Respiratory Outcomes of Infants Born after Oligoanyhydramnios
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A. Study Purpose and Rationale

Background:
Oligohydramnios, or decreased amniotic fluid volume, is a rare complication of pregnancy that is generally defined as an Amniotic Fluid Index (AFI) <5. Anhydramnios, or absent amniotic fluid during pregnancy, is generally defined as AFI of 0. The causes for oligoanhydramnios (OAH) are varied, but often occur as a result of fetal renal disease or premature rupture of membranes (PROM). Beginning in the 12th week of pregnancy, the fetal kidneys begin to produce urine, which is responsible for the production and maintenance of amniotic fluid. An appropriate amount of amniotic fluid is thought to be necessary for stimulation and development of fetal lungs. Disturbances in this pathway resulting in decreased amniotic fluid can then result in lung hypoplasia. Aside from renal disease, PROM can also result in OAH due to continued leakage of amniotic fluid through the cervix.

Overall prognosis of OAH varies, with some studies demonstrating poor outcome and death rates between 30-60%. However, other studies show more encouraging long-term prognosis, with close to 60% survival. Generally, later gestational age at diagnosis of oligo or anhydramnios correlates with better outcomes. The earlier that oligohydramnios is detected, the more severe the pulmonary hypoplasia. Another important prognostic indicator depends on the etiology of OAH. If renal anomalies are the cause of decreased amniotic fluid, the nature of the renal anomaly is very important. Hydronephrosis has been correlated with a favorable outcome, whereas renal agenesis and dysplasia with less favorable outcomes.

Respiratory failure is a common cause of death in the neonatal period, and surviving infants often require significant respiratory support, with studies demonstrating 60- 80% of surviving infants requiring significant ventilator support including conventional vent and HFOV. Although some infants are able to survive on CPAP alone, this is unusual and most infants requiring respiratory intervention depended upon intubation and conventional ventilator support.

Aim:
Overall, while literature on this subject exists, data on prognosis and long-term outcome is still varied and there are still significant gaps in the literature. An evidence-based approach to treatment and management of anhydramnios is evolving and not yet well established, and there is a need for more research in this area in order to better counsel women with second trimester oligo or anhydramnios secondary to PPROM or renal etiologies. In this study, we examine infants born after second trimester PPROM or with renal anomalies leading to OAH and the impact on respiratory outcome.

Main hypothesis:
Our hypothesis is that infants born from gestations complicated by oligoanhydramnios will have poor respiratory outcomes in the immediate neonatal period and at time of discharge from the Neonatal Intensive Care Unit.

B. Study Design and Statistical Analysis

The study design is a retrospective chart review. Data will be obtained through cooperation with Columbia University Department of Obstetrics and Gynecology CORE Data Team. Database will be developed from REDCap (Research Electronic Data Capture).
Those eligible to be included in the study are fetuses, whether terminated or live born, at Columbia University Medical Center between 2007 through 2017 after pregnancies complicated by oligo or anhydramnios. Oligohydramnios will be defined as the amniotic fluid index (AFI), calculated as the sum of the deepest pockets of amniotic fluid in the four quadrants of the uterus, being less than 5 cm. Anhydramnios will be defined as an amniotic fluid index of 0 cm.

Variables of interest during pregnancy include gestational age at diagnosis of OAH, renal anomalies, genetic conditions, severity of OAH based on Amniotic Fluid Index (AFI), gender of fetus, maternal age, and whether or not the pregnancy was terminated, resulted in intrauterine fetal demise (IUFD), or resulted in a live birth. Variables of interest after delivery include comfort care measures only, mortality in the neonatal or newborn period, intubation, continuous positive airway pressure (CPAP) requirement, supplemental oxygen requirement, dialysis requirement, placement of a tracheostomy. At time of discharge from the NICU, variables of interest are respiratory support requirement and mortality.

There are four main outcomes that we will be analyzing in this study: respiratory failure in the neonatal period, mortality in the neonatal period, respiratory support requirement at discharge from NICU, and survival to discharge from the NICU.

Statistical analysis will be conducted using Microsoft Excel and R. Nominal data, for example mean gestational age at diagnosis, will be analyzed using an unpaired t-test. Categorical data, such as existence of renal anomalies, will be analyzed using 2 x 2 contingency tables.
We will assume a p value of <0.05 for significance.

C. Study Procedure: Data will be obtained and analyzed as described above.

D. Study Drugs: None
E. Medical Device: None
F. Study Questionnaires: None
G. Study Subjects: Fetuses and newborns, whether terminated or live born, at Columbia University Medical Center between 2007 through 2017 after pregnancies complicated by oligo or anhydramnios.

H. Recruitment of subjects: Subjects will be recruited from retrospective chart review. This study will apply for waiver of consent.

I. Confidentiality of Study Data:

Chart review will be done only on secure, password protected computers. All connections to the REDCap system occur over encrypted channels, and all collected information is stored on a server hosted at Columbia University. All patient identifiers will be removed from the electronic data set prior to analysis, and each patient will be assigned a unique study ID number. A separate file correlating this study number with patient identifiers will be kept in a secure, password protected database. Only the study personnel will have access to the file, which will be kept on encrypted endpoint devices.

J. Potential Conflict of Interest: None
K. Location of the Study: Columbia/CUMC-Neonatal Intensive Care Unit
L. Potential Risks: Not applicable
M. Potential Benefits: There will be no direct benefit to the participant.
N. Alternative Therapies: Not Applicable
O. Compensation to Subjects: None
P. Costs to Subjects: Not Applicable
Q. Minors as Research Subjects: Not Applicable
R. Radiation or Radioactive Substances: Not Applicable

References:

1. Waldo Sepulveda, Amy E. Wong, Alexandra Casasbuenas, A. S. and J. L. A. Congenital diaphragmatic hernia in a first-trimester ultrasound aneuploidy screening program. *Prenat. Diagn.* **28,** 531–534 (2008).
2. Shrem, G., Nagawkar, S. S., Hallak, M. & Walfisch, A. Isolated Oligohydramnios at Term as an Indication for Labor Induction: A Systematic Review and Meta-Analysis. *Fetal Diagn. Ther.* **40,** 161–173 (2016).
3. Moxey-Mims, M. & Raju, T. N. K. Anhydramnios in the Setting of Renal Malformations. *Obstet. Gynecol.* **131,** 1 (2018).
4. Mehler, K. *et al.* Respiratory and general outcome in neonates with renal oligohydramnios - A single-centre experience. *Nephrol. Dial. Transplant.* **26,** 3514–3522 (2011).
5. Loos, S. & Kemper, M. J. Causes of renal oligohydramnios: impact on prenatal counseling and postnatal outcome. *Pediatr. Nephrol.* **33,** 541–545 (2018).
6. Klaassen, I., Neuhaus, T. J., Mueller-Wiefel, D. E. & Kemper, M. J. Antenatal oligohydramnios of renal origin: Long-term outcome. *Nephrol. Dial. Transplant.* **22,** 432–439 (2007).
7. Chien, L. N., Chiou, H. Y., Wang, C. W., Yeh, T. F. & Chen, C. M. Oligohydramnios increases the risk of respiratory hospitalization in childhood: A population-based study. *Pediatr. Res.* **75,** 576–581 (2014).