Genome-wide survival analysis of dental caries incidence

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Introduction

Socioeconomic status (SES) and environmental factors may contribute to disparities in oral health and may also interact with predisposing genetic factors.

The aim of this study was to use survival analysis to identify the potential risk factors, genetic variants and gene-environment interactions (GEI) associated with dental caries incidence in a birth cohort.

Study Design

Samples

A total of 911 children were included from the Center for Oral Health Research in Appalachia, cohort 2 (COHRA2); each was followed annually from birth with 7 years being the longest follow-up to date. Annual intra-oral examinations were performed to assess dental caries experience, including the approximate time to first carious lesion.

Risk factors

- Sex (Male vs. Female)
- Recruitment site (Pennsylvania vs. West Virginia)
- Household income (<$50K/year vs. ≥$50K/year)
- Home water source (water company vs. well)
- Home fluoride level
- Mother’s educational attainment (<high school, high school–some college, >some college)
- Mother’s toothbrushing frequency
- Mother’s dental caries experience
- Breastfeeding status
- Breastfeeding duration

Statistical analysis

Cox proportional hazards models were used to assess the associations of time to event trait with self-reported risk factors, 4.9 million genetic variants and GEI.

Results

A total of 196 children (21.5%) had their first primary tooth caries event during the follow-up period. The average survival time was 3.23 years.

Risk factors

Household income, home water source, mother’s educational attainment, mother’s toothbrushing frequency, mother’s dental caries experience, breastfeeding status, and breastfeeding duration were individually associated with dental caries incidence in univariate models, while only household income, home water source, and mother’s educational attainment were significantly associated in the multivariate model of all potential risk factors simultaneously (Figure 1).

Figure 1. Survival curves for dental caries incidence stratified by significant risk factors in the multivariate model

Genetic variants and GEI

The heritability (i.e., proportion of variance explained by genetics) of the time to event trait was 54.4% (P<0.0001). There were no specific genetic variants associated with dental caries incidence at genome-wide significant level (P<5e-8), however, an intronic variant (P=1.16e-8) in HMCH2 was identified in the GEI test of interaction with home water source at genome-wide significance level (Figure 2).

Figure 2. Genome-wide survival analysis of dental caries incidence interacted with home water source

Conclusions

Our findings indicate that household income, mother’s educational attainment, and home water source may be independently-operating risk factors for dental caries incidence, and the time to event of first carious lesion is heritable. SES and environmental factors might have roles in the genetic architecture of dental caries.