

Protein that may predict future diabetes risk and death from cancer identified

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New research, published in *Diabetologia*, suggests that people with elevated levels of the protein prostatic acid phosphatase (mainly found in epithelial cells which line the surfaces and organs of the body) may be at higher risk of developing diabetes.

Importantly, the findings also indicate that individuals with elevated levels of both blood sugar and prostatic acid phosphatase appear at significantly greater risk of death from cancer.

The results held true even after adjusting for a wide range of influential factors including age, sex, [waist circumference](#), smoking and drinking habits, LDL (bad) cholesterol, systolic blood pressure, and anti-hypertensive medication.

The study is the first to examine the association between prostatic acid phosphatase blood levels and [cancer mortality](#) in the [general population](#) and analysed blood samples from over 4,000 middle-aged Swedish adults that were taken over a decade ago as part of the ongoing Malmö Diet and Cancer Study—a large population-based prospective study that has been running in Malmö, a city in southern Sweden since 1993.

"This is the most comprehensive analysis of its kind to date and sheds new light on the biological connection between [diabetes](#) and cancer," says co-lead author Professor Gunnar Engström from Lund University in Malmö, Sweden. "Prostatic acid phosphatase may be just an indicator that disease might occur, or could be causally relevant, which is exciting because it raises

the possibility of targeting this protein with future treatments for both diabetes and cancer."

Extensive evidence indicates that diabetes is linked with an increased risk of developing several types of cancer and death from cancer, and that medicines used to treat high blood sugar can alter this association. People with type 2 diabetes are around twice as likely to develop pancreatic, endometrial and liver cancer, have a 30% higher chance of developing bowel cancer and a 20% increased risk of breast cancer. However, the mechanisms that drive this predisposition are poorly understood.

Prostasin is a stimulator of epithelial sodium channels that regulate sodium balance, [blood volume](#) and [blood pressure](#). Moreover, prostasin has been found to suppress hyperglycaemia (high blood sugar)-induced tumour growth and is associated with [glucose metabolism](#). However, little is known about the link between prostasin, diabetes and cancer mortality.

To find out more, a team of Chinese and Swedish researchers conducted a cross-sectional analysis of the association between prostasin blood levels (categorised by quartiles) and diabetes in 4,658 adults (average age 58 years; 40% men) enrolled in the Malmö Diet and Cancer Study Cardiovascular Cohort between 1991 and 1994, of whom 361 (8%) had existing diabetes.

After adjusting for potential confounding factors including age, sex and waist circumference, smoking and drinking habits, LDL-cholesterol, [systolic blood pressure](#), and anti-hypertensive medication, elevated prostasin levels were found to be positively associated with the presence of diabetes, with those in the highest prostasin quartile almost twice as likely to have diabetes compared to the lowest.

Researchers then examined clinical data from the same cohort (excluding 361 participants with existing diabetes) until the end of 2019 to investigate associations with new cases of diabetes. Over an average 22-year follow-up, 702 participants developed diabetes. Longitudinal analyses identified a linear relationship between prostatic acid phosphatase (PAP) and incident diabetes, with participants with PAP in the highest quartile 76% more likely to develop diabetes than those in the lowest quartile.

Interestingly, PAP levels were found to be a better predictor of diabetes in younger participants, and those with lower blood glucose levels and better kidney function. The authors speculate that elevated PAP levels may be a compensatory response to overly high blood sugar (hyperglycaemia) but may be insufficient to stop or reverse worsening glucose control. And because PAP may be secreted into urine, normal kidney function may help to maintain optimal PAP blood levels.

In further analyses examining whether PAP has an effect on mortality (from any cause, cancer mortality, and cardiovascular mortality), researchers found that PAP was significantly associated with both cancer mortality and all-cause mortality. During average follow-up of 24 years, 651 participants died from cancer. Participants with PAP blood levels in the highest quartile were 43% more likely to die from cancer than those in the lowest quartile. For each doubling of PAP concentration, risk of cancer mortality increased by 139% and 24%, respectively, among participants with and without elevated levels of blood glucose (impaired fasting glucose). No association was found for cardiovascular mortality.

"Prostatic acid phosphatase is a new potential risk marker for the development of diabetes and for cancer mortality, especially in individuals with high blood glucose levels", says first author Dr. Xue Bao from The Affiliated Hospital of Nanjing University Medical School in Nanjing, China. "It is

easily accessible, which enhances its potential to serve as a warning marker in the future."

Since prostatic acid phosphatase has a role in regulating several diabetes-associated biological pathways that are also involved in the onset and promotion of some cancers, it may potentially mediate the process from high blood sugar to cancer, or at least may act as a marker for [cancer](#) susceptibility in participants with [high blood sugar](#). To look at this in more detail, it will be useful for future studies to trace the exact origins of prostatic acid phosphatase in [blood](#), and to determine whether the association between prostatic acid phosphatase and diabetes is causal."

The authors note that the study is observational and point to several limitations, including that the study is limited by its use of one dataset from one Swedish city, therefore the findings might not be generalisable to other populations. They also note that prostatic acid phosphatase levels were measured using frozen [blood samples](#) stored for more than a decade and their values may not be the same as measured in fresh samples. Furthermore, the study only measured prostatic acid phosphatase levels at one time point and could not distinguish between diabetes types.

More information: Xue Bao et al, Plasma prostatic acid phosphatase: a novel risk marker for incidence of diabetes and cancer mortality, *Diabetologia* (2022). [DOI: 10.1007/s00125-022-05771-w](https://doi.org/10.1007/s00125-022-05771-w)

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