

Impact of assisted reproduction and specific pregnancy complications on maternal mid-trimester Down's syndrome screening

ABSTRACT

Objective: Pregnant women hope, that propable fetal disorders could be detected as early as possible, and during last decades several biochemical screening methods have been developed to accomplish this. The specific aim of this study was to study the effect of assisted reproduction technologies (ART) on the maternal mid-trimester serum free β -hCG and AFP MoM levels and the usefulness of these markers in the prediction of specific pregnancy complications.

Subjects and methods: 19310 women who participated in the Down's syndrome screening program in 1994-1996 in Helsinki, Oulu, Tampere and Turku University hospital areas. Additionally 194 pregnancies started with ART up to 1998 were included. The singleton ART pregnancies were divided into intrauterine insemination (IUI, n=48), *in vitro* fertilization (IVF, n=58), intracytoplasmic sperm injection (ICSI, n=32) and frozen-thawed embryo transfer (FET, n=26) and IVF twin (n=30) groups. The effect of the ovarian stimulation medication on the marker levels was evaluated, as well as the effect of the number of embryos transferred. The marker levels between spontaneous (n=145) and IVF (n=30) twins were compared. The pregnancy complications analysed were gestational diabetes mellitus (GDM), pregnancy induced hypertension (PIH) and intrahepatic cholestasis of pregnancy (ICP), a common, probably inherited pregnancy complication. PIH pregnancies were further divided into severe and mild pre-eclampsia and gestational hypertension. In the PIH study serum inhibin A and total renin levels were also measured.

Results: The free β -hCG MoM levels were higher in IUI (1.29), IVF (1.19), ICSI (1.07) and FET (1.33) pregnancies and in IVF twins (2.20) as compared to controls (1.00). AFP levels did not differ between the groups. The ovarian stimulation medication could not explain the alterations on the marker levels in the IVF or ICSI groups. The number of embryos transferred had a low correlation with free β -hCG ($r=0.28$) and AFP ($r=0.30$) MoM levels only in the IVF group. The IVF twin group had statistically significantly higher free β -hCG MoM levels than the spontaneous twin group (2.20 and 1.83, respectively). The AFP MoM levels were higher in a subgroup with severe pre-eclampsia (1.68) than in mild pre-eclampsia (1.09) or gestational hypertension (0.94). Both free β -hCG and AFP levels were statistically significantly lower in the group with spontaneous pregnancies and GDM (0.72, $p=0.01$ and 0.93, $p=0.01$, respectively).

Conclusions: In pregnancies achieved with ART the mid-trimester serum MoM levels of β -hCG are higher compared to spontaneous pregnancies and elevated levels of markers may give a false positive result in the Down's syndrome screening. GDM and severe pre-eclampsia may affect maternal mid-trimester serum free β -hCG and AFP MoM levels and consequently may have an impact on the screening result.

Key words: AFP/ART/free β -hCG/Down's syndrome/FET/ICSI/IUI/IVF/pre-eclampsia/gestational diabetes/intrahepatic cholestasis of pregnancy.