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3rd trimester fetal heart rate discriminates between non-carriers, carriers of single and double LQT1 mutations in Swedish Long QT Syndrome families

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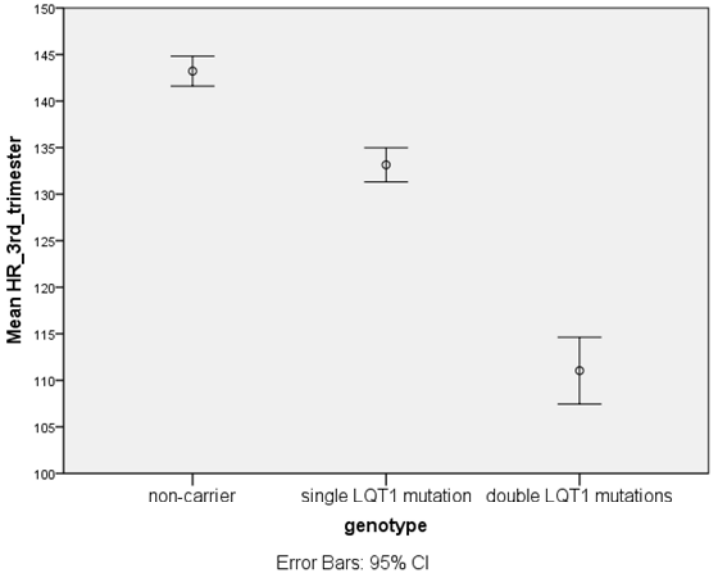
Introduction: Early diagnosis is of utmost importance in the congenital Long QT Syndrome (LQTS), especially for fetuses carrying double mutations, a condition associated with a high risk for life-threatening arrhythmias early in life. Here we investigate 3rd trimester fetal heart rate, routinely recorded within public maternal health care, as a possible early marker for LQTS genotype.

Methods: In large Swedish LQTS families where molecular genetics cascade screening for LQT1 (KCNQ1 gene) mutations had been performed in the clinical setting, fetal heart rates during the 3rd trimester (gestational week 29- birth) were noted for 124 fetuses with ascertained genotype, whereof 45 were non-carriers of the familial mutation(s), 67 were heterozygous mutation-carriers and 12 carried double mutations (3 homozygous and 9 compound heterozygous mutation-carriers). Among the heterozygous mutation-carriers, genotypes included p.Y111C (n=63), p.A525T (n=3) and p.R518X (n=1). Among the carriers of double mutations, genotypes included R518X/R518X= 3, A525T/R518X=4, M159sp/R518X=2, R190W/R518X=1, R530W/R518X=1 and S349W/R518X=1. Sex was equally distributed within each genotype group (females 62%, 46% and 50%, per group). The mean fetal heart rate per individual, calculated from all recordings from gestational week 29 and onwards, noted in the maternal health care records, were summarized and compared between genotype groups (no mutation, single mutation, double mutations) using t-tests and non-parametric tests, as appropriate.



Results: Mean 3rd trimester heart rate correlated with fetal genotype (no mutation 143±5 bpm; one mutation 133±8 bpm; double mutations 111±6 bpm, $p<0.001$). Mean heart rates were statistically lower per added mutation (no mutation vs. single mutation $p<0.001$, single mutation vs. double mutation $p<0.001$). Fetal sex did not significantly affect mean 3rd trimester heart rate ($p=0.246$).

Conclusions: In this study including 124 fetuses with ascertained genotype from Swedish LQT1 families, 3rd trimester fetal heart rate discriminated between fetal genotypes (no mutation, single mutation and double mutations). This finding strengthens the role of fetal heart rate in the early diagnosis of familial LQTS, and importantly for the identification of fetuses with double mutations, at high risk of early life-threatening arrhythmias.