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Adverse Pregnancy Outcomes in the Lupus in prEGnAnCY (LEGACY) Cohort: Anti-Phosphatidylserine/Prothrombin IgG Antibodies are Stronger Predictors than Lupus Anticoagulant.

Adverse pregnancy outcomes (APO) are a major concern in SLE, particularly in the presence of antiphospholipid antibodies. Although lupus anticoagulant (LAC) is among the strongest predictors of APO, emerging evidence suggests that antibodies to the phosphatidylserine/prothrombin complex (aPS/PT) may also identify patients at increased risk. Our aim was to examine whether aPS/PT predicted APO in SLE pregnancies and how they perform compared to LAC in the multi-centre prospective Lupus in prEGnAnCY (LEGACY) cohort.

LEGACY includes Systemic Lupus International Collaborating Clinics in Canada, South Korea, Peru, and Mexico. Pregnant SLE women are consecutively enrolled 30 units. LAC testing was performed at each site using validated assays. APO were a composite outcome of either: 1) fetal death >20 weeks, 2) neonatal death, 3) placenta-mediated preterm delivery <36 weeks, and/or 4) small for gestational age (<5th percentile). We performed multivariable hazards models with frailties and gestational age as the time axis to assess associations between aPS/PT IgG and/or IgM and APO, versus LAC and APO. We used Harrell's C-index to assess model discrimination.

Among 98 SLE pregnancies, 9 (9%) were aPS/PT IgG-positive, 25 (26%) were aPS/PT IgM-positive, and 11 (11%) were LAC-positive. Eight women (8%) were positive for both aPS/PT (IgG and/or IgM) and LAC. Thirteen pregnancies (13%) experienced an APO, including 5/9 (56%) in the aPS/PT IgG-positive group and 5/11 (46%) in the LAC-positive group. In multivariable analysis, aPS/PT IgG positivity was strongly associated with APO (HR 12.2, 95% CI 1.7-87.2), whereas IgM and/or overall aPS/PT positivity showed non-significant trends [HR 1.9 (95% CI 0.3-11.2) and HR 2.2 (95% CI 0.4-11.2), respectively]. LAC positivity was also associated with a substantially higher APO risk (HR 7.8, 95% CI 1.7-35.1), though less strongly than aPS/PT IgG. Discriminative performance was slightly higher for aPS/PT IgG (adjusted C-index 0.80, 95% CI 0.65-0.95) compared with LAC, aPS/PT IgM, and combined aPS/PT IgG and/or IgM models (0.78, 95% CI 0.68-0.89; 0.72, 95% CI 0.59-0.85; and 0.73, 95% CI 0.61-0.86, respectively).

In the prospective LEGACY cohort, aPS/PT IgG demonstrated a stronger independent association with APO and slightly better discriminative performance than LAC. These findings suggest that aPS/PT IgG may outperform LAC in predicting APO and could improve risk stratification in SLE pregnancies.