**Title:** Neurodevelopmental Outcome of Infants Born to Mothers with COVID-19 Infection During Pregnancy: A Meta-Analysis

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**Background and relevance:** Intrauterine viral infections induce an increase in the levels of proinflammatory cytokines which inhibit the proliferation of neuronal precursor cells and stimulate oligodendrocyte cell death leading to abnormal neurodevelopment. Epidemiologic studies suggest maternal immune activation during pregnancy maybe associated with neurodevelopmental effects in infants which is of great concern. Given the large number of exposed individuals, even a modest increase in risk for adverse offspring neurodevelopment would still have a massive public health impact.

**Objective:** To determine the neurodevelopmental outcome of infants born to mothers with COVID-19 infection during pregnancy.

**Methodology:** This study utilized a meta-analysis design. Studies published up to September 30, 2022 were included in the analysis.

**Data Analysis:** STATA MP Statistical Software, Version 13, College Station, TX: StataCorp LP was utilized for all statistical analyses. A p-value ≤0.05 was considered statistically significant. Since estimated heterogeneity is non-significant and not substantial, a fixed-effect model was utilized. Pooled risk ratio was utilized as the summary effect measure for the risk of neurodevelopmental delays and was estimated with their corresponding 95% confidence intervals. Heterogeneity was scrutinized using the following statistical tests: Q statistics test, I2 statistics, and tau squared statistics. I2 values greater than 50% imply substantial heterogeneity, while a Q-statistics with a significant p-value denotes a statistically significant heterogeneity.

**Results:** Two studies with a total population of 7,848 patients met the eligibility criteria. Results indicated that all included studies have good quality of evidence in the areas of selection, comparability, and exposure. Appraisal of the included studies in these areas of evaluation also showed that all studies were of good quality. The pooled risk of neurodevelopmental delays among infants born to COVID- 19 positive mother was 2.00% higher than those born from mothers who were negative for COVID-19 infection. However, this was not statistically significant. Graphical analysis of publication bias showed funnel symmetry, suggestive that publication bias was unlikely. This result was

confirmed with formal statistical tests using Begg's adjusted rank correlation test and Egger's regression asymmetry test.

**Conclusion:** Although not statistically significant, infants born to mothers with COVID-19 infection during pregnancy have increased risk of neurodevelopmental delay. This may be attributed to the limited number of studies and articles available and in part because children born to women infected in the first wave of the pandemic are younger than two years of age. In addition, majority of developmental delay reflected developmental disorders of motor function or speech and language.

**Recommendations:** Given the time-frame since the pandemic has started, little is known about the effect of in- utero exposure to COVID-19 in infants and children. Hence, this research topic remains to be of importance considering the increasing proportion of pregnant women being infected with COVID- 19. The author recommends future studies which assess the neurodevelopmental outcome in children with longer duration of follow-up should be explored.