Serum Markers Predict Severe Preeclampsia

VITALS

Major Finding: The combination of 25-hydroxyvitamin D level and sFlt-1:PlGF ratio early in the second trimester had an area under the ROC curve of 0.834 for predicting severe preeclampsia.

Data Source: A nested, case-control study of 164 pregnant women, one-fourth of whom had developed severe preeclampsia.

Disclosures: Dr. Woodham did not report any relevant financial disclosures.

BY SUSAN LONDON

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SAN FRANCISCO – Levels of serum markers measured early in the second trimester of pregnancy may help identify women who are likely to develop severe preeclampsia, the results of a nested case-control study indicated.

In the study, there was no association between the level of vitamin D and levels of two angiogenic factors that have been previously implicated in the development of preeclampsia, soluble FMS-like tyrosine kinase 1 (sFlt-1) and placental growth factor (PlGF). But both the level of vitamin D and the ratio of sFlt-1 to PlGF predicted the development of severe preeclampsia after other risk factors were taken into account. And in ROC (receiver operating characteristic) curve analysis, the combination outperformed either measure individually.

"These results suggest that 25-hydroxyvitamin D and angiogenic factors play independent roles in the pathogenesis of preeclampsia," said Dr. Padmashree Chaudhury Woodham. "Our findings suggest that the combination of 25-hydroxyvitamin D level and sFlt-1:PlGF ratio is a better predictor of preeclampsia in midgestation than either marker alone."

A low 25-hydroxyvitamin D level has previously been shown to be a risk factor for severe preeclampsia, according to Dr. Woodham, who is a fellow in ob.gyn. at the University of North Carolina at Chapel Hill. But its association with angiogenic factors is unclear.

The investigators drew their study patients from a large cohort of pregnant women who gave blood for routine prenatal screening early in the second trimester (gestational age, 15-20 weeks). They restricted analyses to women with a singleton pregnancy who did not have chronic medical illnesses and whose fetuses did not have congenital abnormalities.

Each woman who developed severe preeclampsia (n = 41) was matched by race/ethnicity with three control women who had uncomplicated births at term (n = 123). Banked frozen serum samples were assayed to determine levels of vitamin D (total 25-hydroxyvitamin D) and the angiogenic markers sFlt-1, PlGF, and vascular endothelial growth factor (VEGF).

The severe preeclampsia and control groups were similar in terms of age, parity, and body mass index, Dr. Woodham reported. Overall, 39% were black, 29% were white, 27% were Hispanic, and 5% were Asian. The season and the median gestational age at the time blood was drawn were also similar. But the median gestational age at delivery was younger in the preeclampsia group (32.6 vs. 39.6 weeks; *P* less than .001).

Relative to their control counterparts, the women who developed preeclampsia had lower levels of vitamin D (*P* less than .001), VEGF (*P* less than .001), and PlGF (*P* = .03), and a higher ratio of sFlt-1 to PlGF (*P* = .02). Levels of vitamin D were not correlated with levels of any of the angiogenic factors or with the sFlt-1:PlGF ratio, contrary to the findings of in vitro and animal studies. However, in a multivariate model, each 1-nmol/L increase in total vitamin D level was associated with a 5% reduction in the odds of preeclampsia, whereas each 1-unit increase in the sFlt-1:PlGF ratio was associated with an 11% increase in the odds.

ROC curve analysis showed that for predicting preeclampsia, the area under the curve was 0.745 for vitamin D alone and 0.669 for the sFlt-1:PlGF ratio alone. But it was higher with their combination (0.834). There was also a small further improvement when VEGF level was added to the mix, with an area under the curve of 0.851. ■