Low Vitamin D Associated With Preeclampsia Risk

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ARLINGTON, VA. — Pregnant women who have insufficient serum levels of vitamin D may have an increased risk of developing preeclampsia, according to findings from the first study of its kind.

If other investigators confirm this association, "preeclampsia may be added to the growing list of nontraditional adverse health effects of vitamin D insufficiency," Lisa M. Bodnar, Ph.D., said at a conference sponsored by the American Society for Bone and Mineral Research.

Medically indicated preterm deliveries for preeclampsia account for about 15% of all premature births in the United States. Delivery is the only known cure for preeclampsia, and little is known about how to prevent the disorder, said Dr. Bodnar of the department of epidemiology at the University of Pittsburgh.

'Vitamin D insufficiency was an important and significant predictor of preeclampsia risk, and ... the risk declined as vitamin D status improved.'

She and her colleagues conducted a nested case-control study of 49 primigravid women with preeclampsia and 392 women who had normal pregnancy outcomes in the prospective Pregnancy Exposure and Preeclampsia Prevention Study cohort.

The investigators enrolled the patients in the cohort at less than 16 weeks of gestation and obtained samples of maternal blood throughout gestation and cord blood at delivery. Preeclampsia was defined as the new appearance of gestational hypertension and proteinuria after 20 weeks of gestation, and the return of these abnormalities to normal in the postpartum period.

In maternal blood samples that were taken at less than 22 weeks of gestation, women who developed preeclampsia had a significantly lower mean concentration of 25-hydroxy vitamin D (25[OH]D) than did control patients (38.5 nmol/L vs. 42.8 nmol/L). The investigators adjusted the comparison for confounding variables such as race/ethnicity, prenatal multivitamin use, prepregnancy body mass index, and the season.

"In our logistic regression model, we found that vitamin D insufficiency was an important and significant predictor of preeclampsia risk, and that the risk declined as vitamin D status improved to about the nadir of the curves between 80 and 100 nmol/L," she said.

Compared with a 25(OH)D concentration of 80 nmol/L, the adjusted odds ratio for the risk of preeclampsia declined from 3.5 at 20 nmol/L to 2.7 at 30 nmol/L, 2.1 at 40 nmol/L, and 1.6 at 50 nmol/L; this was a significant trend.

The neonates of preeclamptic mothers had significantly lower mean levels of 25(OH)D in their cord blood at delivery than babies of control women (36.5 nmol/L vs. 43.1 nmol/L). The infants of preeclamptic mothers also were 2.4 times more likely to have a mean 25(OH)D concentration of less than 40 nmol/L than were infants of control patients.

The placenta has vitamin D receptors and expresses 1-α-hydroxylase, which converts stored 25(OH)D into the active compound $1,25(OH)_2D$. Vitamin D has been shown to regulate the transcription of genes that are important for placental invasion of the uterus and angiogenesis, both of which are critical for normal implantation.

Vitamin D also has ant-inflammatory and immunomodulatory properties, downregulates the blood pressure hormone renin, and is involved in insulin secretion, she said.

The first of two stages that are thought to occur in preeclampsia starts with reduced perfusion of the placenta, which is often secondary to abnormal implantation of the placenta and failed remodeling of maternal blood vessels that supply oxygen and nutrients to the placenta.

The placenta then produces materials that cause oxygen distress, endothelial activation and injury, activation of inflammatory markers, and a reduced perfusion of nearly all organs of the body. The endothelial dysfunction initiates a coagulation cascade and the ensuing second stage of multisystem sequelae, said Dr. Bodnar. ■