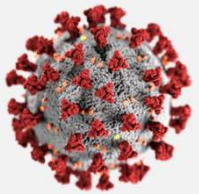
The associations of prenatal exposure to SARS-CoV-2 infection and COVID-19 vaccination with child neurodevelopment: a systematic review and meta-analysis

Marco Rizzo[1], Rushna Tubassum[1], Carly A Kaplan[1], Moussa Konde[2], Lily Martin[3], Frederieke Gigase[4], Lot de Witte[1,5,6], Veerle Bergink[1,7,8], Anna-Sophie Rommel[1]

[1]Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York City, New York, USA; [2]Center for Excellence in Youth Education, Icahn School of Medicine at Mount Sinai, New York City, New York, USA; [3]Levy Library, Icahn School of Medicine at Mount Sinai, New York City, New York, USA; [4]Child and Adolescent Psychiatry and Psychology, Erasmus MC, Rotterdam, the Netherlands; [5]Department of Psychiatry Radboud UMC, Nijmegen, the Netherlands; [6]Department of Human Genetics, Radboud UMC, Nijmegen, the Netherlands; [7]Department of Obstetrics, Gynecology and Reproductive Science, Icahn School of Medicine at Mount Sinai, New York, New York, USA; [8]Department of Psychiatry at Erasmus MC, Rotterdam, the Netherlands

Icahn School of Medicine at Mount Sinai



BACKGROUND

SARS-CoV-2 has infected millions of people, including many pregnant individuals. This raises concerns about possible sequelae of prenatal exposure to SARS-CoV-2 infection with lifelong consequences for the child.

Our previous research showed no association between SARS-CoV-2 infection and COVID-19 vaccination during pregnancy and adverse birth outcomes, although other studies have suggested that severe infection may increase the risk of preterm birth and low birthweight.

Yet, the longer-term neurodevelopmental consequences of prenatal exposure to SARS-CoV-2 and COVID-19 vaccines on auditory, motor, behavioural, cognitive and brain development of the child remain to be investigated.

METHODS

We systematically searched MEDLINE, EMBASE, PsycINFO, Web of Science, Scopus, and Cochrane CENTRAL for original research on neurological, auditory, motor, cognitive, behavioural, psychosocial and neuroimaging outcomes in children prenatally exposed to SARS-CoV-2 infection and/or COVID-19 vaccination published in any language since 2019 and before 8th Nov 2024.

Blinded reviewers screened titles and abstracts, assessed full texts for eligibility, and rated the quality of the selected articles using the Newcastle-Ottawa Scale (NOS).

We performed a meta-analysis on any outcome reported in three or more studies with controls. We applied a random-effects model using the reciprocal of the estimated variance, allowing us to combine effect size estimates without individual-level data.

RESULTS

We identified 70 studies (Figure 1), published over 4 years (2021-2024). We categorized studies by outcome into neurological (n=7), neuroimaging (n=12), motor development (n=3), neurodevelopmental disorders (n=2), audiological assessments (n=29), and neurodevelopment (n=35). Some studies reported more than one outcome. The median sample size was N=117 (IQR: 44-340) with ages ranging 0-36 months.

- **Neurological** outcomes (0-3 months) were generally normal
- Most children (0-9 months) prenatally SARS-CoV-2 exposed show no atypical clinical manifestations in **brain morphology & functioning**
- Prenatal SARS-CoV-2 exposure may be associated with early **motor delays**, which seem to be transient (0-12 months)
- Higher risk of motor and language **disorder** at 12 months, which was no longer significant at 18 months
- Higher risk of failing first **hearing** test in exposed children but no differences at follow-up (0-36 months) (Figure 2)
- Higher risk of **developmental delays** in fine motor and problem-solving skills in exposed children (0-36 months) (Figure 3)

Figure 1. PRISMA 2020 flow diagram

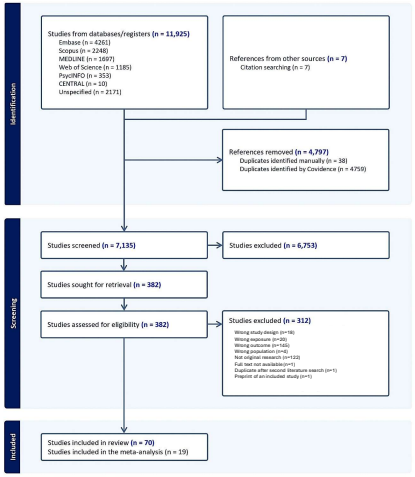


Figure 2. Forest plots for the first (a) and second (b) auditory screening

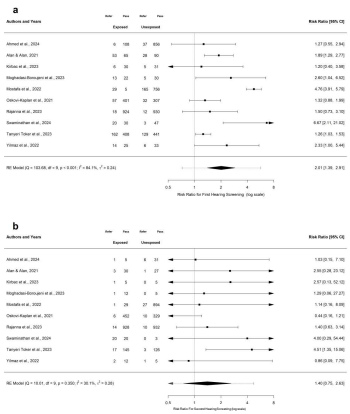
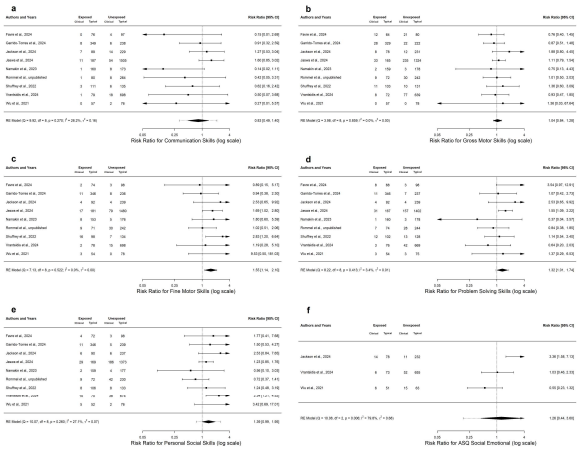


Figure 3. Forest plots for the categorical ASQ-3 (a-e) and ASQ:SE-2 (f) outcomes with 95% CIs. Plots are shown for the (a) communication, (b) gross motor, (c) fine motor, (d) problem-solving, and (e) personal-social subdomains of the ASQ-3.



CONCLUSIONS

We observed transient auditory impairments and delays in fine motor and problem-solving skills following prenatal SARS-CoV-2 exposure. Due to the heterogeneity and quality of the evidence, as well as the potential for unmeasured confounding, these association are unlikely to be causal. We found no link between prenatal SARS-CoV-2 exposure and neurological or neuroimaging outcomes. Additionally, no adverse neurodevelopmental effects were reported following prenatal exposure to COVID-19 vaccination.

CLINICAL RELEVANCE

The evidence for a causal relationship between prenatal SARS-CoV-2 exposure and adverse neurodevelopment is limited, and observed associations are likely transient. Our findings highlight the need for long-term follow-up of prenatally exposed children to determine the extent, nature, and persistence of any developmental deviations.

ACKNOWLEDGEMENTS

This work was supported by a grant from the NICHD (R01HD109613).

NIH

REFERENCES

COVID-19 cases | WHO COVID-19 dashboard. COVID-19 cases. 2025. Available from: https://data.who.int/dashboards/covid19/cases

Al-Haddad R, et al. Long-term Risk of Neuropsychiatric Disease After Exposure to Infection In Utero. JAMA Psychiatry. 2019 Jun 1;76(6):594–602.

Auriti et al. Maternal–Fetal Infections (Cytomegalovirus, Toxoplasma, Syphilis): Short-Term and Long-Term Neurodevelopmental Outcomes in Children Infected and Uninfected at Birth. Pathogens. 2022 Nov;11(11):1278.

Devaraju et al. Beyond TORCH: A narrative review of the impact of antenatal and perinatal infections on the risk of disability. Neurosci Biobehav Rev. 2023 Oct;153:105390.

Gigase et al. SARS-CoV-2 infection, inflammation and birth outcomes in a prospective NYC pregnancy cohort. J Reprod Immunol. 2024 Jun 1;163:104243.

Marchand et al. Maternal and neonatal outcomes of COVID-19 vaccination during pregnancy, a systematic review and meta-analysis. Npj Vaccines. 2023 Jul 15;8(1):1–9.