

## Fiest trimester placental growth factor in combined screening of aneuploidies and preeclampsia

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### Objective

Evaluate if the implementation of PLGF in different strategies with different markers is capable of reducing results of intermediate risk for down syndrome (T21), subsequently diminishing fetal DNA tests. Secondly, it assesses if the diagnostic capacity of T21 and other aneuploidies would improve if PLGF is introduced. Thirdly, it evaluates if the median of MoMs, from the following biochemical markers: protein associated to pregnancy (PAPP-A), free beta-subunit of human chorionic gonadotropin (free  $\beta$ hCG) and PLGF, differentiates between these groups: non-preeclamptic women; patients with diagnosis of preeclampsia; patients with isolated hypertension (adding patients with preeclampsia in this same group) and a third group of patients with a neonate diagnosed of low birth weight.

### Methods

Retrospective and observational, case-control study. 467 frozen samples ( $-80^{\circ}\text{C}$ ) were obtained from a cohort of pregnant women screened between January 2011 and November 2015. Control groups ( $n=278$ ) were formed ruling out aneuploidies, preeclampsia, hypertension, low birth weight ( $<2.500$  g at term), diabetes mellitus or unregistered delivery. The following magnitudes were determined (PAPP-A,  $\beta$ hCG libre, PLGF) using the Delfia X Press auto-analyzer, through the Perkin Elmer® platform. The intra/inter analytic variability is inferior to 4%, for all the markers. The statistic calculation was done using the SPSS v19. A statistical significance of  $p<0.05$  was assumed and the median comparison was performed using students t- distribution. We calculated T21 risk, using LifeCycle v4.0 software, integrating in this calculation NT, maternal age and biochemical markers.

### Results

A reduction of positive results in intermediate risk, with a cutoff of 1/31-1/1.000: 6,4%. A comparison of first trimester biochemical markers in preeclampsia, hypertension and low birth weight: MoM PLGF: Control: 1,05; T21: 0,72 ( $p<0,001$ ); T18+T13+ Other: 0,70 ( $p=0,007$ ); PE: 0,73 ( $p=0,005$ ); PE + HTA: 0,84 ( $p=0,002$ ); Low birth weight: 0,76 ( $p=0,026$ ); The MoM of PLGF in all the groups present differences, compared to the controls. The combination of all biochemical markers, do not put forward significant differences. As we added variables, the area beneath the curve reached 0.931, however no statistical significance was attained. The ROC curves were created using the biochemical markers; however the confidence intervals are not significant, as they overlap.

### Conclusion

The implementation of PLGF in a contingent strategy would permit a reduction of the intermediate risk in those women who are candidates to fetal DNA. An overlap in confidence intervals regarding the calculation of the risk of T2, using a combination of different markers, could be explained by: a small sample size or the lack of discrimination of the biochemical markers. The diagnosis efficiency of T21 increases, however when we increase the number of markers used to calculate the risk, no significance is reached. The implementation of PLGF can be useful in the early screening of preeclampsia; hypertension and low birth weight. However, we should increase sample size in order to select the best combination of markers which would be capable to screen for preeclampsia and other obstetric complications. In a short-term future we will have the results of a multicenter, prospective study which would validate or not the use of Aspirin in the prevention of preeclampsia ("Aspre" [www.aspre.eu](http://www.aspre.eu)). Such studies would become more important and will have more connotations if a preventable treatment is introduced.