CONGENITAL HYPOTHYROIDISM IN TWIN COUPLES AND TRIPLETs


1Italian National Institute of Health, Rome; 2Vita-Salute University, IRCCS San Raffaele Hospital, Milan; 3University of Bologna, Bologna; 4University “La Sapienza”, Rome; 5Ganoboli Hospital, Catania; 6IRCCS Istituto Auxologico Italiano and University of Milan, Italy.

Introduction
Over the years special screening procedures for preterm and twin babies (re-screening at 2-4 weeks of life) have been adopted by many screening laboratories worldwide. However, no extensive studies have been performed to verify how many co-twins with negative test at first screening (3-5 days of life) become positive at re-screening, and the utility of a long-term follow-up also in co-twins with negative test at screening and re-screening.

Objectives
1) to estimate the concordance rate for CH within the first month of life in twin couples/triplets discordant for CH at the first screening;
2) to verify whether a long-term follow-up of co-twins with negative test at screening and re-screening may be useful to verify the occurrence of thyroid hypofunction in these children during development;
3) to characterize probands and co-twins by next generation sequencing (NGS) analysis of a panel of candidate genes (NXX2-1, FOXE1, PAX8, GLIS3, JAG1, TSHR, SLC26A4, DUOX2, DUOX2A2, TPO, TG)

Methods
Thirty-eight twin couples and 4 triplets discordant for CH at first screening (42 CH probands) were recruited for the study. The range of the long-term follow-up in the couples/triplets was 3-21 years (median 8.1 y).

Pairwise concordance rate (PCWR) was calculated as the proportion of concordant pairs over the sum of concordant and discordant pairs. Case wise concordance rate (CWR) is the probability that one twin in a pair is affected, given that his/her co-twin is affected. Survival analysis using Kaplan-Meier method was performed to describe the occurrence of thyroid hypofunction in co-twins.

Results
Among the couples/triplets discordant at first screening 5 co-twins resulted positive at re-screening. PCWR and CWR for CH confirmed at re-screening are reported in FIG.1

During the long-term follow-up a thyroid hypofunction was observed in 4 co-twins and a treatment with L-thyroxine was started at the age of 2 months for two co-twins, 9 months, 12 years. PCWR and CWR for permanent thyroid hypofunction are reported in FIG.2. Details of concordant twin pairs are reported in TABLES 1-2. Kaplan-Meier survival curves concerning the long term follow-up are shown in FIG.3.

The systematic NGS analysis revealed variations consistent with the observed phenotype in 50% of concordant twin couples. Most of the discordant MZ cases remain unexplained by NGS analyses (TABLES 3-4).

Conclusions. These results show:
1. the importance of the re-screening at 2-4 weeks of life in both MZ and DZ twins;
2. the possible benefit of a long-term follow-up also in co-twins with negative test at screening and re-screening, especially if MZ;
3. the need of further studies in order to uncover the largely unexplained pathogenesis of CH.

The authors declare no conflict of interest.