, with more than a two-fold increased risk (relative risk = 2.4). Generally, for both triglycerides and

glucose the relative risk was about 1.7 for all breast cancer.

"We know a great deal about breast cancer, but we can't identify who is likely to get it. The effect of different variables associated with increased glucose and insulin levels needs to be evaluated further in larger studies," Kabat said. "We need to deepen our understanding of these different interrelated behaviors and physiological factors to see how they affect breast cancer."

Tim Byers, M.D., M.P.H., associate dean of the Colorado School of Public Health and interim director of the University of Colorado Cancer Center, believes these findings are important because the results show possible mechanisms that might explain the observation that increased weight is a risk factor for postmenopausal breast cancer.

"We have assumed that the relationship between weight and breast cancer risk is due to increased circulating estrogens among postmenopausal women who are overweight or obese," he said. "An alternative explanation is explored here: that some other aspect of the metabolic syndrome might be involved, such as growth-stimulating effects of insulin, or insulin-like growth factors."

Based on the results of this study, Byers stated that researchers now need to look more closely at dynamic changes in insulin over time, in factors tied to inflammation, and in the specific ways in which estrogen metabolism is tied to features of the metabolic syndrome.

"Though estrogens are produced in adipose tissues, just how these are metabolized in various subgroups of women needs better study," he said. "In addition, the hyper-inflammatory state of obesity and the metabolic syndrome need to be better described relative to cancer risk."

Source: American Association for Cancer Research (news : web)