

Maternal and placental inflammatory biomarkers in spontaneous preterm delivery

Predictive ability, stability and neonatal associations

Akademisk avhandling

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av

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This thesis is based on the following papers:

- I.** Prediction of spontaneous preterm delivery in women with threatened preterm labor: a prospective cohort study of multiple proteins in maternal serum
Tsiartas P, Holst R-M, Wennerholm U-B, Hagberg H, Hougaard D M, Skogstrand K, Pearce B D, Thorsen P, Kacerovsky M, Jacobsson B
BJOG 2012; 119:866-873
- II.** Maternal inflammatory response to microbial invasion of the amniotic cavity: analyses of multiple proteins in the maternal serum
Cobo T, Tsiartas P, Kacerovsky M, Holst R-M, Hougaard D M, Skogstrand K, Wennerholm U-B, Hagberg H, Jacobsson B
Acta Obstet Gynecol Scand 2013; 92:61-68
- III.** The effect of latency of time, centrifugation conditions, supernate filtration, and addition of protease inhibitors on amniotic fluid interleukin-6 concentrations
Tsiartas P, Kacerovsky M, Hallingström M, Liman V, Cobo T, Jacobsson B
Am J Obstet Gynecol 2015; 213(2): 247-8
- IV.** The association between histological chorioamnionitis, funisitis and neonatal outcome in women with preterm prelabor rupture of membranes
Tsiartas P, Kacerovsky M, Musilova I, Hornychova H, Cobo T, Sävman K, Jacobsson B
J Matern Fetal Neonatal Med, 2013; 26(13): 1332-1336

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ABSTRACT

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Preterm delivery (PTD), spontaneous or iatrogenic, causes short- and long-term morbidity and underlies almost 75% of neonatal deaths. The prevalence in the Nordic countries is about 6% but it differs among countries. In the USA, for instance, it is around 9.6%.

The origin of spontaneous PTD is mostly unknown. However, infection and inflammation are leading causes, mainly at early gestational ages. Microbial invasion of the amniotic cavity (MIAC) occurs in 12-14% of symptomatic women with preterm labor (PTL) and in 37-43% of women with preterm prelabor rupture of membranes (PPROM). MIAC elicits an inflammatory response mediated by cytokines, chemokines and other peptides, known as intra-amniotic inflammation (IAI). IAI causes early onset of symptoms, early gestational age at delivery and, consequently, worse neonatal outcome. Chemokines induce chemotaxis in neutrophils and macrophages, enhancing their migration to the placenta and fetal membranes. This process, known as histological chorioamnionitis (HCA), occurs in more than half of spontaneous PTD cases. Early detection of spontaneous PTD presents a challenge because most women who deliver preterm have no obvious risk factors that can be identified early. Indeed, more than half of spontaneous PTDs occur in low-risk pregnancies.

One aim of the studies in this thesis was to study whether non-invasive strategies could predict the occurrence of spontaneous PTD within 7 days, as well as the rate of MIAC. We found that a combination of maternal serum proteins and cervical length constituted the most accurate prediction model for spontaneous PTD within 7 days of testing. However, we observed few differences between maternal serum protein levels in MIAC-positive PTL and PPRM cases.

An additional aim was to study the effect of different pre-analytical handling procedures on concentrations of interleukin-6 (IL-6), the cytokine most reported as a biomarker of IAI. We found that differences in handling procedures did not affect amniotic fluid IL-6 levels.

Furthermore, these studies investigated the relationship between neonatal outcome and placental histological findings in women with PPRM. We found that HCA and funisitis increased the risk of early-onset neonatal sepsis and retinopathy of prematurity in PPRM pregnancies.

Keywords: Preterm birth, prediction, proteins, multiplex, microbial invasion of the amniotic cavity, histological chorioamnionitis, neonatal outcome, cytokine stability, interleukin-6 (IL-6)

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