

INTRODUCTION

Down syndrome (DS) is the first cause of intellectual deficiency involving a supernumerary material of chromosome 21. The best practice laboratories guidelines recommend nuchal translucency screening combined with first-trimester serum screening. In the second trimester, sequential serum screening can be performed. A risk $\geq 1/250$ was considered increased and fetal karyotyping is required. Pregnancy loss following invasive sampling (amniocentesis or chorionic villosity sampling) is estimated to 0.5-1%. The application of massively parallel sequencing (next-generation sequencing; NGS) to non invasive prenatal diagnostic of Fetal circulating DNA in Maternal serum represents the major advanced progress of human genetics.

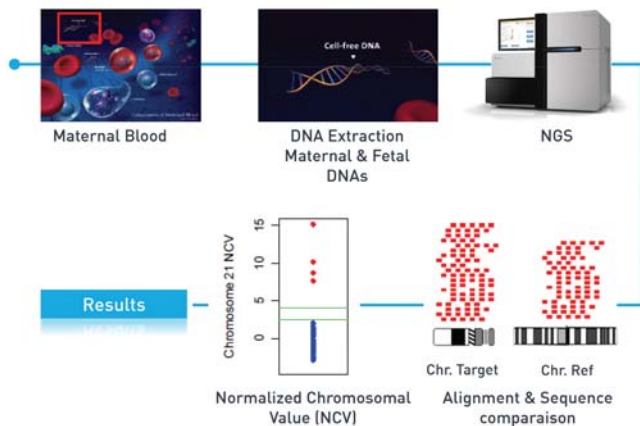
OBJECTIVES

Noninvasive assessment of the fetal genomic constitution is now possible using next-generation sequencing (NGS) technologies. Here we report our clinical performance of non-invasive prenatal testing (NIPT) in detecting trisomy 21, 18 and 13 and discuss its performance in high-risk pregnancies.

METHODS

Between November 2014 and July 2015, 746 NIPT samples were screened for fetal trisomy 21, 18 and 13 using whole-genome sequencing of plasma cell-free DNA. With HiSeq 2500 (Illumina), millions of amplified genetic fragments were sequenced aligned and Normalized Chromosome Value for each chromosome was used for NIPT. Positive results were systematically confirmed by karyotype.

NIPT process at Biomnis Laboratory



RESULTS

A total of 746 high-risk pregnancies including other indications from 12 to 30 weeks of amenorrhea were tested: abnormal serum screen (606 cases; 81,2%), personal history of trisomy 21 (44 cases; 5,9%), advanced maternal age (23 cases; 3,1%), *twin pregnancies* (53 cases; 7,1%), and familial history of trisomy T13, T18 or standard serum screening out of limits (20 case; 2,7%).

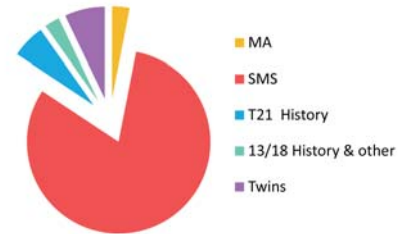
NIPT detected 20 fetuses with trisomy: 18 fetuses with Down syndrome, 1 fetus with trisomy 18 and 1 fetus with T13. One T18 detected by NGS were not confirmed by karyotype. Test failure concerned only 2 cases and no false negative result was observed.

CONCLUSION

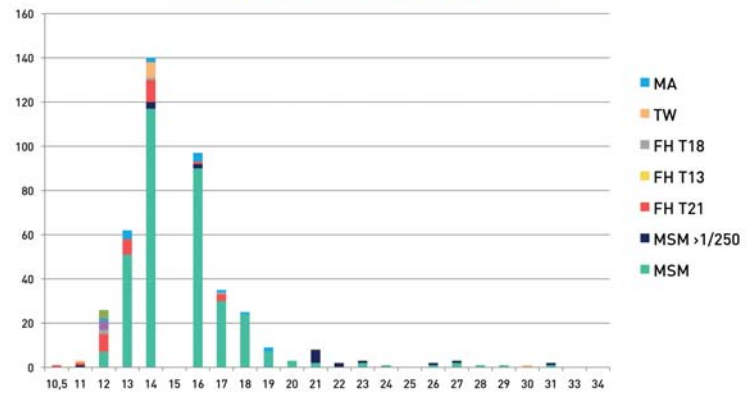
NIPT is a reliable and very useful in clinical settings. It allows the detection of T21, T18 and T13 in maternal blood and thus reduces the risk of fetus from invasive sampling and reduce parental anxiety.

Indications for 746 pregnant woman NIPT tested at Biomnis laboratory

MA	SMS	T21 History	13/18 History & other	Twins
23	606	44	20	53

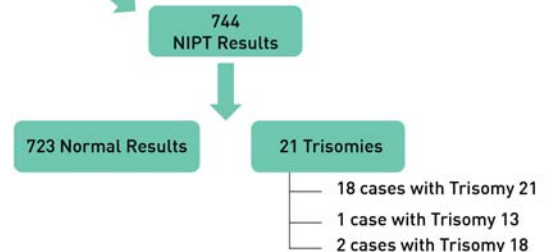
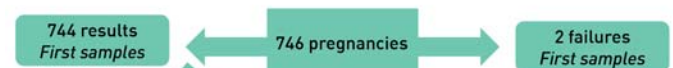
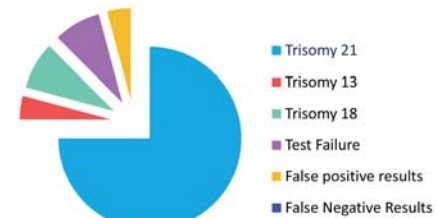


Distribution of Amenorrhea weeks of NIPT



Number of positive NIPT Results

Trisomy 21	Trisomy 13	Trisomy 18	Test failure	False positive results	False negative results
18	1	1	2	1	0



Karyotype Results

- 20 Trisomies confirmed
- 1 False positive of Trisomy 18