Underlying factors of the association between Cesarean section and autism spectrum disorder

Objective: Recent epidemiological studies indicated that birth by Cesarean section (CS) is a risk factor of autism spectrum disorder (ASD). However, the underlying factors of this association remain vague. The goal of this study was to explore the contribution of various prenatal, perinatal and neonatal variables to the link between CS and ASD.

Method: We studied a wide range of prenatal, perinatal and neonatal characteristics in 347 children diagnosed with ASD, 117 children diagnosed with other forms of developmental delay (DD), and 2226 matched controls (matched by sex, age, and ethnicity). Both cases and controls were sampled from all single-live-born children at the Soroka University Medical Center between the years 2009-2016. Diagnosis of ASD and DD was determined according to DSM-V criteria. Conditional logistic regression models were used to assess the adjusted risk of CS on both ASD and DD.

Results: Delivery by CS was significantly associated with ASD but not with DD (P-value=0.019 and P-value=0.540 respectively). Additional variables that were associated with ASD included general anesthesia (GA), parity number, and amniocentesis. Stratification of CS deliveries to those conducted with and without GA revealed that only CS+GA elevate the risk of ASD (OR=1.618, 95%CI=1.176-2.226). Further stratification of CS+GA to emergency and elective surgeries implied small but not significant difference between the two (OR=1.97 vs. OR=1.56 respectively; Breslow-Day test of homogeneity P-value=0.174). Finally, dividing the ASD group into subgroups according to their DSM-V severity levels, indicated that exposure to CS+GA affects only the most severely diagnosed children with ASD (OR = 2.52; 95%CI=1.488-4.275).

Conclusions: Our findings suggest that exposure to GA during CS is likely the underlying factor of the association between CS and ASD. However, this factor is unlikely causing ASD, but rather contributes to the emergence of more severe symptoms among children with ASD.