34 Advanced maternal age and the risk of major congenital anomalies: survival of the fittest?

Katherine Goetzinger[1], Anthony Shanks[1], Anthony Odibo[1], George Macones[1], Alison Cahill[1]
[1]Washington University in St. Louis, Obstetrics & Gynecology, St. Louis, MO

OBJECTIVE: Advanced maternal age (AMA) is a well-established risk factor for fetal chromosomal abnormalities secondary to defects in cell division; however, the relationship between AMA and major congenital anomalies remains unknown. The objective of this study was to determine if AMA is an independent risk factor for major congenital anomalies diagnosed at the time of second trimester anatomic survey, in the absence of aneuploidy.

STUDY DESIGN: This is a retrospective cohort study of all patients with a singleton gestation presenting for second trimester anatomic survey over an 18 year period. Cases of aneuploidy were excluded. Study groups were defined by maternal age <35 versus ≥35 years. The primary outcome was the presence of one or more major fetal anomalies diagnosed at second trimester ultrasound. Univariate and multivariate logistic regression analyses were used to estimate the risk of major fetal anomalies in women who were AMA. The distribution of fetal anomalies by organ system was also compared between the study groups.

RESULTS: Of 76,156 euploid fetuses, 2.4% (n=1,804) were diagnosed with a major anomaly. There was a significant decrease in the incidence of major fetal anomalies with increasing maternal age until the threshold of age 35. (p<0.001) AMA was significantly associated with an overall decreased risk for major fetal anomalies (aOR 0.59, 95% CI 0.52-0.66) after controlling for potential confounders. Specifically, the incidence of central nervous system (CNS), renal, and abdominal wall anomalies were decreased in women ≥35 years. This was contrasted by the similar rate of cardiac anomalies between the study groups. (Table).

CONCLUSION: AMA is associated with an overall decreased risk for major fetal congenital anomalies, driven by a decrease in CNS, renal and abdominal wall defects. These surprising findings may suggest that the "all or nothing" phenomenon plays a more robust role in embryonic development with advancing oocyte age, with anatomically normal fetuses being more likely to survive.

	AMA (n=20,803)	Age <35 (n=55,353)	RR (95% CI)<b/>	aOR (95% CI)	p-value
Any Major Anomaly (n=1,804)	1.7%	2.6%	0.66 (0.59-0.74)	0.59* (0.52-0.66)	<0.001
CNS Anomaly (n=496)	0.4%	0.7%	0.55 (0.43-0.69)	0.49* (0.38-0.62)	<0.001
Renal Anomaly (n=226)	0.2%	0.3%	0.66 (0.48-0.92)	0.58† (0.41-0.81)	0.002
Abdominal Wall Defect (n=189)<b/>	0.1%	0.3%	0.21 (0.12-0.37)	0.23¶ (0.13-0.40)	<0.001
Cardiac Anomaly (n=302)<b/>	0.4%	0.4%	0.92 (0.72-1.20)	--	0.56

*Adjusted for alcohol use, gestational diabetes, pre-gestational diabetes, and African American race; †Adjusted for gestational diabetes, pre-gestational diabetes, and African American race; ¶Adjusted for tobacco use, parity, and African American race.

35 Correlation between initial neonatal and early childhood outcomes among children delivered <34 weeks gestation

Tracy Manuck[1], Xiaoming Sheng[2], Bradley Yoder[2], Michael Varner[1]
[1]University of Utah, Obstetrics and Gynecology, Salt Lake City, UT, [2]University of Utah, Pediatrics, Salt Lake City, UT

OBJECTIVE: Obstetric researchers commonly use neonatal morbidities as surrogate endpoints for longer-term outcomes. We sought to correlate neonatal diagnoses prior to hospital discharge with early childhood cognitive and motor function.

STUDY DESIGN: Secondary analysis of a multicenter RCT of antenatal magnesium sulfate (Mg) vs. placebo administered to women at imminent risk for early PTB to prevent death and cerebral palsy (CP) in their offspring. All women were at high risk for PTB <32.0 wks. Singletons delivered 24.0-33.9 wks who survived to hospital discharge post-birth and had 2-year-old outcome data were included. Those surviving to age 2 were assessed by trained physicians and Bayley Scales of Infant Development Mental Development and Psychomotor Development Indices (MDI, PDI). Neonatal diagnoses at each baby's initial hospital discharge were examined singly and in combination to determine those most predictive of severe composite childhood morbidity, defined as a childhood diagnosis of moderate/severe CP and/or Bayley MDI and/or PDI scores >2 SD below the mean. Data were analyzed by multiple logistic regression and area under ROC curves (AUC).

RESULTS: 1400 children met criteria. Children were delivered at a mean of 29.9 (range: 24.0-33.9) wks gestation. 58 (4.1%) had moderate/severe CP. On Bayley testing, 245 (19.2%) had a MDI Score >2 SD and 229 (17.8%) a PDI Score >2SD below the mean. A total of 349 (24.9%) had severe composite childhood morbidity. Multivariable regression results demonstrating the relationship between neonatal diagnoses and severe childhood morbidity are shown in the Table.

CONCLUSION: Approximately 1 in 4 children born <34 weeks had severe childhood morbidity at age 2. Individual neonatal morbidities (BPD, NEC, sepsis, severe IVH, and PVL) had modest predictive value for subsequent adverse early childhood outcomes; combinations of multiple morbidities were only marginally more prognostic. Prediction of childhood outcomes from neonatal diagnoses remains imperfect.

Multivariable regression results

Neonatal Morbidities	n (%)	OR (95% CI)	AUC (95% CI)
None	768 (54.9)	0.63 (0.47 - 0.83)	0.66 (0.62 - 0.69)
Single Morbidity or Death			
Bronchopulmonary dysplasia (BPD)	262 (18.7)	1.76 (1.24 - 2.51)	0.67 (0.64 - 0.70)
Sepsis	222 (15.9)	1.30 (0.93 - 1.82)	0.66 (0.63 - 0.70)
Brain Injury*	48 (3.4)	4.04 (2.18 - 7.52)	0.67 (0.64 - 0.71)
Necrotizing enterocolitis (NEC)	114 (8.1)	1.47 (0.97 - 2.23)	0.66 (0.63 - 0.70)
Retinopathy of Prematurity (ROP)	336 (24.0)	1.64 (1.17 - 2.30)	0.67 (0.63 - 0.70)
Multiple Morbidities or Death			
BPD + brain injury	22 (1.6)	4.19 (1.64 - 10.7)	0.67 (0.63 - 0.70)
BPD + NEC + ROP	30 (2.1)	2.15 (1.01 - 4.60)	0.66 (0.63 - 0.70)
BPD + NEC + ROP + brain injury	4 (0.30)	4.94 (0.50 - 48.5)	0.66 (0.63 - 0.70)

Relationship between neonatal diagnoses and the probability of severe composite childhood morbidity are shown. All models are shown for individual predictors; the best model is shown for the combination of 2, 3, and 4 neonatal morbidities.

*brain injury = severe intraventricular hemorrhage and/or periventricular leukomalacia

Other co-variables in regression models included delivery gestational age, maternal education, randomization to magnesium, and chorioamnionitis.