



**Karolinska  
Institutet**

**Institutionen för neurobiologi vårdvetenskap och samhälle**

# Gestational age at birth and risk of esophageal inflammation and cancer

**AKADEMISK AVHANDLING**

som för avläggande av medicine doktorsexamen vid Karolinska  
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av

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# ABSTRACT

**Background** In a hypothesis generating study by my colleagues a 7-fold increase in the risk of esophageal adenocarcinoma (EAC) was found in a cohort of individuals born preterm or with a low birth weight. Preterm born individuals regurgitate more than term born infants, and infant gastroesophageal reflux disease (GERD) might continue into childhood and even adulthood. GERD, a major public health problem in adult westernized populations, is a risk factor for esophagitis, Barrett's esophagus (BE), and EAC. There are no previous studies assessing risk of inflammation, metaplasia, and cancer among adults in relation to perinatal characteristics.

**Aims** This thesis aims to explore the effect of gestational age and size at birth, on the risk of being diagnosed with esophagitis, BE or EAC later in life.

**Patients and Methods** We performed four population-based case-control studies. As cases we identified patients with endoscopy verified esophagitis, BE of intestinal metaplasia type, and EAC from the Swedish Cancer Register, the Patient Register and from two local Barrett Registers. Control individuals were randomly selected from the source population, and matched on age, sex and location of birth. We collected exposure data from birth records, including the variables gestational age, birth weight and length, and maternal diseases, among others. Using conditional logistic regression we modeled the risk of being a case based on exposure status, and calculated odds ratios (OR) and 95% confidence intervals (CI). A p value of 0.05 was considered statistically significant.

**Results** Compared to birth at term with adequate birth weight for gestational age, preterm birth and being SGA increased the risk of being diagnosed with esophagitis (OR 2.7, 95% CI 2.2-3.5 and OR 1.5, 95% CI 1.3-1.7, respectively), and even more so among those diagnosed before 10 years of age (OR 6.8, 95% CI 4.7-10.0 and OR 2.0, 95% CI 1.6-2.5, respectively). We found an increased risk of being diagnosed with BE among those born SGA and <3<sup>rd</sup> percentile (OR 3.0, 95% CI 1.4-6.4), as well as those in the 3<sup>rd</sup> to <10<sup>th</sup> percentile (OR 1.8, 95% CI 1.0-3.1). The risk of BE was also increased among those with a birth weight <2,500 grams (OR 8.2, 95% CI 2.8-23.9). The risk of EAC was increased by 13% per week preterm birth, compared to birth at term (OR 1.1, 95% CI 1.0-1.3). No effect of size at birth was seen for EAC, or for cardia adenocarcinoma and esophageal squamous cell carcinoma.

**Conclusions** Altogether, these data indicate that gestational age and size at birth are strongly associated with risk of esophagitis and BE later in life. Furthermore, the results indicate that preterm birth is associated with a risk of EAC and cardia adenocarcinoma, but not esophageal squamous cell carcinoma.