

174 PROTEOMIC PROFILE OF MATERNAL SERUM IN WOMEN WITH RECURRENT PRETERM BIRTH LEONARDO PEREIRA¹, AMANDA ALEXANDER¹, MELISSA STANDLEY², JODI LAPIDUS³, ASHOK REDDY², SRINIVASA NAGALLA², ¹Oregon Health & Science University, Obstetrics and Gynecology, Portland, Oregon, ²Proteogenix, Inc., Beaverton, Oregon, ³Oregon Health & Science University, Portland, Oregon

OBJECTIVE: Patients with prior preterm birth (PTB) are at increased risk for recurrent preterm birth (RPTB). Our objective was to identify potential serum profiles characteristic of RPTB compared to non-recurrent PTB among symptomatic women in preterm labor (PTL).

STUDY DESIGN: Serum samples from prospectively enrolled women in spontaneous PTL at 20-34 weeks gestational age (GA) were analyzed. Ten women (5 RPTB, 5 non-recurrent PTB) were matched for GA. PTB was defined as delivery <34 weeks GA. Proteomic analysis of maternal serum was performed using fluorescent 2-dimensional gel electrophoresis (2D-DIGE). Image analysis and spot quantification was performed using Phoretix software. Protein identification was performed utilizing liquid chromatography tandem mass spectrometry (LC-MS/MS) and MALDI-TOF-MS.

RESULTS: Women were recruited at a mean GA of 27.8 weeks +/- 3.1 SD, and delivered at a mean GA of 29.8 weeks +/- 2.9 SD. There were no significant differences in demographic or reproductive factors between groups. 2D-DIGE demonstrated differential expression of multiple proteins representing a unique signature of RPTB. Potential biomarkers included inflammatory mediators and coagulation proteins. Preliminary analysis of potential biomarkers using immunoassays are correlative of 2D-DIGE data.

CONCLUSION: RPTB has a distinct maternal serum proteome profile compared to non-RPTB. Validation of potential biomarkers in a larger cohort could lead to better understanding of the mechanisms of RPTB.

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175 PREDICTING SURVIVAL AMONG NEONATES BORN AT 23 WEEKS GESTATION JENNIFER MCNAMARA¹, KATHLEEN SMITH¹, DEBORAH FELDMAN², YU MING VICTOR FANG², CHARLES INGARDIA², ADAM BORGIDA², ¹University of Connecticut Health Center, Obstetrics and Gynecology, Farmington, Connecticut, ²Hartford Hospital, Maternal Fetal Medicine, Hartford, Connecticut

OBJECTIVE: To evaluate the model derived from the Neonatal Research Network Extremely Preterm Birth Outcome Data in its ability to predict survival in a cohort of neonates born at 23 weeks gestation.

STUDY DESIGN: We identified all neonates born at 23 0/7 to 23 6/7 weeks gestation who were resuscitated at our institution from January 1995 through December 2006. Data regarding gestational age at delivery, birth weight, neonatal gender, singleton versus multiple gestation, maternal administration of corticosteroids and survival to discharge were obtained from the medical record. The model recently published by Tyson et al., (N Engl J Med. 358:1672-81, 2008), was used to generate the predicted survival for individual neonates. The mean predicted survival for all infants defines the expected survival rate for the cohort. The observed rate of survival was compared to the expected survival rate for the cohort using the Chi-square test. The mean predicted survival for survivors versus nonsurvivors was also compared.

RESULTS: We identified 33 neonates born at 23 0/7 to 23 6/7 weeks gestation who were resuscitated. Mean (\pm SD) birth weight was 559 gm (\pm 68.4). Maternal corticosteroids were administered in 15 (45.5%) of cases. Of the 33 infants, 16 (48.5%) were female, and 18 (54.5%) were singletons. The predicted survival rate for the cohort was 30.5%. The observed survival rate was 18/33 (54.5%), which was significantly higher than the predicted survival rate ($p = 0.003$). The mean predicted survival rate for survivors was 31.4%, versus 29.3% for nonsurvivors ($p = 0.53$).

CONCLUSION: The observed rate of survival to discharge among neonates delivered at 23 weeks gestation at our institution was significantly higher than the rate predicted using the published model, which may reflect institutional differences in selecting infants for resuscitation. There was no difference in predicted survival for survivors and nonsurvivors, suggesting that the published model may not be generalized to all populations.

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176 DIAGNOSIS OF EARLY-ONSET NEONATAL SEPSIS IN PREMATURE NEONATES FROM PROTEOMIC ANALYSIS OF UMBILICAL CORD BLOOD PETER ROBILIO¹, ASHOK REDDY², ARCHANA THOMAS², THOMAS JACOB², MELISSA STANDLEY², JOHN MICHAELS², XINFANG LU², JODI LAPIDUS², DAVID ESCHENBACH¹, MICHAEL GRAVETT¹, SRINIVASA NAGALLA², ¹University of Washington, Obstetrics and Gynecology, Seattle, Washington, ²Proteogenix, Inc., Beaverton, Oregon

OBJECTIVE: Early-onset neonatal sepsis (EONS), an important cause of mortality and morbidity in premature infants, is strongly associated with intra-amniotic infection. Identification of sepsis-associated biomarkers within neonatal cord blood from those who acquired EONS in utero could facilitate early treatment. We conducted a systematic analysis of the umbilical cord blood proteome in premature infants to identify potential biomarkers associated with EONS.

STUDY DESIGN: Umbilical cord blood samples from a prospective observational cohort of 82 women in spontaneous preterm labor at 20-34 weeks gestation were analyzed. EONS was defined as a positive neonatal blood culture within 72 hours of delivery. Cord blood proteome analysis was performed using fluorescence 2 D gel electrophoresis (2-DIGE), multidimensional liquid chromatography tandem mass spectrometry (2D LC-MS/MS) and label-free quantification (spectral counting). Pair-wise comparison was performed using χ^2 goodness-of-fit tests after adjusting for multiple comparisons via the false-discovery rate (FDR) method. Immunoassays were used for accurate quantification and evaluated using the Receiver Operating Characteristic (ROC) curves.

RESULTS: Of 82 subjects, 71 delivered at < 34 weeks and 5 of these had EONS. 2-DIGE analysis revealed the presence of a unique cord blood proteome for EONS. 2D LC-MS/MS and label-free quantification identified 52 proteins differentially expressed ($p < 0.05$) in neonates with EONS. These included immunoregulatory, acute phase, and extra-cellular matrix proteins. Immunoassay of 12 of these potential biomarkers showed good discriminant capability between those with and without sepsis (AUROC's 0.80 to 0.91). Immunoassay multi-analyte analysis further increased the discriminant ability (AUROC > 0.99).

CONCLUSION: Cord blood proteome analyses identified the presence of multiple novel proteins predictive of EONS. These may form a basis to develop rapid non-invasive immunoassays to accurately diagnose EONS independently of culture, allowing for earlier treatment.

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177 REPRODUCTIVE CONSEQUENCES OF ELECTIVE CESAREAN: A DECISION ANALYSIS WILLIAM GROBMAN¹, AARON CAUGHEY², KATHERINE HAHN¹, ¹Northwestern University, Chicago, Illinois, ²University of California, San Francisco, San Francisco, California

OBJECTIVE: To determine the pregnancy outcomes, throughout reproductive life, related to a nulliparous woman's decision to proceed with elective cesarean (ECS) versus trial of labor (TOL).

STUDY DESIGN: A decision-analytic model was developed to compare the consequences of a nulliparous woman choosing ECS versus TOL. In this model, all women who had an ECS initially or who had a cesarean after attempting a TOL, had repeat cesareans in future pregnancies. Literature was used to determine probabilities of successful trial of labor, placenta previa, placenta accreta, and major obstetric complications, including transfusion, operative injury, DVT, hysterectomy, and mortality. Probabilities of these events were dependent upon both parity and the number of prior cesareans that a woman had experienced. The probability of a major obstetric complication was determined for each pregnancy, as was the cumulative probability of a major obstetric complication based on the number of deliveries a woman could have. Sensitivity analyses were performed using reasonable ranges for all variables.

RESULTS: At baseline estimates, there is a slightly greater probability of complications with the choice of an ECS than from a TOL, although this difference is small (0.77% versus 0.53%). With more pregnancies, the difference in risk of morbidity becomes increasingly greater for women who initially chose an ECS, largely related to the risk of placenta previa and accreta. For example, at a second pregnancy, the risk of placenta previa with accreta for those who had chosen an ECS vs. TOL at their first birth was 0.07% and 0.02%; at a third pregnancy the risks were 0.55% and 0.15%; and at fourth the risks were 1.99% and 0.54%. The risk of a major complication during a second pregnancy, for those who had chosen an ECS vs. TOL at their first birth, was 1.78% vs. 1.17%; during a third pregnancy, 3.10% vs. 1.88%; and during a fourth pregnancy 5.26% vs. 2.83%.

CONCLUSION: Choosing an ECS for an initial birth increases the probability of significant obstetric complications throughout a woman's reproductive life.

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