Urinary PlGF Predicts Early-Onset Preeclampsia

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VIENNA — Decreased urinary placental growth factor at midgestation is strongly associated with the subsequent development of early-onset preeclampsia, S. Ananth Karumanchi, M.D., reported.

"Low urinary PlGF antedates the clinical diagnosis of preeclampsia and may serve as a screening test to predict who will develop early-onset disease," Dr. Karumanchi said at the 14th World Congress of the International Society for the Study of Hypertension in Pregnancy.

The findings, published soon after the congress, come from a nested case-control study within the Calcium for Preeclampsia Prevention trial of healthy nulliparous women enrolled at five U.S. university medical centers during 1992-1995. Frozen serum and urine samples from 120 women with preeclampsia were compared with those of 120 matched normotensive controls (JAMA 2005;293:77-85).

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In all the women, urinary PlGF levels increased during the first two trimesters, with a more rapid increase after 21-24 weeks and a peak at 29-33 weeks. However, those levels were significantly lower among the women who subsequently developed preeclampsia at weeks 25-28, 29-32, and 33-36. Differences were particularly large between the controls and the women who subsequently developed preeclampsia before 37 weeks or who had preeclampsia with a small-for-gestational age (SGA) infant.

Alterations in urinary PlGF levels at 21-32 weeks were also more pronounced in women who subsequently developed preeclampsia before 37 weeks (87 pg/mL) than among those who had onset of preeclampsia at term (223 pg/mL).

At 33-42 weeks, those levels were 22 vs. 118 pg/mL, lead author Richard J. Levine, M.D., of the National Institute of Child Health and Human Development, Bethesda, Md., and his associates reported in the published article.

The women were divided by quartiles of urinary PlGF obtained at 21-32 weeks' gestation and the results adjusted for gestational age at specimen collection, storage time, body mass index, and maternal age.

Compared with women in the upper three quartiles, the odds ratio was 22.5 for later development of preterm preeclampsia among the women with PlGF concentrations in the lowest quartile (less than 118 pg/mL). The association was even stronger when restricted to just morning urine specimens, with an odds ratio of 39.5.

For term preeclampsia, the adjusted odds ratios of lowest vs. the upper three quartiles of PlGF concentration were 2.2 at 21-32 weeks and 2.3 at 33-42 weeks' gestation. The data also suggested a strong association between low urinary PlGF and a substantially increased risk for preeclampsia with an SGA infant, but the numbers were too small to make a stable estimate, Dr. Levine and his associates noted.

Adjusting the results for urinary creatinine concentration did not change the strength of the associations, they said.

Previous data from this research group showed that increased circulating serum levels of the angiogenic factor soluble fms-like tyrosine kinase (sFlt-1) were predictive of subsequent preeclampsia (N. Engl. J. Med. 2004;350:672-83).

But because the sFlt-1 molecule is too large to be filtered into urine, the current study focused on PlGF, which binds to sFlt-1, as a more clinically feasible alternative. If a reliable dipstick assay could be developed for urine screening of all pregnant women for urine PlGF, then subsequent serum measurements of both PlGF and sFlt-1 could minimize false-positive results from urine testing, the researchers said.

At the congress, Dr. Karumanchi, a nephrologist at Beth Israel Deaconess Medical Center, Boston, said, "Obviously, this is a retrospective study done using specimens frozen for several years, and we don't know if it can be reproduced prospectively. Nevertheless, it does prove the hypothesis that angiogenic factors play a critical role in the pathogenesis of this syndrome." ■