

How Body Mass Index (BMI) Influences the Content of Cell-Free Fetal DNA (cffDNA) in Maternal Blood – Consequences for the PrenaTest® Analysis

Introduction

According to latest research, one out of three persons worldwide is overweight. Among adults, the prevalence of obesity is generally higher among women than among men.¹ It is well known that obesity increases the risk for diseases and complications during pregnancy. Furthermore, ultrasound examinations can't always deliver clear results for obese pregnant women. But are there consequences of overweight on the performance of non-invasive prenatal tests (NIPT)?

NIPT are based on the analysis of cell-free fetal DNA (cffDNA) circulating in the maternal blood. In general, the determination of the percentage of cffDNA in relation to the total amount of cell-free DNA is one of the first steps of the analysis. With every PrenaTest® result this percentage is given to the physician. The prerequisite for a successful PrenaTest® analysis (on the basis of *random massively parallel sequencing, rMPS*) is a cffDNA level of $\geq 4\%$ in singleton pregnancies and $\geq 8\%$ in twin pregnancies.

BMI influences the cffDNA level in maternal blood

All samples from singleton pregnancies which have been analyzed with rMPS in our Constance Laboratory within a certain time frame, have been assessed (n=45,936). The results confirm that a higher BMI affects the cffDNA content in maternal blood and, thus, might affect the feasibility of the PrenaTest®.

All in all, 99.1 % of all blood samples (n=45,518/45,936) had a cffDNA content of at least 4 % and were analyzed successfully. Only 0.9 % of the samples (n=418/45,936) had a cffDNA content below 4 % so that the analysis had been stopped at that point. The pregnant women from whom the blood samples were taken were offered to repeat the test at a later point of time, since the cffDNA content usually rises during pregnancy. From all pregnant women having a cffDNA content in the blood of at least 4 %, 7.8 % had a BMI ≥ 30 (n=3,544/45,518). Compared to that, the percentage of women with a cffDNA content below 4% and a BMI ≥ 30 was 28.2 % (n=118/418) (see table 1).

Thus, within the group of pregnant women with a BMI ≥ 30 the cffDNA content was nearly 5 times more often below 4 % than in the group with a BMI < 30 (3.2 % vs. 0.7 %).

	cffDNA content $\geq 4\%$	cffDNA content $< 4\%$
All samples (n=45,936)	99.1 % (n=45,518/45,936)	0.9% (n=418/45,936)
Samples from women with BMI < 30 (n=42,274)	99.3% (n=41,974/42,274)	0.7% (n=300/42,274)
Samples from women with BMI ≥ 30 (n=3,662)	96.8% (n=3,544/3,662)	3.2% (n=118/3,662)

Table 1: Number of analyzed blood samples with regard to cffDNA content and BMI

In studies analyzing the accuracy of NIPT in overweight or obese women it has been proven before that the average cffDNA content decreases with increasing weight. An explanation might be the fact that the blood volume increases with higher body mass. Ashoor et al. found that the average cffDNA level in the blood of a pregnant woman with 60 kg weight is about 12 %, whereas it is only about 4 % in women with 160 kg weight (measured at a gestational age of 11+0 to 13+6).²

Recommendation

Although – according to our internal statistics – the majority of pregnant women with a BMI ≥ 30 will obtain a valid PrenaTest® result after the first blood collection (see table 1), we recommend to inform patients with a higher BMI about their individual risk to receive no test result at the first attempt. However, all women with a cffDNA content below 4 % have the possibility to repeat the test with a blood sample drawn later in pregnancy at no additional charge. Please inform your patients that the costs for the PrenaTest® analysis will only be charged when a valid test result is reported.

Literature

- 1 The GBD 2015 Obesity Collaborators. Health Effects of Overweight and Obesity in 195 Countries over 25 Years. N Engl J Med 2017; 377:13-27 July 6, 2017 DOI: 10.1056/NEJMoa1614362
- 2 Ashoor G, Syngelaki A, Poon LC, Rezende JC, Nicolaidis KH. Fetal fraction in maternal plasma cell-free DNA at 11-13 weeks' gestation: relation to maternal and fetal characteristics. Ultrasound Obstet Gynecol. 2013b Jan;41(1):26-32.