Fetal fraction of cell-free DNA and placental function in IVF/ICSI and spontaneous pregnancy

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Objective

Fetal fraction (FF) is a direct measure of placental mass and, perhaps, also of placental function. There is a direct correlation between FF and maternal serum PAPP–A and PlGF in the general population. The aim of our study was to evaluate correlation of FF with PAPP-A, free β-hCG, mean uterine artery pulsatility index (UAPI) and mean arterial pressure (MAP) in IVF/ICSI pregnancies compared with pregnancies conceived spontaneously.

Methods

This was a single-centre retrospective study from 2013 to 2018 of pregnancies undergoing both the combined screening test at 11-13+6 weeks (FMF criteria) and cfDNA (Harmony, Roche). Chromosomal defects were excluded. Data was shown by median (IQR) and frequencies (%). Characteristics of the two groups were compared by the χ2 test or Fisher's exact test, for categorical variables, and by the Mann-Whitney U-test for continuous variables. Measured biomarkers (FF, PAPP-A, free β-hCG, UAPI and MAP) were first converted to multiples of the median (MoM) after adjustment for pregnancy characteristics. MoM of FF were calculated using medians provided by Lee et al. (Hum Rep, 2018) and log-transformed. Biomarkers MoM of IVF/ICSI pregnancies were compared to those of spontaneous conceptions by univariate mixed linear analysis.

Results

181 pregnancies were included for analysis. There were 45 IVF/ICSI pregnancies and 136 spontaneously conceived pregnancies. The two groups differed in maternal age [IVF/ICSI: 39 yrs (36-41); controls: 37 yrs (34-39), p = 0. 001] and parity [nulliparous, IVF/ICSI: 39 (88. 6%); controls: 73 (56. 2%), p <0. 0001], but did not differ for BMI [IVF/ICSI: 21. 2 (19. 1-22. 8); controls: 21. 7 (19. 6-23. 4), p =0. 447] and gestational age in days at cfDNA [IVF/ICSI: 88 (78-100); controls: 86 (81-98. 5), p = 0. 709]. In the IVF/ICSI group, 13 out of 45 (29%) pregnancies were obtained by egg donation. There were no differences of FF MoM [IVF/ICSI: 1. 13 (0. 84-1. 41); controls: 1. 04 (0. 79-1. 24), p =0. 237], PAPP-A MoM [IVF/ICSI: 1. 02 (0. 6-1. 36); controls: 1. 16 (0. 84-1. 56), p =0. 091], free β-hCG MoM [IVF/ICSI: 0. 99 (0. 6-1. 3); controls: 1. 02 (0. 7-1. 45), p=0. 478] and UAPI MoM [IVF/ICSI: 1 (0. 77-1. 26); controls: 1. 11 (0. 89-1. 26), p =0. 072] between the two groups. MAP MoM was significantly higher in IVF/ICSI than in spontaneous group [IVF/ICSI: 1. 01 (0. 95-1. 11); controls: 0. 95 (0. 9-1), p =0. 003]. Considering the trend of log10 FF MoM as increasing log10 PAPP-A MoM, both groups showed a statistically significant increase in the slope of the regression line [coefficient (95% CI); IVF/ICSI: 0. 158 (-0. 022-0. 338); controls: 0. 126 (0. 006-0. 253), p=0. 027]; but there was no difference in the slope between IVF/ICSI and spontaneous pregnancies (p=0. 765). Moreover, there was no significant difference in the slope of the regression line of both log10 free β-hCG MoM (p=0. 487), log10 UAPI MoM (p= 0. 639) and log10 MAP MoM (p= 0. 284) against log10 FF MoM in the two groups.

Conclusion

The positive correlation of FF with PAPP-A is particularly evident in IVF/ICSI pregnancies. This finding may be related to differences in placental development of these high risk pregnancies, but further studies are needed.