



## Cell-free fetal DNA testing in singleton in-vitro fertilisation conceptions

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### Objective

In-vitro fertilisation (IVF) is responsible for 4.4% of births in Australia. IVF conceptions are associated with maternal anxiety and have higher rates of aneuploidy than spontaneous conception. Cell-free fetal DNA (cffDNA) testing, which analyses circulating cell-free fetal DNA in maternal blood, has been shown to have very high accuracy for detection of trisomy 21 in the general obstetric population. There remains to be focused and conclusive evidence regarding the test characteristics of cffDNA testing in IVF conceived pregnancies. The aim of this study is to compare fetal fraction, test failure rate and positive predictive value of cffDNA testing in pregnancies conceived spontaneously and through IVF, and to investigate the effect of IVF modalities on these test characteristics.

### Methods

This was a single-centre, retrospective cohort study including spontaneously and IVF conceived singleton pregnancies where screening for trisomies 21, 18 and 13, as well as sex chromosome aneuploidies (SCA) was performed with cffDNA testing after 10 weeks' gestation. Samples were collected consecutively between April 2013 and November 2016 at a private obstetric and gynecological ultrasound clinic in Melbourne, Australia. Multivariate regression analysis was used to determine significant predictors of logarithmically transformed fetal fraction and test failure. Comparison of test characteristics between study groups was performed adopting a significance level of 5%.

### Results

A total of 4,633 spontaneously conceived and 992 IVF pregnancies were included. Median fetal fraction was lower (10.3% [interquartile range (IQR), 7.7-13.5] vs. 11.9% [IQR, 9.1-15.0];  $p=0.005$ ), test failure rate was higher (5.2% vs. 2.2%;  $p<0.001$ ) and positive predictive value (PPV) for trisomies 18, 13 and SCA was poorer in IVF pregnancies compared to those spontaneously conceived. Multivariate linear regression analysis demonstrated that lower fetal fraction was related with IVF conception, increased BMI, earlier gestational age and South and East Asian ethnicities. Multiple logistic regression analysis found IVF conception and increased BMI to be associated with test failure. Positive predictive value was high for trisomy 21 in IVF conception (100.0%), but was lower for other trisomies when compared with the non-IVF population.

### Conclusion

Fetal fraction is significantly lower, failure rate is higher and positive predictive value of cffDNA testing is lower in singleton pregnancies conceived by IVF than those conceived spontaneously. These limitations should be taken into account during pre-test counseling in pregnant women who conceive by IVF.