

Background: Understanding the extent that multiple gestations mediate risk of obstetric complications following exposure to fertility treatment may provide etiological insights and assist clinical decisions concerning treatment strategies and pregnancy monitoring.

Objectives: Implementing a structural approach to mediation analysis, we aimed to (1) assess the association between treatment and adverse outcome independent of underlying infertility and (2) quantify that the extent associations are mediated by multiple gestation.

Methods: From the nearly 1 million pregnancies recorded in the Medical Birth Register between 1996 and 2006 in Sweden, we selected the 8% ($N=84\,689$) that occurred after more than 12 months of trying to achieve pregnancy (i.e., self-reported infertility). Fertility treatments were identified from self-reports, general medical records, and procedural information from fertility clinics.

Results: Compared to pregnancies achieved spontaneously, those assisted by fertility treatment had higher odds of all studied complications except gestational diabetes and urogenital infections. Associations to placenta previa (OR, 2.31; 95%CI: 1.89–2.82) and placental abruption (OR, 1.77; 95%CI: 1.46–2.16) were almost entirely independent of multiple gestations. Conversely, multiple gestations mediated the majority (86% and 75%, respectively) of the associations to preterm birth (OR, 1.90; 95%CI: 1.78–2.02) and Cesarean (OR, 1.43; 95%CI: 1.34–1.49) and all of the modest association with preeclampsia (OR, 1.14; 95%CI: 1.06–1.22). Both direct and mediated pathways contributed to the remaining positive associations with chorioamnionitis, labor induction, and postpartum hemorrhage. Restricting exposure to assisted reproductive technologies only and evaluating primiparous and multiparous women separately yielded similar results.

Conclusions: Interventions to restrict the occurrence of multiples could diminish or greatly reduce risks of numerous obstetric complications following fertility treatment. Independent association with serious placental complications still suggests that all pregnancies achieved after fertility treatment should be monitored as high risk.

482. Asthma Medication Use Before and After the Onset of Type 1 Diabetes in Children and Adolescents: A Population-based Cohort Study

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Background: It has been reported that patients with type 1 diabetes (T1DM) have a decreased lung function. Studies on the association of T1DM and asthma in children show controversial results.

Objectives: The aim of this study was to quantify asthma medication use in children and adolescents with and without (reference cohort) T1DM 5 years before and after the onset of diabetes.

Methods: A population-based cohort study was conducted in the Dutch PHARMO Record Linkage System. All children (<19 years) with at least two insulin prescriptions between 1999 and 2009 were included in the T1DM cohort ($n=915$). Up to four times larger reference cohort ($n=3590$) with the same age and sex distribution was sampled from the PHARMO RLS.

Results: The 5-year prevalence rate of asthma medication use in the T1DM cohort was substantially higher (23.2%), with a peak in the first year, compared with the reference cohort (18.3%) after the onset of diabetes. In both cohorts, children aged 4 years and younger used asthma medication statistically significantly more frequent compared with children in ages of 5–9, 10–14, and 15–18 years before the onset of diabetes, 68.0% compared with 22.6%, 24.7%, and 27.0%, respectively, in the T1DM cohort and 54.3% compared with 25.4%, 21.3%, and 28.3%, respectively, in the reference cohort. After the onset of diabetes, these rates were 31.0%, 17.1%, 24.3%, and 28.0% in diabetic patients and 21.6%, 16.1%, 16.5%, and 22.3% in the reference cohort, respectively.

Short acting muscarinic antagonists were used more frequently in the T1DM cohort compared with the reference cohort after the onset of diabetes (5.5% vs 0.62%, $p < 0.001$). The incidence rate of asthma medication use was 2.5 times higher in the first year after the onset of diabetes compared with the reference cohort (46.3 vs 17.9 per 1000 person-years) but not in later years of follow-up.

Conclusions: T1DM was associated with statistically significantly higher prevalence and incidence rates of asthma medication use after the onset of type 1 diabetes, with a peak in the first year after the onset of diabetes.