Higher manganese levels in early pregnancy linked to lower preeclampsia risk

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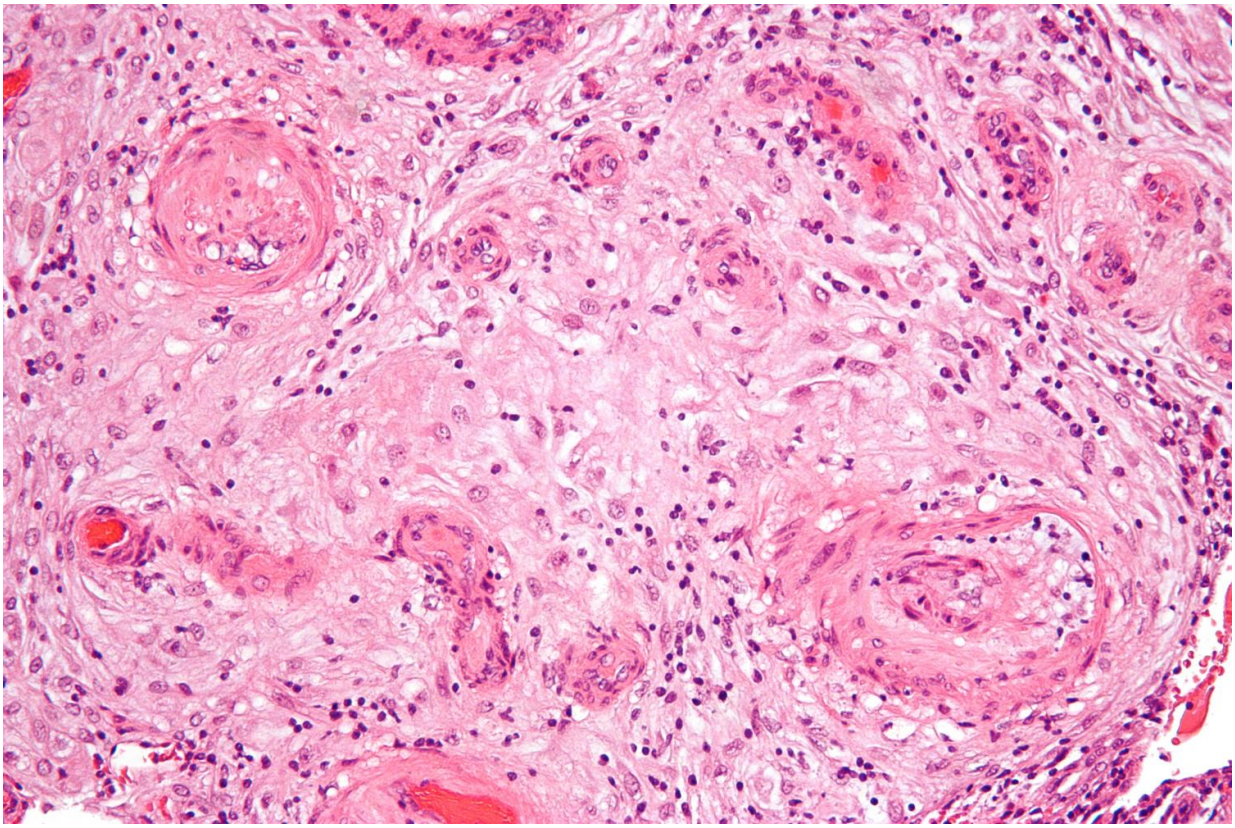

High magnification micrograph of hypertrophic decidual vasculopathy, as seen in pregnancy-induced hypertension. Credit: Wikipedia

An analysis of data from more than 1,300 women followed prospectively through pregnancy found that women with lower levels of the essential

mineral manganese in early pregnancy were more likely to develop the serious high blood pressure syndrome called preeclampsia in late pregnancy, according to a new study led by researchers from Johns Hopkins Bloomberg School of Public Health.

The study, published online in the journal *Epidemiology*, suggests the possibility that boosting manganese levels in women before and during pregnancy could potentially reduce preeclampsia risk.

Preeclampsia usually occurs after the 20th week of pregnancy and affects more than 100,000 women in the U.S. each year and an estimated 2 to 8 percent of pregnancies worldwide—and is trending towards higher rates. It features high blood pressure and associated organ damage, for example to the kidneys, and if untreated preeclampsia can lead to fatal complications such as stroke for mothers and/or premature birth for offspring. Risk factors include obesity, diabetes, and a family history of preeclampsia, but its root biological causes are unknown.

The new paper is thought to be the first to link preeclampsia to lower manganese levels in early pregnancy, long before preeclampsia appears. Prior epidemiological studies have found that women with preeclampsia tend to have lower manganese levels compared to women who don't have preeclampsia. This earlier research did not establish whether the variation in manganese levels preceded the development of preeclampsia.

"If our findings are confirmed by other prospective pre-birth cohorts, then this association between low manganese and preeclampsia should be examined experimentally, first in mice and then in humans," says study senior author Noel Mueller, Ph.D., assistant professor in the Department of Epidemiology at the Bloomberg School.

"These new findings are especially relevant, considering that

preeclampsia rates are increasing and we still lack any good strategy for preventing it," says study first author Tiange Liu, MHS, a research data analyst at the Bloomberg School.

Mueller, Liu, and colleagues previously found, in a study published in 2019, that in a sample of more than 1,000 women from the Boston Birth Cohort, levels of manganese in red blood cells, as measured shortly after delivery, tended to be lower in women who had had preeclampsia.

For their new analysis, the researchers looked at data from another Massachusetts-based study called Project Viva, which was conducted in 1999-2002. The Project Viva dataset included preeclampsia outcomes and also levels of manganese in blood drawn in the first trimester of pregnancy. If preeclampsia in these cases tended to be preceded by low manganese levels months earlier, that would be an even stronger hint that low manganese levels can be a causative factor for this condition.

The sample included 1,312 women, of whom 48 (3.7 percent) developed preeclampsia.

The researchers in their analysis found that higher manganese levels in the first trimester were associated with a lower risk of preeclampsia later in the pregnancy, depending on the dose. This suggests that incrementally more manganese would bring incrementally less risk. The researchers divided the women into three equally sized groups according to their measured manganese levels—low, medium, and high—and found that those in the high-manganese group had just half the risk of preeclampsia, compared to those in the low-manganese group.

The study was observational and did not establish a causal relationship between higher manganese levels and lower preeclampsia risk. The findings suggest that further studies that could establish a causal relationship, including of high-manganese diets, might soon be advisable.

Many common foods such as mussels, brown rice, sweet potatoes, pine nuts, and spinach are relatively rich in manganese.

Manganese has multiple biological roles in human cells—in enzyme complexes, for example, that help protect cells from harmful oxygen-containing molecules. But how it would ward off preeclampsia is so far unclear. Studying cellular mechanisms during pregnancy would help illuminate how differences in manganese levels could account for changes in preeclampsia risk, the researchers say.

More information: Tiange Liu et al. Prospective Association Between Manganese in Early Pregnancy and the Risk of Preeclampsia, *Epidemiology* (2020). DOI: 10.1097/EDE.0000000000001227

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