Validating the ratio of insulin like growth factor binding protein 4 to sex hormone binding globulin as a prognostic predictor of preterm birth in Viet Nam: a case-cohort study

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August 7, 2023

Abstract

Objective To validate a serum biomarker developed in the USA for preterm birth (PTB) risk stratification in Viet Nam. *Design* Case-cohort study *Setting* Tu Du Hospital, Ho Chi Minh City, Viet Nam *Population* Women with a viable singleton pregnancy (n=5000). *Methods* Maternal serum was collected between $19\,^{+0}$-$22\,^{+6}$ weeks' gestation and participants followed to neonatal discharge. Relative insulin-like growth factor binding protein 4 (IGFBP4) and sex hormone binding globulin (SHBG) abundances were measured by mass spectrometry and their ratio compared between PTB cases and term controls. Discrimination (area under the receiver operating characteristic curve, AUC) and calibration for PTB <37 and <34 weeks were tested, with model tuning using clinical factors. *Main outcomes measures* All PTBs (any birth [?]37 weeks' gestation) and spontaneous PTBs (birth [?]37 weeks' gestation with clinical signs of initiation of parturition). *Results* Complete data were available for 4984 (99.7%), cohort PTB rate=6.7%; n=335. We observed an inverse association between IGFBP4/SHBG ratio and gestational age at birth (p=0.017); AUC 0.60 (95% CI, 0.53-0.68). Including previous PTB (multiparous women) or prior miscarriage (primiparous women) improved performance (AUC 0.65 and 0.70, respectively, for PTB <37 and <34 weeks' gestation). Optimal performance (AUC 0.74) was between 19-20 weeks' gestation, for BMI >21kg/m^2 and age 20-35 years. *Conclusions* We have validated a novel serum biomarker for PTB risk stratification in a very different setting to the original study. Further research is required to determine appropriate ratio thresholds based on the prevalence of risk factors and the availability of resources and preventative therapies.
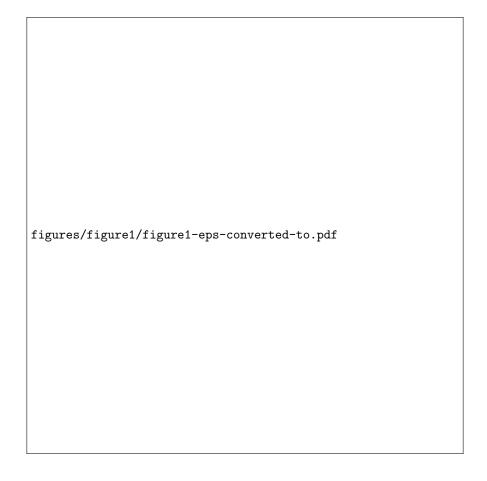
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