Göteborg, 2021

Methodological considerations in epidemiological studies in perinatal medicine

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i 2119, Hus 2, HVB, Hälsovetarbacken, Arvid Wallgrens backe 5, Göteborg, den 31 maj 2021, klockan 9.00

av Dominika Modzelewska

Fakultetsopponent: Senior researcher, Deputy director Siri Eldevik Håberg
Department of Centre for Fertility and Health, Norwegian Institute of Public Health, Olso, Norway

Avhandlingen baseras på följande delarbeten

I. Modzelewska D, Sole-Navais P, Zhang G, Muglia LJ, Nilsson S, Jacobsson B. Importance of the environment for gestational duration variability and correlation between relatives - results from the Medical Swedish Birth Registry, 1973-2012. PLoS One. 2020 Jul 24;15(7).

II. Modzelewska D, Sole-Navais P, Sandstrom A, Zhang G, Muglia LJ, Flatley C, Nilsson S, Jacobsson B. Changes in data management contribute to temporal variation in gestational duration distribution in the Swedish Medical Birth Registry. PLoS One. 2020 Nov 6;15(11).

III. Modzelewska D, Bellocco R, Elfvin A, Brantsæter AL, Meltzer HM, Jacobsson B, Sengpiel V. Caffeine exposure during pregnancy, small for gestational age birth and neonatal outcome - results from the Norwegian Mother and Child Cohort Study. BMC Pregnancy Childbirth. 2019 Feb 26;19(1):80.

IV. Modzelewska D, Solé-Navais P, Brantsæter AL, Flatley C, Elfvin A, Meltzer HM, Sengpiel V, Barman M*, Jacobsson B*. Maternal dietary selenium intake during pregnancy and neonatal outcomes in the Norwegian Mother, Father, and Child Cohort Study. Nutrients. Multidisciplinary Digital Publishing Institute; 2021 Apr;13(4):1239

(*Shared last authorship)

SAHLGRENSKA AKADEMIN
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Methodological considerations in epidemiological studies in perinatal medicine

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Abstract

This thesis is based on two projects, each consisting of two papers. In these two projects we investigated factors affecting the variability in gestational duration, and associations between maternal diet and neonatal outcomes.

In the first project we investigated factors affecting the variability in gestational duration with a particular interest in the genetic contributions. The contribution of genetic factors to trait's variability is estimated by heritability analysis. For gestational duration, heritability estimates are up to 36%. However, genetic studies have identified a limited number of genetic variants. In the first project we aimed to assess whether an essential assumption underlying heritability analysis, constant environmental conditions, holds. In Paper I, we observed a substantial variability in the correlation estimate in gestational age at delivery between relatives with respect to their year of birth or age gap. This variability suggests the existence of temporally changing environmental factors. In Paper II, we showed that obstetrical practices and data handling contribute to changes in gestational duration over time. Two studies in this project suggest that the assumption of constant environmental conditions might not hold. This might explain the dissonance between the conclusions of heritability and genetic studies.

The second project was an extension of previous studies performed in our research group. In these studies, we detected associations between maternal caffeine or selenium intakes and small for gestational age (SGA), and SGA and neonatal outcomes. Therefore, we hypothesized that the selected maternal food components and neonatal outcomes would be associated. In both studies (Papers III and IV), we did not detect associations between maternal caffeine or selenium intake and neonatal outcomes. The lack of associations may be the result of SGA babies having different neonatal outcomes based on the underlying SGA cause. One type of SGA might be related to maternal caffeine/selenium intake and not associated with neonatal outcomes; the other types might be caused by more aggressive factors leading to worse performance in the neonatal period. The results warrant caution when using SGA as a representation for neonatal outcomes.

Keywords: gestational duration, preterm delivery, familial aggregation, heritability, variability, birthweight, small for gestational age, neonatal outcomes

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