

### 5 Stillbirth collaborative research network: proximate causes of death in a prospective, population based, multi-center, case-control study with a standardized protocol

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**OBJECTIVE:** To determine causes of death in a racially and geographically diverse, population-based stillbirth cohort.

**STUDY DESIGN:** Prospective, multicenter, population based case-control study of all stillbirths and a representative sample of live births occurring in 5 geographically diverse regions in 59 hospitals averaging > 80,000 deliveries per year from 03/06 to 08/08. Cases underwent a standardized protocol including maternal interview, medical record abstraction, postmortem and placental pathology, and biospecimen testing. Causes of fetal death were assigned using evidence-based explicit definitions. Conditions potentially associated with fetal death are categorized as being either present, or a possible or probable cause of death.

**RESULTS:** 512 stillbirths had complete postmortem examinations including 459 (89.6%) antepartum and 53 (10.4%) intrapartum deaths. Overall, 58% had a probable and 80% a possible or probable cause of death. 27% had more than one possible or probable cause identified. Probable causes were found more often in deaths 24 weeks versus > 24 weeks gestation (67.2 vs 51.7%;  $p = 0.0006$ ), and in intrapartum compared to antepartum cases (81 vs 55%;  $p = 0.0003$ ). The most common possible/probable causes of stillbirth were placental insufficiency (27%), obstetric complications (23%), maternal/fetal infection (17%), maternal medical conditions (15%), genetic/structural anomalies (14%), and cord abnormalities (8%). Infection and obstetric complications were more common in intrapartum cases while placental insufficiency was more common in antepartum stillbirth. Causes also differed by gestational age. Autopsy and placental histology were critical in determining a cause of death in the majority of cases.

**CONCLUSION:** After systematic evaluation using strict criteria, a possible or probable cause of death can be found in the majority of stillbirths. Many stillbirths derive from potentially preventable causes. Research efforts should target placental insufficiency, obstetric complications, infection, and medical disorders.

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### 6 A randomized controlled trial of wound complication rates of subcuticular suture vs staples for skin closure at cesarean delivery

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**OBJECTIVE:** To determine the wound complication rates for different methods of skin closure at cesarean delivery (subcuticular sutures vs. staples).

**STUDY DESIGN:** This is a randomized prospective trial. Women were enrolled on admission to the hospital and randomized to closure with subcuticular suture (4.0 monocril) or staples at the time of cesarean delivery. Women undergoing cesarean delivery in labor as well as scheduled cesarean delivery were eligible. Surgical and postpartum care was otherwise at the discretion of the provider. Demographic, intrapartum and delivery data were collected during the hospitalization. Wound complication data (including wound separation, wound infection, antibiotic use, need for a wound-related physician visit, and readmission) were collected via telephone interview 2-4 weeks postoperatively by a single investigator. Student t test, chi square and regression analysis were used to analyze the data.

**RESULTS:** A total of 425 patients were randomized. Wound complication data was complete for 98% of subjects (219 suture and 197 staples). Maternal demographic data was similar in both groups. Use of staples resulted in a higher wound separation rate (16.8 v. 4.6%,  $p < 0.001$ ), higher composite wound complication rate (21.8 v. 9.1%,  $p < 0.001$ ), and increased post-operative physician visits (36.0 v. 10.6%,  $p < 0.001$ ); these associations persisted after adjusted analysis. Staple closure was associated with a more than 4-fold increased risk of wound separation (adjusted OR 4.66, 95%CI 2.07, 10.52,  $p < 0.001$ ). Median operative time was 8 minutes shorter in the staple group (49 vs. 57 min  $p < 0.0001$ ).

**CONCLUSION:** Use of staples for cesarean delivery closure is associated with an increased risk of wound complications and post-operative physician visits. Subcuticular suture may therefore be the preferred method of skin closure for cesarean delivery.

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### 7 Identification and characterization of proteomic biomarkers in amniotic fluid that are differentially expressed before and after antenatal corticosteroid administration

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**OBJECTIVE:** Antenatal corticosteroid therapy decreases the incidence of neonatal complications in preterm infants. To better understand the effects on the developing fetus, proteomic analysis of amniotic fluid (AF) was performed before and after steroid administration.

**STUDY DESIGN:** AF was collected by amniocentesis for threatened PTB < 34 weeks both before and in the same subject within 7 days of steroid administration ( $n = 12$ ). There was no evidence of intra-amniotic infection/inflammation. Proteomic analysis was performed by SELDI-TOF (surface-enhanced laser desorption/ionization time-of-flight) mass spectrometry. Proteomic biomarkers before and after steroid administration were isolated, characterized and quantified.

**RESULTS:** Five biomarkers differentially expressed in the AF before and after antenatal corticosteroid therapy were identified by proteomic analysis, all of which were significantly decreased. These were designated peaks A(6,879 Da), B(13,756 Da), C(22,206 Da), D(12,454 Da) and E(44,450 Da). Fractions containing the biomarkers of interest were then separated by FPLC and subjected to SDS-PAGE gel electrophoresis, in-gel tryptic digestion, immunodepletion assays, ELISA and MS/MS. Peaks A and B were identified as isoforms of transthyretin; peaks C, D and E were identified as triple-charged albumin, prothrombin fragment 2 and lumican, respectively. ELISA confirmed a significant decrease in AF concentrations of albumin and prothrombin following antenatal corticosteroid therapy, but the differences in transthyretin and lumican measurements did not achieve statistical significance.

**CONCLUSION:** This study uses proteomic technology to identify for the first time protein biomarkers in the AF before and after antenatal corticosteroid therapy. The biomarkers were identified as transthyretin, albumin, prothrombin and lumican. A better understanding of the molecular and cellular mechanisms by which antenatal steroids prevent neonatal complications will facilitate the development of new and innovative interventions to improve perinatal outcome in infants destined to deliver preterm.

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