Angiogenic Imbalances Predict Preeclampsia in SLE

BY DIANA MAHONEY New England Bureau

BOSTON — Alterations in circulating antiangiogenic protein levels in pregnant women with lupus and antiphospholipid antibody syndrome may predict preeclampsia, a pregnancy complication for which they are at increased risk, according to data presented at the annual meeting of the American College of Rheumatology.

The findings suggest that identification of angiogenic imbalances early in gestation and subsequent interventions targeting the inflammatory pathways that trigger the imbalances could potentially reduce the incidence of preeclampsia in women with these autoimmune conditions, reported Dr. Jane E. Salmon of the Hospital for Special Surgery in New York.

In a nested case-control study of pregnant women with systemic lupus erythe-

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matosus (SLE) and/or antiphospholipid antibody (APLA) syndrome, women with elevated levels of circulating soluble fms-like tyrosine kinase 1 (sFlt-1) and soluble endoglin (sEng) at midpregnancy were at significantly

increased risk for preeclampsia later in pregnancy, compared with age- and ethnicity-matched disease control patients who had SLE and/or APLA but not preeclampsia, reported Dr. Salmon.

Subjects for the investigation were enrolled in the multicenter observational PROMISSE (Predictors of Pregnancy Outcome BioMarkers in Antiphospholipid Antibody Syndrome and Systemic Lupus Erythematosus) study. In the larger study, 211 women with SLE and/or APLA who were less than 12 weeks pregnant at enrollment were followed throughout their pregnancy to determine the association between alterations in antiangiogenic factors and the later development of preeclampsia. In the nested case-control study, each of the 16 women with SLE and/or APLA syndrome from the larger cohort who developed preeclampsia was matched to both another SLE woman



and/or an APLA-positive woman who didn't develop preeclampsia and to a healthy control who had neither autoimmune disease or pregnancy complications, Dr. Salmon explained.

Compared with the healthy controls, elevations in levels of circulating sFlt-1 were observed in all of the autoimmune patients as early as 12-15 weeks' gestation. Additionally, the rate of increase in levels of that protein throughout pregnancy was significantly higher in patients who went on to develop preeclampsia, and it was higher in all patients with autoimmune disorders, compared with healthy controls, reported Dr. Salmon. Among the patients with autoimmune disorders, elevated levels of sFlt-1 and sEng at 20-23 weeks' gestation were independently associated with increased risk of developing preeclampsia, she noted.

The findings indicate that sFlt-1 and sEng are biomarkers predictive of preeclampsia in patients with lupus and/or APLA and that "imbalances [in the levels of these biomarkers] early in pregnancy increase the vulnerability of these patients to preeclampsia," said Dr. Salmon. 'Because inflammatory mediators trigger production of antiangiogenic factors, early intervention to block specific pathways of inflammation could prevent angiogenic imbalance in lupus pregnancies at risk for preeclampsia.²

Obstetrics

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Dr. Salmon reported having no financial disclosures relative to this presentation.



[†]Adequate calcium and vitamin D as part of a healthful diet throughout life, along with physical activity, may reduce the risk of osteoporosis later in life.

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References: 1. IMS data; NDT 2001-2006. 2. Sunyecz JA, Weisman SM. The role of calcium in osteoporosis drug therapy. *J Womens Health*. 2005;14:180-192. 3. Data on file, Wyeth Consumer Healthcare.