Title

North American Fetal Therapy Network: Maternal Outcomes in Fetal Aqueductal Stenosis.

Journal

Fetal therapy, 51(6)

Authors

Emery, Stephen

Lopa, Samia

Peterson, Erika

et al.

Publication Date

2024

DOI

10.1159/000540196

Peer reviewed

HHS Public Access

Author manuscript

Fetal Diagn Ther. Author manuscript; available in PMC 2024 December 11.

Published in final edited form as:

Fetal Diagn Ther. 2024 ; 51(6): 612–616. doi:10.1159/000540196.

North American Fetal Therapy Network: Maternal Outcomes in Fetal Aqueductal Stenosis

Stephen P. Emery, MD[a], **Samia Lopa, PhD**[b], **Erika Peterson, MD**[c], **Jena L. Miller, MD**[d], **Marjorie C. Treadwell, MD**[e], **Juliana Gebb, MD**[f], **Henry Galan, MD**[g], **Eric P. Bergh, MD**[h], **Amanda Criebaum, MSN, RN**[i], **Amelia McLennan, MD**[j], **Joseph B. Lillegard, MD**[k], **Yair J. Blumenfeld, MD**[l], **Ozhan M. Turan, MD**[m], **David C. Streitman, MD**[n]

[a]Department of Obstetrics, Gynecology, and Reproductive Sciences/University of Pittsburgh School of Medicine/UPMC Magee-Womens Hospital, Pittsburgh (PA,) USA

[b]Department of Biostatistics and Computational Biology/University of Rochester, Rochester (NY,) USA

[c]Department of Obstetrics and Gynecology/Medical College of Wisconsin/Children's Hospital of Wisconsin, Milwaukee (WI,) USA

[d]Department of Gynecology and Obstetrics/Johns Hopkins University/The Johns Hopkins Hospital, Baltimore (MD,) USA

[e]Department of Obstetrics and Gynecology/University of Michigan/University of Michigan Hospital, Ann Arbor (MI,) USA

[f]Division of Pediatric General, Fetal and Thoracic Surgery/University of Pennsylvania/Children's Hospital of Philadelphia, Philadelphia (PA,) USA

[g]Department of Obstetrics and Gynecology/University of Colorado School of Medicine/Children's Hospital Colorado, Denver (CO,) USA

[h]Department of Obstetrics and Gynecology/University of Texas at Houston/Children's Memorial Hermann Hospital, Houston (TX,) USA

[i]Department of Obstetrics and Gynecology/St. Louis Fetal Care Institute, St. Louis (MO,) USA

Corresponding Author: Stephen P. Emery, MD, Department of Obstetrics, Gynecology, and Reproductive Sciences, University of Pittsburgh School of Medicine, UPMC Magee-Womens Hospital, 300 Halket Street, Pittsburgh, PA 15213 USA, emerysp@upmc.edu.

Author Contributions:

Emery contributed to manuscript conception, data review, manuscript writing, coordination of co-author input, and approval. Lopa performed the statistical analysis, manuscript review, and approval. Peterson, Miller, Treadwell, Gebb, Galan, Criebaum, Bergh, McLennan, Lillegard, Blumenfeld, Turan, and Streitman contributed to data acquisition and manuscript review and approval.

Statement of Ethics:

The University of Pittsburgh Institutional Review Board (IRB) approved of the study to be conducted locally (STUDY20050409). Registry approval was obtained through the University of Pittsburgh IRB (STUDY20020214) for the University of Pittsburgh to serve as the coordinating center for the study. Each collaborating center completed their local IRB approval for site enrollment, data extraction, and registry entry. A data use agreement (DUA) was obtained between the University of Pittsburgh and each collaborating center with local IRB approval being a prerequisite of DUA execution. Written informed consent was obtained for participation in the study. Registry data was entered into the database by collaborating centers in a de-identified manner. This study protocol was reviewed and approved by ethics committees at each of the participating sites. The full list of participating sites and ethics committees can be found at https://docs.google.com/document/d/13ss4t9Z13KV-sulmBgsnCvaaaeXtqRQO0DmWbXbwcPk/edit?usp=sharing.

Conflict of Interest Statement:

The authors have no conflicts of interest to declare.

[j]Department of Obstetrics and Gynecology/University of California Davis/UC Davis Medical Center, Sacramento (CA,) USA

[k]Department of Surgery/ Children's Minnesota, Minneapolis (MN,) USA

[l]Department of Obstetrics and Gynecology/Stanford University/Stanford Medicine Children's Health, Palo Alto, (CA,) USA

[m]Department of Obstetrics, Gynecology, and Reproductive Sciences/University of Maryland School of Medicine/University of Maryland Medical Center, Baltimore (MD,) USA

[n]Department of Obstetrics and Gynecology/Indiana University School of Medicine/Riley Children's Hospital, Indianapolis (IN,) USA

Abstract

Introduction: Fetal aqueductal stenosis (AS) affects approximately 1:1,000 pregnancies. Obstruction of cerebral spinal fluid (CSF) circulation occurs at the aqueduct of Sylvius, leading to progressive hydrocephalus and macrocephaly, which often necessitates cesarean section (CS). The purpose of this study is to describe maternal outcomes associated with fetal AS.

Methods: This study is conducted through the North American Fetal Therapy Network (NAFTNet). Subjects with a prenatal diagnosis of severe fetal central nervous system (CNS) ventriculomegaly were recruited and followed longitudinally. Maternal events around the delivery of fetuses with AS were recorded and analyzed.

Results: Thirty-seven subjects with fetal AS confirmed by neonatal neuroimaging were analyzed. The average gestational age at delivery was 36.7 weeks. Overall, 86% were delivered by CS, and 62% of these were elective. Ninety-one percent of CSs were performed through a Pfannenstiel abdominal incision. A classical uterine incision was required in 13% of cesarean deliveries. The peripartum complication rate was 27%.

Conclusion: Women carrying a fetus with AS were at risk for preterm birth, cesarean delivery, a classical uterine incision, and peripartum complications. This data highlights the maternal morbidity associated with fetal AS and the potential benefit of in-utero therapy not only for neonatal outcomes but also for maternal outcomes.

Keywords

fetal aqueductal stenosis; ventriculomegaly; hydrocephalus; maternal complications

Introduction:

Severe fetal central nervous system (CNS) ventriculomegaly (lateral ventricle >15 mm) affects approximately 1 in 1000 pregnancies.[1] Neonatal neurologic outcomes are generally poor, including seizure disorder, developmental delay, and ophthalmological abnormalities.[2–6] Ventriculoamniotic shunting for fetal severe ventriculomegaly was attempted in the 1980s but was abandoned due to a perceived lack of effect. Technological limitations of fetal imaging at the time precluded an accurate diagnosis of fetal aqueductal stenosis (AS). A de facto moratorium was placed on ventriculoamniotic shunting in 1986.[7]

In fetal AS, cerebral spinal fluid (CSF) circulation is obstructed at the level of the aqueduct of Sylvius. The accumulation of excess CSF leads to supratentorial hypertension, hydrocephalus, and macrocephaly.[8] Macrocephaly often necessitates delivery by cesarean section (CS) because the fetal head is too large to pass through the maternal pelvis.[9] Cesarean section exposes the mother to quantifiable risks during and after the procedure, such as hemorrhage, infection, thromboembolism, and wound complications. Cesarean scars are a risk factor for complications in subsequent pregnancies such as placenta accreta and cesarean scar ectopic pregnancy. [10–13] In some instances, a classical (vertical) uterine incision is necessary to atraumatically deliver the enlarged fetal head. A classical cesarean scar is a risk factor for uterine rupture and potentially catastrophic outcomes in subsequent pregnancies.[14, 15] In-utero shunting of excess CSF into the amniotic cavity with a ventriculo-amniotic shunt could decrease the fetal head circumference, thereby decreasing the need for performing a CS. This study aims to describe peripartum maternal morbidity in pregnancies complicated by fetal AS. Characterizing the maternal risks of severe fetal CNS ventriculomegaly is a necessary component for constructing a comprehensive risk-benefit assessment of in-utero shunting for fetal AS.

Methods:

We conducted a multicenter, prospective, observational study of prenatally diagnosed severe fetal CNS ventriculomegaly through the North American Fetal Therapy Network (NAFTNet). Inclusion criteria were pregnancies complicated by severe CNS ventriculomegaly (VM, lateral ventricle diameter >15 mm) not secondary to a primary diagnosis such as myelomeningocele or encephalocele, and the ability to obtain longitudinal data through pregnancy, delivery, and at one and two years of age of the child. Pregnancies in which long-term follow-up was not possible (pregnancy termination) or unlikely (major extracranial diagnosis) were excluded. Subjects with incomplete information regarding a prenatal or postnatal diagnosis or those recruited after 37 weeks were excluded. Maternal demographic information, initial and subsequent ultrasound findings, genetic testing results, infection studies, fetal MRI if performed, delivery information, neonatal data (including postnatal diagnosis by neonatal neuroimaging), and neurologic development at ages one and two years were collected. De-identified study data was collected and managed using REDCap electronic data capture tools hosted at the University of Pittsburgh, which served as the coordinating center (University of Pittsburgh IRB-approved STUDY20040214 Coordinating Center for NAFTNet Prenatal Diagnosis of Aqueductal Stenosis). Each study center required IRB approval and a data use agreement with the University of Pittsburgh.

Events around delivery (gestational age, indication, intended route of delivery, actual route of delivery, skin incision, uterine incision, and maternal complications) were extracted from patient records and analyzed for this study. Gestational age at delivery was recorded in weeks. The indication for delivery was recorded as spontaneous labor, induced labor, CS before labor, or CS after labor. Route of delivery was recorded as vaginal delivery (VD), CS, or CS after trial of labor (TOL). The skin incision was recorded as Pfannenstiel, high transverse, or vertical. The uterine incision was recorded as low transverse, classical, “T” and “J.” Maternal complications were recorded as hemorrhage, wound, thromboembolic, febrile, other, or none. Results are expressed in number and percent.

Results:

The study enrolled participants from April 2015 through January 2024. Thirteen NAFTNet centers contributed 57 subjects with sufficient data for this analysis. Subject demographics are described in a prior publication from this initiative.[16] The mean subject age was 29.3 years, ranging from 19-41 years. A majority were Caucasian. The mean year of pregnancy was 2019, with a median of 2020 and a mode of 2021. In 37 of the 57 subjects, the postnatal diagnosis was AS by neonatal neuroimaging. These 37 subjects represent the cohort for the current manuscript.

The average GA at delivery was 36.7 weeks. Regarding route of delivery, 32 (86%) subjects were delivered by CS and 5 (14%) were delivered vaginally. Twenty-three (62%) were electively delivered by CS before labor, 5 (13%) entered labor spontaneously, 5 (13%) were induced, and 4 (10%) proceeded to CS after IOL. The skin incision was Pfannenstiel in 29 (91%), high transverse in 2 (6%), and vertical in 1 (3%) of cesarean deliveries. The uterine incision was low transverse in 28 (87%) and classical in 4 (13%) of cesarean deliveries, three through a Pfannenstiel incision and one through a vertical midline incision. There were no “T” or “J” uterine incision extensions. Ten (27%) subjects experienced a peripartum complication (five hemorrhage, two wound, one febrile, one retained placenta requiring manual extraction, and one placental abruption). (Table 1)

Discussion:

Shunting for fetal hydrocephalus was attempted in the 1980s but was abandoned due to a perceived lack of effect.[7] In retrospect, the problem was likely improper patient selection due to limitations of accurate prenatal diagnosis at the time. Emery and colleagues proposed an evidence-based reassessment of ventriculo-amniotic shunting for fetal aqueductal stenosis in 2015[17]. This study is part of a larger NAFTNet initiative that includes assessing the accuracy of prenatal diagnosis of fetal AS, describing maternal outcomes, developing a scoring system for fetal AS based on ultrasound and MRI findings, and pediatric neurodevelopment scores at ages 1 and 2 years. This study aims to define maternal outcomes associated with the diagnosis of fetal AS. This information will be necessary to construct a thorough risk-benefit assessment for future in-utero shunting.

Timing of delivery is a consideration in fetal AS. The risks of prematurity must be weighed against ongoing neurological damage from supratentorial hypertension, ischemia, and neuronal shear.[18] In the past, preterm birth was advocated in hopes of optimizing neurologic outcomes. More recently, nearterm or term delivery has been preferred, as preterm infants are poorer surgical candidates for ventriculoperitoneal shunting or endoscopic third ventriculostomy than term infants.[19] Our cohort’s gestational age of delivery was 36.7 weeks, which reflects this current trend.

Eighty-six percent of subjects were ultimately delivered by cesarean section, and sixty-two percent were delivered by elective cesarean section, consistent with anecdotal experience of a high incidence of CS with fetal AS.

Thirteen percent of cesarean sections were performed through a classical uterine incision, which is substantially higher than the <2% rate in a large cohort of >19,000 cesarean deliveries.[10] Classical uterine incisions are prone to rupture in subsequent pregnancies, resulting in catastrophic maternal and neonatal consequences, and are therefore generally avoided.[14, 20–23] In these cases, the surgeons likely determined that the macrocephalic head could not be safely delivered through a low transverse uterine incision and that a vertical uterine incision was necessary. Ventriculoamniotic shunting for fetal AS may decrease the need for cesarean section and a classical incision with its associated consequences by preventing macrocephaly.

Peripartum complications were significant in this cohort (27%), with hemorrhage occurring in 5 (14%). Two (6%) developed wound complications, both with a Pfannenstiel incision. One vaginal delivery was complicated by shoulder dystocia and retained placenta, necessitating manual extraction. One subject experienced placental abruption at 32 weeks.

A strength of this study is its multicenter, prospective methodology through NAFTNet, whose member centers have experience in prenatal diagnosis.[24] To our knowledge, this is the first prospective cohort of fetuses with a proven postnatal diagnosis of AS, which allows for evaluating the obstetric implications of this specific diagnosis. Prior studies were retrospective and included other causes of severe fetal CNS ventriculomegaly.[4, 5] In addition, these studies were focused on fetal-neonatal evaluation and did not address maternal or obstetric outcomes. In contrast to the study by Hannon et al., where the overall and elective CS rates (62.3% and 45.3%) in this current study focused on AS, these cesarean rates were much higher (86% and 62%, respectively. [4] Our study is limited by small numbers. As an observational study, it cannot determine causation.

In conclusion, women carrying a fetus with AS are at risk for elective preterm delivery, cesarean section, classical uterine incision, and peripartum complications. This information will help construct a risk-benefit equation for in-utero shunting for fetuses with AS.

Acknowledgement:

The authors would like to acknowledge Virali Patel, BS for her assistance with writing, reviewing, and referencing this manuscript.

Funding Source:

The North American Fetal Therapy Network is supported by a grant (5R13HD059293-05) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development. Jena L. Miller is supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development of the National Institutes of Health under award number R01HD100540. The contents of the publication are solely the responsibility of the authors and do not necessarily represent the official views of the NIH. Jena L. Miller is supported by Janssen Research and Development, LLC for a project unrelated to this research.

Data Availability Statement:

The data that support the findings of this study are not publicly available due to concerns for subject confidentiality but are available from the Corresponding Author upon reasonable request.

References

1. Isaacs AM, et al. , Age-specific global epidemiology of hydrocephalus: Systematic review, metanalysis and global birth surveillance. PLoS One, 2018. 13(10): p. e0204926. [PubMed: 30273390]
2. Tonetti DA, et al. , Clinical Outcomes of Isolated Congenital Aqueductal Stenosis. World Neurosurg, 2018.
3. Levitsky DB, et al. , Fetal aqueductal stenosis diagnosed sonographically: how grave is the prognosis? AJR Am J Roentgenol, 1995. 164(3): p. 725–30. [PubMed: 7863902]
4. Hannon T., et al. , Epidemiology, natural history, progression, and postnatal outcome of severe fetal ventriculomegaly. Obstet Gynecol, 2012. 120(6): p. 1345–53. [PubMed: 23168759]
5. Carta S., et al. , Outcome of fetuses with prenatal diagnosis of isolated severe bilateral ventriculomegaly: systematic review and meta-analysis. Ultrasound Obstet Gynecol, 2018. 52(2): p. 165–173. [PubMed: 29484752]
6. Kennelly MM, Cooley SM, and McParland PJ, Natural history of apparently isolated severe fetal ventriculomegaly: perinatal survival and neurodevelopmental outcome. Prenat Diagn, 2009. 29(12): p. 1135–40. [PubMed: 19821481]
7. Manning FA, Harrison MR, and Rodeck C, Catheter shunts for fetal hydronephrosis and hydrocephalus. Report of the International Fetal Surgery Registry. N Engl J Med, 1986. 315(5): p. 336–40. [PubMed: 3724830]
8. Shinar S, et al. , Fetal macrocephaly: Pathophysiology, prenatal diagnosis and management. Prenat Diagn, 2023. 43(13): p. 1650–1661. [PubMed: 38009873]
9. Chervenak FA and McCullough LB, Ethical analysis of the intrapartum management of pregnancy complicated by fetal hydrocephalus with macrocephaly. Obstet Gynecol, 1986. 68(5): p. 720–5. [PubMed: 3763090]
10. Liu S, et al. , Maternal mortality and severe morbidity associated with low-risk planned cesarean delivery versus planned vaginal delivery at term. CMAJ, 2007. 176(4): p. 455–60. [PubMed: 17296957]
11. Silver RM, et al. , Maternal morbidity associated with multiple repeat cesarean deliveries. Obstet Gynecol, 2006. 107(6): p. 1226–32. [PubMed: 16738145]
12. Timor-Tritsch IE, et al. , Cesarean Scar Pregnancy: Diagnosis and Pathogenesis. Obstet Gynecol Clin North Am, 2019. 46(4): p. 797–811. [PubMed: 31677755]
13. Silver RM, Implications of the first cesarean: perinatal and future reproductive health and subsequent cesareans, placentation issues, uterine rupture risk, morbidity, and mortality. Semin Perinatol, 2012. 36(5): p. 315–23. [PubMed: 23009962]
14. Patterson LS, O'Connell CM, and Baskett TF, Maternal and perinatal morbidity associated with classic and inverted T cesarean incisions. Obstet Gynecol, 2002. 100(4): p. 633–7. [PubMed: 12383525]
15. Nunes I, et al. , FIGO good practice recommendations on surgical techniques to improve safety and reduce complications during cesarean delivery. Int J Gynaecol Obstet, 2023. 163 Suppl 2: p. 21–33. [PubMed: 37807585]
16. Emery SP, et al. , Prenatal Diagnosis of Fetal Aqueductal Stenosis: A Multicenter Prospective Observational Study through the North American Fetal Therapy Network (NAFTNet). Fetal Diagn Ther, 2024.
17. Emery SP, Greene S, and Hogge WA, Fetal Therapy for Isolated Aqueductal Stenosis. Fetal Diagn Ther, 2015. 38(2): p. 81–5. [PubMed: 25997519]
18. Emery SP, et al. , Histologic Appearance of Iatrogenic Obstructive Hydrocephalus in the Fetal Lamb Model. Fetal Diagn Ther, 2019: p. 1–9.
19. Morgan CD, et al. , Early elective delivery for fetal ventriculomegaly: are neurosurgical and medical complications mitigated by this practice? Childs Nerv Syst, 2018. 34(5): p. 829–835. [PubMed: 29196812]
20. Greene RA, Fitzpatrick C, and Turner MJ, What are the maternal implications of a classical caesarean section? J Obstet Gynaecol, 1998. 18(4): p. 345–7. [PubMed: 15512105]

21. Halperin ME, Moore DC, and Hannah WJ, Classical versus low-segment transverse incision for preterm caesarean section: maternal complications and outcome of subsequent pregnancies. Br J Obstet Gynaecol, 1988. 95(10): p. 990–6. [PubMed: 3191053]

22. Lao TT, et al. , Uterine incision and maternal blood loss in preterm caesarean section. Arch Gynecol Obstet, 1993. 252(3): p. 113–7. [PubMed: 8503702]

23. Shah YG, et al. , Acute maternal morbidity following classical cesarean delivery of the preterm infant. Obstet Gynecol, 1990. 76(1): p. 16–9. [PubMed: 2359565]

24. Baschat AA, et al. , Care Levels for Fetal Therapy Centers. Obstet Gynecol, 2022. 139(6): p. 1027–1042. [PubMed: 35675600]

Results

Table 1:

Variable	N=37
Gestational age at delivery in weeks	36.7
Cesarean section n, (%)	32 (86)
Elective cesarean section, n, (%)	23 (62)
Pfannenstiel incision, n, (%)	29 (91)
Low transverse uterine incision	28 (87)
Classical uterine incision, n, (%)	4 (13)
Peripartum complications, n, (%)	10 (27)