UC San Diego
UC San Diego Previously Published Works

Title

267 Multiple fetal anomalies are associated with actionable postnatal genome sequencing results

Permalink

https://escholarship.org/uc/item/9vh083zj

Journal

American Journal of Obstetrics and Gynecology, 224(2)

ISSN

0002-9378

Authors

Zhang-Rutledge, Kathy
Dimmock, David
Kingsmore, Stephen F
et al.

Publication Date

2021-02-01

DOI

10.1016/j.ajog.2020.12.289

Peer reviewed

RESULTS: Maternal age, parity, BMI, gestational age at delivery, neonatal birthweight, and APGAR scores were similar between the two groups. None of the patients developed preeclampsia or required acute treatment for hypertension. Accounting for Bonferroni correction, we found statistically significant elevations of 1.45-2.03 fold in 9 of the targeted unsaturated fatty acids in the chronic hypertension group compared to controls.

CONCLUSION: Using metabolomic profiling, we found that 9 unsaturated fatty acid were elevated in the serum of fasting pregnant women with chronic hypertension. This free fatty acid profile mirrors that of people with chronic hypertension outside of pregnancy. This may represent a possible pathway explaining how pregnant women with well controlled chronic hypertension remain at high risk for complications such as preeclampsia. Larger studies are needed to compare the fatty acid profile in women with chronic hypertension who developed pre-eclampsia.

Free fatty acid chemical formula	Fold change (Hypertension/control)	P
C16:0 (area)	1.63	<0.01
C16:1	1.85	0.03
C18:1	1.56	<0.01
C18:2	1.71	<0.01
C18:3	1.79	0.05
C20:3	2.03	<0.01
C20:4	1.45	0.03
C22:5	1.78	<0.01
C22:5 isomer	1.89	<0.01
* p-value with Bonferroni correction		

267 Multiple fetal anomalies are associated with actionable postnatal genome sequencing results

Kathy Zhang-Rutledge[1], David Dimmock[2], Stephen F. Kingsmore[2], Louise C. Laurent[1]
[1]University of California, San Diego, La Jolla, CA, [2]Rady Children's Institute for Genomic Medicine, San Diego, CA

OBJECTIVE: Prenatal whole exome sequencing (WES) and whole genome sequencing (WGS) have not been adopted into routine obstetrical practice due to high cost and suspected low diagnostic yield. However, the actual diagnostic yield of these methods in pregnancies with specific prenatal findings is not known. The goal of this study is to determine whether specific types of prenatal complications are associated with actionable postnatal WES/WGS results.

STUDY DESIGN: This is a case control study comparing critically ill neonates in the NSIGHT2 study who had actionable versus negative postnatal WES/WGS results. We excluded neonates without available prenatal ultrasound reports. We reviewed the ultrasound reports for abnormal findings. We calculated the odds ratio and used Fisher's exact test to compare findings between the two groups.

RESULTS: 213 neonates were sequenced in the NSIGHT2 study. 80 of those neonates had available prenatal ultrasounds. Of these, 21 had an actionable finding from genome sequencing: 7 WES and 14 WGS. 59 neonates had negative sequencing results: 32 WES and 27 WGS. 66.7% of neonates with actionable WES/WGS results had anomalies suspected on fetal ultrasound, while 55.9% of neonates with negative sequencing had suspected fetal anomalies. Among those with suspected fetal anomalies, neonates with actionable WES/WGS results were 4.5 times more likely to have multiple anomalies and 6.7 times more likely to have anomalies of the extremities compared to those with negative findings. Fetal growth restriction was present in 19% of neonates with actionable WES/WGS and in 6.8% with negative sequencing results.

CONCLUSION: In our study population, neonates with actionable findings on WES/WGS were statistically more likely to have multiple anomalies and anomalies of the extremities. These findings suggest that pregnancies with multiple fetal anomalies on ultrasound may benefit from WES/WGS. Larger studies are needed to determine utility of introducing WES/WGS to clinical practice.

	Positive Results[a]	Negative Results[a]	OR (95% CI)	P[b]
Central Nervous System	7 (33.3)	9 (15.3)	2.78 (0.88-8.79)	0.11
Face	2 (9.5)	0	N/A[c]	0.07
Heart	7 (33.3)	21 (35.6)	0.91 (0.32-2.59)	1.0
Chest	1 (4.8)	2 (3.4)	1.43 (0.12-16.6)	1.0
Gastrointestinal	2 (9.5)	3 (5.1)	1.97 (0.31-12.7)	0.60
Genitourinary	5 (23.8)	5 (8.5)	3.38 (0.87-13.1)	0.12
Extremities	4 (19)	2 (3.4)	6.71 (1.13-39.8)	0.04*
Spine	1 (4.8)	0	N/A[c]	0.26
Umbilical Cord	3 (14.3)	4 (6.8)	2.29 (0.47-11.2)	0.37
Placenta	1 (4.8)	0	N/A[c]	0.26
Amniotic Fluid Index	4 (19)	6 (10.2)	2.08 (0.52-8.25)	0.44
Other Body System	0	2 (3.4)	N/A[c]	1.0
Any Anomaly	14 (66.7)	33 (55.9)	1.58 (0.56-4.47)	0.45
Multiple Anomaly	10 (47.6)	10 (16.9)	4.46 (1.49-13.3)	0.01*
Fetal Growth Restriction	4 (19)	4 (6.8)	3.24 (0.73-14.3)	0.20
[a] Data presented as N (percentage)				
[b] Analysis by Fisher's exact test				
[c] Not estimable due to zero cells				
* Statistically significant				

268 Utility of the INCODE algorithm to identify cause of stillbirth in clinical settings

Hannah Sweeney[1], Hannah Kenny[1], Allison Bosch[2], Donald Dudley[1]
[1]University of Virginia, Charlottesville, VA, [2]Emory University, Atlanta, GA

OBJECTIVE: The Initial Causes of Fetal Death Evaluation (INCODE) algorithm was developed by the Stillbirth Collaborative Research Network (SCRN) as a research tool to assign causes of death of stillbirth in which standardized postmortem examination (PME) is performed. Our goal was to assess the utility of INCODE in a retrospective cohort of stillbirths (SB) at a single tertiary hospital where PME was not routinely performed.

STUDY DESIGN: Chart reviews were performed for all cases of SB from Dec 2013 to Oct 2019. Narrative summaries and PME results were recorded. Cause of death was assigned based on INCODE as described by SCRN investigators.

RESULTS: Of the 99 identified SB, probable cause of death was identified in 70 (70.7%; 95% CI, 61.7-79.7%) and possible or probable cause in 92 (92.9%; 95% CI, 87.9-98.0%). The most common causes of SB were placental (n=40 [40.4%; 95% CI, 30.7-