A Noninvasive Prenatal Screen that Achieves ≥4% Fetal Fraction in >99.9% of Patients

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All authors were employed by Myriad Genetics, Inc. at the time of this study

**RESULTS**

- For millions of pregnant women, noninvasive prenatal screening (NIPS) based on cell-free DNA (cfDNA) detects whether their pregnancies are at elevated risk for fetal chromosomal abnormalities.
- Fetal fraction (FF), the proportion of cfDNA originating from the placenta, can impact the accuracy of NIPS, and many laboratories fail samples with low FF, commonly defined as FF <4%.
- FF has been shown to negatively correlate with body mass index (BMI), pregnancies with trisomy 18 or 13, and early gestational age, resulting in higher test failure rates in these populations.
- A whole-genome sequencing (WGS)-based NIPS that employs FF amplification (FFA) technology for all samples has been shown to increase FF by 3.9-fold for samples with low FF.

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**METHODS**

- We retrospectively analyzed results from 104,710 patients who underwent NIPS with FFA during an eight-month period.
- The FFA technology increased FF by preferentially sequencing short cfDNA fragments, known to be enriched for fetal-derived cfDNA.
- FF was assessed for patients who received a screening result (N= 104,557).
- BMI data were available for 65,773 patients.

**RESULTS**

- Median maternal age was 31 years and median gestational age was 12 weeks.
- No patients had tests failed due to FF <4%.
- Less than 0.1% of patients had FF below 4%.
- Ninety-nine percent of patients had FF >6.4% (Fig 1A, dashed line).
- In patients with gestational age less than 12 weeks (N= 48,722), 99% of patients had FF >6%.
- In patients with BMI ≥30 (N= 23,380), 99% of patients had FF >5.4%.
- Even in patients with BMI ≥ 40 and gestational age of 10 weeks, 99% of patients had FF > 4.6%.

**CONCLUSIONS**

- A commercial NIPS using high-throughput FFA achieves sufficiently high FF levels to provide confident results regardless of a woman’s risk factors, preventing unnecessary test failure.

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