Fetal gender and maternal serum screening markers

To the Editor:

Although results from several studies have suggested that fetal gender may have an effect on the maternal serum concentration of pregnancy-related products,[1–8] we could not find a controlled study in which clinical confounding variables that may affect the concentration of maternal serum screening markers for chromosomal and pregnancy complications had been excluded from analysis before the evaluation of the possible effect of fetal gender. For this reason, we performed a nested study in which the clinical records of 213 pregnant women who had consented to donate blood for biochemical research purposes during pregnancy were reviewed in a protocol approved by the institutional review board of Texas Tech University. Gestational age at maternal blood sampling and estimated date of delivery were calculated in all pregnancies using ultrasound measurements as documented in the medical records. Figure 1 summarizes the study design and clinical classification of patients. Sixty-two percent of patients were white, 29% were Hispanic, 4% were African American, and 5% were of other cultural backgrounds. For the purpose of this study, the maternal serum samples from the 135 patients with uncomplicated singleton pregnancies that resulted in term deliveries of appropriately grown neonates without congenital anomalies were thawed and used to measure the concentration of the five maternal serum analytes. Of these 135 patients, 123 had donated blood during the first trimester of pregnancy at a mean gestational age of 11.9 weeks (standard deviation = 1.5), and 129 had donated blood during the second trimester at a mean gestational age of 16.8 weeks (standard deviation = 1.3). First-trimester serum samples (10–14 weeks) were analyzed for free β-human chorionic gonadotropin and pregnancy-associated placental protein-A by enzyme-linked immunosorbent assay. Second-trimester serum samples (15–20 weeks) were analyzed for alpha-fetoprotein and human chorionic gonadotropin by enzyme-linked immunosorbent assay and for unconjugated estriol by second antibody radioimmunoassay. All assays were from Diagnostic Systems Laboratories, Inc. (Webster, TX). Intraassay coefficients of variation averaged less than 5%, and interassay coefficients of variation were between 7% and 11%. All samples were analyzed in duplicate. Clinical and maternal serum biochemical data were entered into the Statistical Package for the Social Sciences (SPSS Inc.,

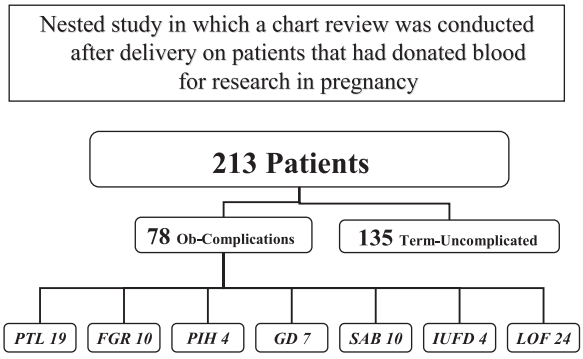

Fig. 1. This was a nested study in which the clinical records of 213 pregnant women who had consented to donate blood for biochemical research purposes during pregnancy were reviewed. Ob, obstetric; PTL, preterm labor (<37 completed weeks); FGR, fetal growth restriction; PIH, pregnancy-induced hypertension; GD, gestational diabetes; SAB, spontaneous abortion; IUFD, intrauterine fetal demise; LOF, loss of follow-up.

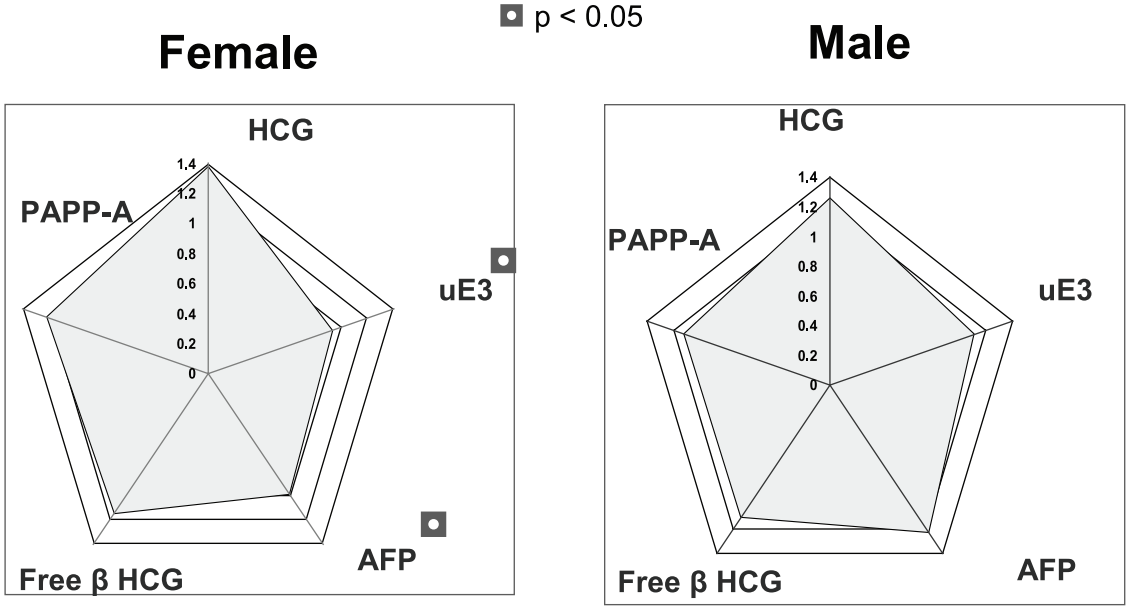

Fig. 2. With a geometric figure, radar-type graphs from the Chart Wizard option in Excel (Microsoft Corporation, Redmond, WA) were used to demonstrate the effects of gender on the mean (multiples of the median) concentration of the five maternal serum markers. The mean serum concentration in mothers bearing male (N = 72) versus female (N = 63) fetuses expressed in multiples of the median were PAPP-A = 1.12 versus 1.22; free β-hCG = 1.1 versus 1.15; uE3 = 1.1 versus 0.94; AFP = 1.23 versus 0.99; and hCG = 1.25 versus 1.37. Significant differences (■ = $P < .05$) were noted for second-trimester alpha-fetoprotein and unconjugated estriol. PAPP-A, pregnancy-associated placental protein-A; β-hCG, β-human chorionic gonadotropin; uE3, unconjugated estriol; AFP, alpha-fetoprotein.

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Chicago, IL), and summary statistics were calculated. Biochemical data were stratified by gestational age at the time of maternal blood sampling and expressed as multiples of the median for the week interval. Multiples of the median were then entered into Excel (Microsoft Corporation, Redmond, WA) in rows with males and females in separate columns. Analysis of variance was used to determine group differences. The significance level was set at P less than .05. No differences in maternal age, time of blood donations, gestational age at delivery, newborn weights, or 5-minute Apgar scores were observed between women bearing male versus female fetuses. Graphic depictions of the mean concentration of the five analytes classified by fetal gender are shown in Figure 2. These findings suggest that mothers bearing female fetuses may have lower alpha-fetoprotein and unconjugated estriol serum concentrations. In addition, our data concur with previous studies reporting higher β-human chorionic gonadotropin and human chorionic gonadotropin concentration in mothers bearing female fetuses.

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