TITLE: ASSOCIATION BETWEEN SERUM HORMONE LEVELS IN EARLY PREGNANCY AND RISK OF HYPERTENSIVE DISEASES OF PREGNANCY IN WOMEN UNDERGOING ASSISTED REPRODUCTION: A RETROSPECTIVE COHORT STUDY

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Background: Preeclampsia (PE) is an important cause of morbidity in pregnancy[1], yet its pathophysiology remains unclear and predicting who will develop PE is challenging[2]. Assisted reproductive technology (ART) use, however, is a known risk factor[2]. Developing screening tools, especially among women using ART, could facilitate timely prevention with aspirin.

Objective: To examine the association between progesterone (P4), estradiol (E2), and human chorionic gonadotropin (hCG) levels in early pregnancy and the development of hypertensive diseases of pregnancy (HDP) among women undergoing ART.

Materials and Methods: This retrospective study included patients who underwent frozen embryo transfer (ET), ovulation induction (OI), or unassisted conception (UC) and had a live singleton birth at a single academic institution from 9/6/2013-12/17/2021. First hormone levels were drawn 9 days after blastocyst ET, and at approximately 4 weeks gestation for those who conceived via OI or UC. Primary outcome was the development of HDP (gestational hypertension, PE, HELLP, or eclampsia). Patient characteristics were compared between ET, OI, and UC patients with Chi-square (or Fisher's exact) test for categorical variables and Wilcoxon rank-sum (or Kruskal-Wallis) test for continuous variables. The ET group was further split into programmed frozen embryo transfer (P-FET) and natural cycle frozen embryo transfer (NC-FET), and hormone levels were compared between these two subgroups. Logistic regressions were also conducted to evaluate whether each hormone level, dichotomized at the quartile of highest risk, was associated with HDP after controlling for age, BMI and gravidity. P-value less than 0.05 was considered statistically significant.

Results: 681 patients were included; 189 had ET, 193 had OI, and 299 had UC. The median age of those who conceived after ET was 37, while the median age of those who conceived after both OI and UC was 35 (p<0.001). Median BMI, history of HDP, and history of chronic hypertension did not vary between groups. Those with UC were most likely to be primigravid and those undergoing ET were most likely to be multiparous (p=0.025). While median hormone levels for E2 and P4 were significantly different between P-FET and NC-FET patients (E2: 252 vs 317 pg/mL, P4: 64 vs 29 ng/mL, respectively; both p<0.001), rates of HDP did not significantly differ between those two groups. In the multivariate analyses, P4, E2, and hCG were not significantly associated with development of HDP.

Conclusions: P4, E2, and hCG levels in early pregnancy did not correlate with development of HDP. While development of HDP is thought to be associated with hormone levels in the 2nd and

3rd trimesters[1], this study suggests that the hormonal milieu of early pregnancy may be less important to HDP risk. Future prospective studies are needed for better assessment.

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