Screening for trisomy 21: maternal weight adjustment of PAPP-A and free β-hCG hampers diagnosis in obese women

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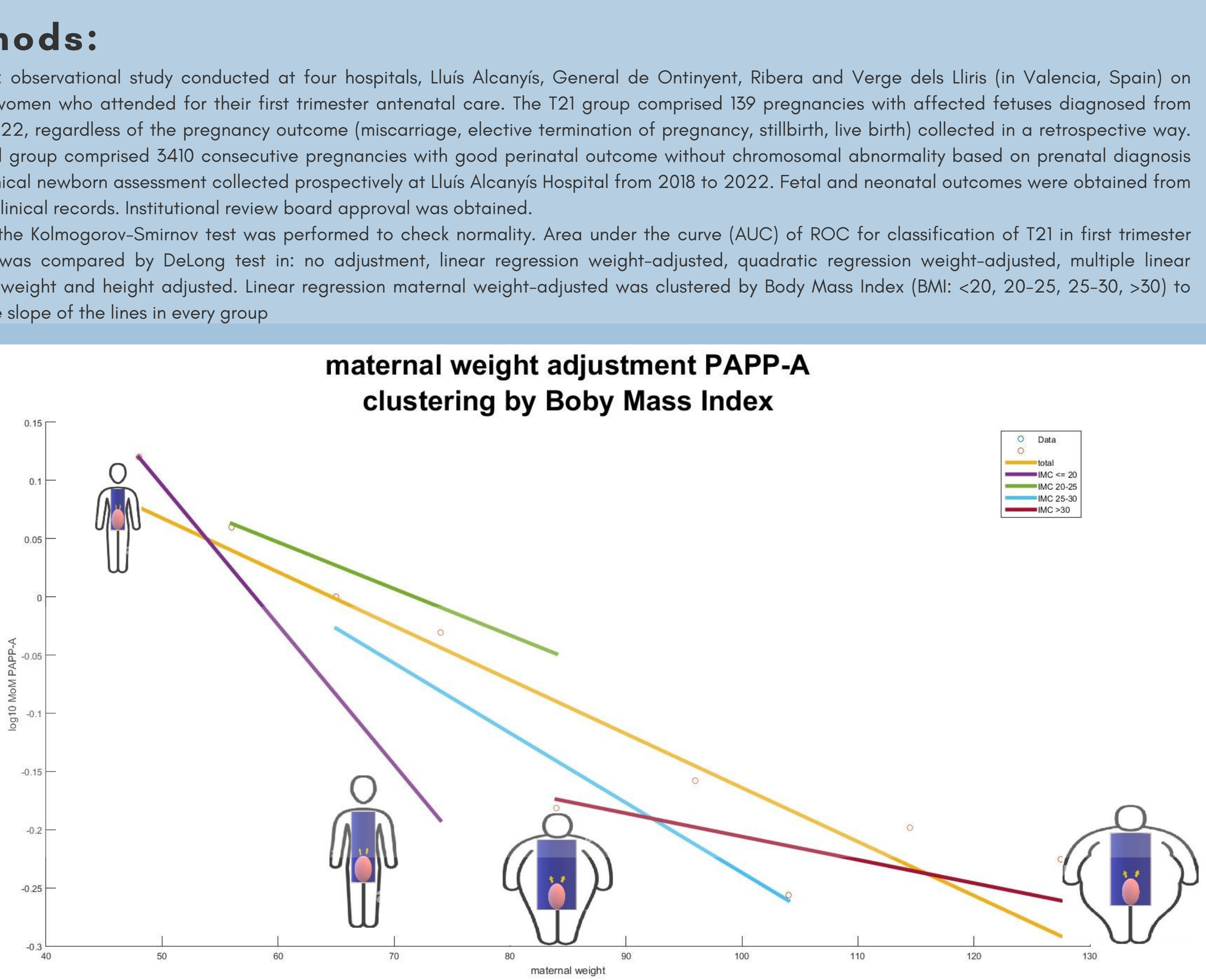
Objective:

To find an appropriate strategy to reduce false negative rate in screening for trisomy 21 (T21), exploring in particular the effect of the adjustments of biochemical markers as a function of maternal size. The aim is to look for the best size descriptor to explore the effect of biochemical markers adjustment in the accuracy of screening

Methods:

Population: observational study conducted at four hospitals, Lluís Alcanyís, General de Ontinyent, Ribera and Verge dels Lliris (in Valencia, Spain) on pregnant women who attended for their first trimester antenatal care. The T21 group comprised 139 pregnancies with affected fetuses diagnosed from 2010 to 2022, regardless of the pregnancy outcome (miscarriage, elective termination of pregnancy, stillbirth, live birth) collected in a retrospective way. The control group comprised 3410 consecutive pregnancies with good perinatal outcome without chromosomal abnormality based on prenatal diagnosis and/or clinical newborn assessment collected prospectively at Lluís Alcanyís Hospital from 2018 to 2022. Fetal and neonatal outcomes were obtained from review of clinical records. Institutional review board approval was obtained.

Statistics: the Kolmogorov-Smirnov test was performed to check normality. Area under the curve (AUC) of ROC for classification of T21 in first trimester screening was compared by DeLong test in: no adjustment, linear regression weight-adjusted, quadratic regression weight-adjusted, multiple linear regression weight and height adjusted. Linear regression maternal weight-adjusted was clustered by Body Mass Index (BMI: <20, 20-25, 25-30, >30) to explore the slope of the lines in every group



Results

first-trimester screening for trisomy 21 identified 81% (95% CI 74.2-87.6) of cases. The main factors associated with false negative diagnoses were maternal obesity and late screening close to 14th week.

Area under the curve of ROC for classification of T21 by first trimester screening with adjustment for maternal size descriptors tested (linear or quadratic regression weight-adjusted and multiple linear regression weight and height adjusted,) were not significantly different between them nor with unadjusted figures.

Slope of linear regression weight-adjusted (figure 1) was significantly different for BMI: as average, in women with a Body Mass Index over 30, the slope of the line relating weight to log10 of the multiples of the median of biochemical markers is very close to 0 (more maternal weight is not associated with a significant increase in volume of distribution of them)

In a posteriori view, false negative cases would have been identified in obese women

Conclusion:

In pregnant women with a Body Mass Index over 30, misidentification rate of trisomy 21 by first trimester screening decreases if PAPP-A and free β-hCG levels are not adjusted by maternal weight or other size descriptors