

Can SARS-CoV-2 Be a Potential Cause of Microcephaly?

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Dear Editor,

Microcephaly (MC) is defined as a head circumference with a standard deviation score (SDS) below -2 according to some experts and below -3 according to others (1-3). In our clinic, we use the criterion of head circumference below -2 SDS to define MC. MC can be classified as primary if present at birth, or as secondary if it develops postnatally (2, 4, 5). Several risk factors have been associated with MC, including genetic disorders, teratogenic exposure, maternal age, maternal phenylketonuria, and hypoxic-ischemic encephalopathy. Keskindemirci et al. also highlighted that socioeconomic factors may play a role in the risk of MC (6). Among these, maternal infections during pregnancy are the leading causes of microcephaly, with Rubella, Zika virus, and cytomegalovirus (CMV) being the most recognized infectious etiologies (2, 4).

The impact of COVID-19 on fetal development during pregnancy has not been fully elucidated. There are reports in the literature suggesting that SARS-CoV-2 infection during pregnancy may lead to complications (7). We read with interest the recent article by Edlow et al., which concluded that “COVID-19 exposure may be associated with neurodevelopmental changes and highlights the need for prospective investigation of outcomes in children exposed to COVID-19 in utero” (8). Moreover, Auger et al., in their time series analysis, observed an increased frequency of microcephaly during the COVID-19 pandemic period (9).

Considering these findings, we wish to share our own observations, which are consistent with those reported by Edlow et al. and Auger et al. Our well-child unit has noted a relative increase in the number of primary microcephaly cases during the COVID-19 pandemic. From January 2002 to March 2020, we identified 49 children with microcephaly, 30 of whom were diagnosed with primary microcephaly. Between 2006 and

2021, the median incidence of primary microcephaly was 2 cases per year, and the range was 0-4. However, in 2021, 8 new cases of primary microcephaly were documented—all of which involved infants born in that year. Further investigation revealed that all the mothers were pregnant and gave birth during the pandemic period (March 2020 to March 2022). Among these mothers, three were confirmed to have had COVID-19 during the second trimester via laboratory tests, while two others reported upper respiratory infections during the same period, although laboratory tests were not conducted.

In conclusion, our observations suggest that maternal COVID-19 infection during pregnancy may contribute to the increased incidence of microcephaly during the pandemic. To better

Supplementary Table: The distribution of primary microcephaly diagnoses by year

Years of Birth	n
2006	1
2007	1
2008	1
2009	3
2010	3
2011	3
2012	1
2013	4
2014	1
2015	2
2016	3
2017	1
2018	3
2019	3
2020	0
2021	8
2022	0
Total	38

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understand the potential association between COVID-19 and microcephaly, we recommend conducting multicenter studies involving larger cohorts. The supplementary table presents the distribution of primary microcephaly diagnoses by years.

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