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"Clinical experience with the cell-free DNA testing at IASO Maternity feto-maternal department, Greece"

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Aims

Non-invasive prenatal tests (NIPT) demonstrate detection rates for fetal aneuploidies, such as Trisomy 21 (Down Syndrome) of greater than 99% with very low false-positive rates (less than 0.1%) (1). The Harmony Prenatal Test (ARIOSA Diagnostics Inc., Roche) assesses the probability of fetal trisomy 21, 18, 13 and sex chromosome aneuploidy (2,3). IASO hospital (www.iaso.gr) has been sending its NIPT to the Ariosa CLIA laboratory in San Jose, California, USA since May 2015. This study aims to analyze patient demographic and quality data, of test results and first trimester screening versus amniocentesis.

Methods: From May 2015 to March 2017 NIPT using the Harmony Prenatal Test (Ariosa Diagnostics Inc., Roche) was provided to pregnant women as the preferred cffDNA test at IASO hospital. All blood samples were collected according to standard operating procedures and shipped to the Ariosa CLIA laboratory in San Jose, California, USA. Nuchal translucency, free beta-chorionic gonadotropin (b-HCG), PAPP- A and amniocentesis were performed by the competent and the FMF-certified personnel of IASO according to established guidelines and operating procedures.

RESULTS: Nine hundred four (904) cfDNA tests were performed in twp years. Results figure out in tables 1,2,3. Forty four tests were submitted to cross-checking or with missing patient information or required new blood drawing. Ninety eight samples were from the Institute of Life. Overall during this period 441 amniocentesis were performed for various reasons. From them 76 demonstrated various 1st trimester screening pathologies and twelve of them came back positive for aneuploidies by amniocentesis.

CONCLUSIONS: We report a two year clinical experience with cfDNA testing from IASO Maternity hospital. One of the biggest maternities in Europe (10 000 deliveries/year, and a modern assisted reproduction setting (Institute of Life). However, first trimester screening is not performed for all pregnant women in our premises, for several reasons. In this study, singleton high-probability first trimester screening results for Trisomy 21 were all confirmed by cfDNA testing and amniocentesis or CVS. One specimen from a twin pregnancy with a high probability cfDNA testing result for Trisomy 18 was determined by amniocentesis as normal (male, female). This result is representing a "case" and cannot be compared to previous reports (4) and could be discordant due to the presence of cfDNA from a vanishing twin (3). cfDNA test turn- around time was approx. 3.5 mean days and "lab-to-lab line" was efficient in specimen handling, clinical evaluation, providing scientific information and updating. Among 904, about 9% (98 patients) preferred cfDNA testing combined to the first trimester test as a primary screening test in the 1st trimester. Maternal age as well as IVF status was strongly associated with the preference of women to the cfDNA test compared to amniocentesis. Surprisingly, a high % of cfDNA tests was performed later than the 17th week of gestation. This might be due to cultural and demographic characteristics of female population.

Table 1. Gestational age: 11-31 w

N. samples	Gestational age
601	11-16
290	17-31

Table 2. cf DNA % from mother's blood

Cf DNA %	Number of samples (904)
4-10%,	340
10.1-20%	469
20.1-37%	34

Table 3. 5/904 tests with high probability Harmony result.

1	True positive confirmed by amniocentesis
2	True positive confirmed by amniocentesis
3	True positive confirmed by CVS
4	False positive twins confirmed by amniocentesis
5	No follow up

References:
1. Gil et al, 2017
2. Juneau et al, 2014
3. Stokowski et al, 2015
4. Gil et al, 2014