Title: Advanced Maternal Age is Not Independently Associated with Age at First Evaluation that Notes Autism Traits among Children with ASD

Authors: Eric Rubenstein, Maureen Durkin, Rebecca Harrington, Russell Kirby, Laura Schieve, Julie Daniels

Introduction: Advanced maternal age (AMA), defined as childbirth at 35 years or older, is a well-known risk factor for poor pregnancy and child health outcomes [1, 2], including increased risk of autism spectrum disorder (ASD) [3]. Many mothers of AMA are aware of their higher risk for suboptimal pregnancy outcomes compared to younger mothers [4-6]. Whether this awareness results in earlier age at identification of ASD in children of AMA mothers has not been studied. Our objective was to estimate effects of AMA on timing of the child’s first evaluation that notes ASD traits using data from the Autism and Developmental Disabilities Monitoring (ADDM) Network, independent of confounding socio-economic factors.

Methods: The ADDM network systematically collects data to determine ASD prevalence among 8-year-old children in multiple sites across the United States. The active surveillance process involves review of medical and health records against a standardized ASD case definition by trained experts. We utilized data on ASD cases with available birth certificate data from surveillance years 2008, 2010, and 2012. Age at first evaluation that noted autism traits was determined by systematic record review of all child evaluations, looking for trigger words that indicated ASD. Linear regression and Cox proportional hazard models were adjusted for maternal education, race/ethnicity, prior live births, study site, and child year of birth. We additionally stratified by intellectual disability (ID) status.

Results: Over the three surveillance years, 10,358 children met surveillance criteria for ASD and had maternal age data from the birth certificate, of which 19.7% had mothers of AMA. These mothers had higher levels of education, more prior live births, and older age of the child’s father at childbirth than non-AMA mothers. In crude analyses, children with AMA mothers had an earlier first evaluation that noted ASD traits (41.3 months compared to 46.5 months, mean difference -2.43 months, 95% Confidence Interval [CI]: -3.43, -1.43) with significantly different distributions (Hazard ratio [HR]: 1.12, 95% CI: 1.06, 1.18). However, after adjusting for maternal education, race and other covariates, these associations were attenuated (mean difference -0.11 months, 95% CI: -1.24, 1.03, HR 1.02, 95% CI: 0.96, 1.10). When stratifying by child ID status, age at first evaluation that noted ASD traits was later for those without ID, but there were no significant difference by AMA status in either ID stratum (Mean difference with ID: 0.11, 95% CI: -1.73, 1.93; without ID: -0.03, 95% CI: -1.68, 1.61).

Discussion: AMA was not associated with earlier age at first evaluation that noted ASD traits after adjustment for confounders. Older maternal age may act as a proxy for greater educational achievement, socio-economic status, and having had more children, all of which are associated with younger age at child’s first evaluation. It is important to target early evaluations and screenings to children at high risk of ASD from lower socio-economic demographics to improve age at diagnosis.

References/Citations: