18 YEARS OF NEONATAL SCREENING FOR CONGENITAL ADRENAL HYPERPLASIA IN NORTH-EASTERN ITALY: RECALL RATE REDUCTION THANKS TO LIQUID CHROMATOGRAPY-TANDEM MASS SPECTROMETRY AS SECOND TIER TEST

Paolo Cavarzere, Laura Palma, Silvana Lauriola, Rossella Gaudino, Monica Vincenzi, Francesca Teofoli, Franco Antoniazzi and Marta Camilot

Division of Paediatric, Department of Mother and Child, University Hospital of Verona, Verona, Italy

The Authors declare that there is no conflict of interest that could compromise the impartiality of the research reported and that for this study no financial supports were requested

INTRODUCTION

- In North-Eastern Italy newborn screening for congenital adrenal hyperplasia (CAH) has been performed since 2001.
- The screening program based on 17-OHP levels in dried blood spots has made early diagnosis for classic form of 21-hydroxylase deficiency (21-OHD) possible, allowing precocious treatment and reduction of mortality rate.
- A high false positive rate at screening test, especially in preterm, low-birth-weight and critically ill newborns, is described.

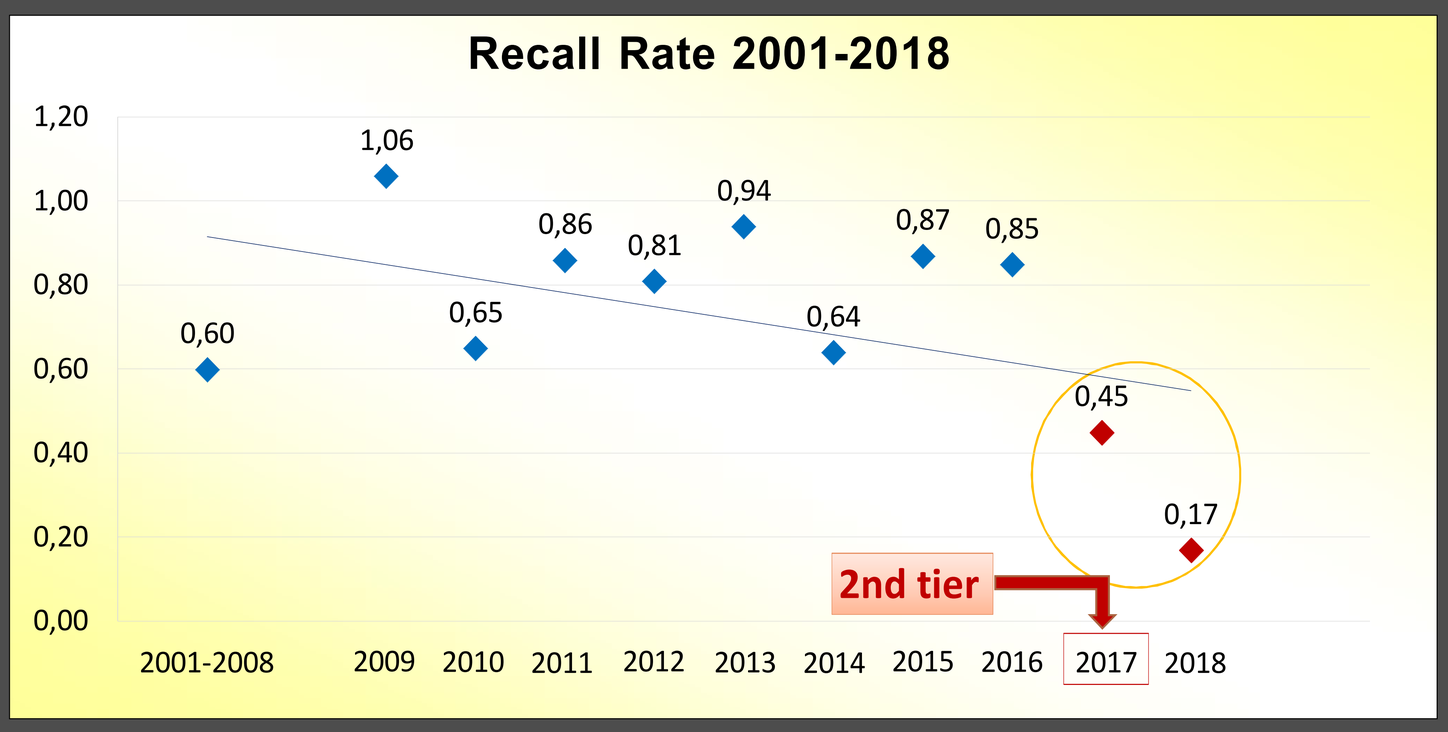
AIMS OF THE STUDY

- To summarize the results of the newborn screening for CAH held in the last 18 years in North-Eastern Italy.
- To evaluate the diagnostic utility of simultaneous determination of 17-OHP, cortisol, 11-deoxycortisol, delta 4-androstenedione and 21-deoxycortisol by liquid chromatograpy-tandem mass spectrometry (LC-MS/MS) as second tiers test performed on the same blood spot.

METHOD AND MATERIALS

- Since 2001 dried blood spots from newborns have been screened with a time-resolved fluoroimmunoassay method (DELFIA) for 17-OHP determination.
- Over the years, the cut-off levels of 17OHP have been adjusted according to gestational age
- Since 2017, samples resulted above the cut-off have been immediately analyzed by LC-MS/MS in order to differentiate affected patients from false positive newborns.

RESULTS



- Since 2001, 786.302 newborns have been screened.
- 34 diagnosis of classic form of 21-OHD and a total incidence of 1:23126
- The subsequent adjustments of cut-off values for 17-OHP based on gestational age and the use of LC-MS/MS, as a second-tier test for positive CAH screening, have significantly reduced the recall rate.

CONCLUSIONS

- Screening for CAH proved to be useful in the neonatal diagnosis of classic form of 21-OHD, allowing a precocious treatment and significantly reducing mortality.
- The use of LC-MS/MS as a second tier test improved the positive predictive value of the screening program.
- LC-MS/MS cannot be seen as a replacement for the conventional method, but it is extremely useful as a second-tier test, in particular in preterm, low-birth-weight and critically ill neonates, preventing unnecessary blood draws, medical evaluations and stress to families.