

Growth and neurodevelopmental outcomes of infants born to mothers with COVID-19 during pregnancy^a

 Hazal Eryılmaz Yıldır¹,  Rukiye Saç²,  Ayşe Esra Tapcı^{*2},  Özge Bayram³,  Dilek Kahvecioğlu⁴,  Ayşin Taşar⁵

¹Department of Pediatrics, Freelance Physician, Hasselt, Belgium

²Department of Pediatrics, Ankara Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

³Department of Developmental Pediatrics, Ankara Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

⁴Department of Neonatology, Ankara Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

⁵Department of Pediatric Emergency, Ankara Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

Cite this article: Eryılmaz Yıldır H, Saç R, Tapcı AE, Bayram Ö, Kahvecioğlu D, Taşar A. Growth and neurodevelopmental outcomes of infants born to mothers with COVID-19 during pregnancy. *J Controv Obstetr Gynecol Ped.* 2026;4(4):83-89. doi:10.51271/JCOGP-0079

*Corresponding Author: Ayşe Esra Tapcı, esratapci@gmail.com

Received: 28/06/2026

Accepted: 29/07/2026

Published: 28/10/2026

ABSTRACT

Aims: To evaluate the impact of intrauterine SARS-CoV-2 exposure on infant growth and neurodevelopment by comparing anthropometric measurements and Denver Developmental Screening Test II (DDST-II) results between infants born to mothers with COVID-19 during pregnancy and unexposed controls.

Methods: This retrospective case-control study included 40 term infants born to mothers with confirmed COVID-19 during pregnancy and 40 term infants born to mothers without COVID-19 infection. The well-child follow-up records from July 2020 to July 2022 were reviewed. Demographic characteristics, anthropometric measurements, and DDST-II results were analyzed.

Results: The groups were comparable in terms of demographic characteristics, birth weight, gestational age, and gender (all $p>0.05$). In the study group, 45% of mothers had COVID-19 during their third trimester. At one month, head circumference (HC), length, and weight percentiles were similar between the groups. At six months, HC below the third percentile was more common in the exposed group (22.2% vs. 3.6%, $p=0.045$), whereas length and weight percentiles did not differ. No significant differences were observed in anthropometric measurements at nine months. DDST-II showed age-appropriate neurodevelopment in 39 infants in each group; one infant in the exposed group had a suspicious result, and one control infant had an abnormal result.

Conclusion: Prenatal SARS-CoV-2 exposure was not associated with significant differences in infant growth or neurodevelopment during the first year of life. Larger prospective studies with longer follow-up periods are required to determine the long-term outcomes.

Keywords: Anthropometric measurements, COVID-19, development, growth

^aThis study was presented as a poster presentation at the Congress of Joint European Neonatal Societies, Rome, Italy, September 19, 2023.

INTRODUCTION

COVID-19 symptoms during pregnancy are the same as those observed in non-pregnant adults. Although more than 90% of patients with COVID-19 recover without hospitalization, the severity of the disease may escalate in the presence of risk factors. Older age, obesity, hypertension, and diabetes mellitus are risk factors for symptomatic COVID-19 during pregnancy. Furthermore, an increase in obstetric complications, such as preterm birth, premature rupture of membranes, fetal distress, and preeclampsia, has been reported in pregnant females with COVID-19.¹⁻⁴

Certain antenatally acquired viral infections can have permanent, potentially destructive effects on the developing fetal brain.^{5,6} Other viral infections that fail to cross the

placental barrier, including influenza, have also been consistently associated with adverse neurodevelopmental outcomes.⁷⁻¹¹ Infection and inflammation negatively affect motor development.¹²

It is generally accepted that respiratory viruses such as SARS-CoV-2 do not have intrauterine transmission. In a systematic review evaluating the effects of COVID-19 on maternal, perinatal, and neonatal outcomes, no conclusive evidence was identified regarding the maternal-fetal transmission of the virus.¹³ Moreover, no increase in the incidence of congenital anomalies has been reported.² However, it has been observed that the newborns of mothers who contracted COVID-19 during pregnancy were more likely to require admission



to the neonatal intensive care unit (NICU).¹⁴ There are also studies reporting an increase in intrauterine fetal and neonatal deaths in the presence of COVID-19 infection.^{4,15}

Although some studies have investigated the effects of intrauterine COVID-19 exposure on infant development, no consensus has yet been reached. While some studies indicate that infants exposed to COVID-19 are more neurodevelopmentally delayed,¹⁶ others have not found evidence of a neurodevelopmental delay but have shown that these infants have lower scores in areas such as fine motor skills and problem solving.¹⁷

The long-term effects of COVID during pregnancy on newborns remain uncertain. Several studies have reported negative neurodevelopmental outcomes.¹⁸⁻²⁰ However, there is insufficient information concerning the long-term effects of COVID-19 during pregnancy and its impact on physical growth and neurodevelopment in childhood. Some studies have reported an increase in the rates of neurodevelopmental diseases.^{17,18} In the current study, we retrospectively examined the well-child polyclinic follow-up data, demographic characteristics, anthropometric measurements, and Denver Developmental Screening Test II (DDST-II) results of healthy term infants under one year of age whose mothers had contracted SARS-CoV-2 during pregnancy. We aimed to evaluate the effect of COVID-19 infection during pregnancy on fetal growth and development by comparing the results with those of healthy controls.

METHODS

This study was approved by the Ethics Committee of Ankara Training and Researches Hospital of the University of Health Sciences (Date: 07.09.2022, Decision No: E-22-1072). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This was a retrospective, single-center study. Between July 2020 and July 2022, data obtained from the electronic medical records of term infants aged 0–12 months who were followed up at the Well-Child Polyclinic of the Department of Pediatric Health and Diseases at Health Sciences University Ankara Training and Research Hospital were examined in this study. The study group comprised infants born to mothers who had COVID-19 during pregnancy, and the control group comprised infants in the same age range who were followed up during the same period and whose mothers did not have a history of COVID-19 during pregnancy. Both groups included only infants with complete data from at least two of the first, sixth, and ninth month controls. Furthermore, all infants included in the sample had undergone anthropometric measurements at the well-child polyclinic and had completed well-child follow-up forms. They were all evaluated as “healthy” with a normal birth weight between the 10th and 90th percentiles according to their gestational age, and they also underwent DDST-II. Infants who were not followed up regularly or whose information could not be accessed, and those with complications at birth, hypoxia, or NICU admission were not included in the study. Infants with comorbidities, a history of premature birth (gestational age <37 weeks), low birth weight for gestational age, below the 10th percentile for intrauterine growth, who

had not undergone DDST-II, and who were older than 12 months were excluded.

General physical examination findings, percentile values of body weight (BW), body length (BL), and head circumference (HC) measurements, and DDST-II results were routinely recorded in the well-child polyclinic for infants aged 0–1 year of age. In addition, regular breast milk intake and vitamin D and iron supplementation were questioned and recorded during the follow-up period.

During all follow-up examinations, the BW of the infants was measured without clothing using a regularly calibrated Wunder BABY scale (barcode number: 1012616913) sensitive to 10 g. BL was measured in the supine position on a hard-floored bed, with the head fixed at a 90-degree angle to the bed, while the infant's whole body was stretched. In this position, the distance from the top of the head to the tip of the heel was measured by a physician using a non-flexible tape measure. HC was measured using a non-flexible tape measure from the most protruding point of the frontal bone at the front to the occipital protuberance at the back of the head.

All measurements were conducted according to the Neyzi percentile values for each month.²¹ The study and control groups were considered normal if their BW, BL, and HC values fell within the range of 3p-97p and non-normal if they were below 3p, and a statistical comparison was performed. As there were no infants with values above 97p in the study or control groups, this threshold was not included in the grouping.

During follow-up, breast milk intake was assessed every month. Infants who were constantly breastfed between 0 and 6 months were evaluated as having received breast milk regularly, whereas the remaining infants were considered to have received breast milk irregularly.

At our hospital, the DDST-II is performed by certified child development specialists who have successfully completed a comprehensive training program. In the current study, DDST-II was performed on infants aged six–nine months. The DDST-II was scored as “pass,” “fail,” “impossible,” and “untestable,” and the test result was interpreted as “normal,” “suspicious,” “abnormal,” and “untestable.”²² The DDST-II is a general developmental screening tool used in Türkiye and is applied twice to infants under follow-up in our clinic at ages 6-9 months and 18 months.

As this was a retrospective study based on available medical records, no a priori sample size or power calculations were performed. Instead, all eligible infants who met the inclusion criteria during the study period were included in the analysis.

Statistical Analysis

Data analysis was performed using SPSS v. 24.0, and the results were evaluated at a 95% confidence level. Kurtosis and Skewness coefficients were calculated to determine the suitability of quantitative variables for a normal distribution. It was concluded that the values were normally distributed since they were between -3 and +3. The relationship between normal and non-normal status according to percentile values

and other demographic data was analyzed using the Chi-square test. Statistical significance was set at $p < 0.05$.

RESULTS

The study included 80 infants, of whom 40 were in the study group and 40 were in the control group. The gender distribution was 55% ($n=22$) males and 45% ($n=18$) females in the study group and 57.5% ($n=23$) males and 42.5% ($n=17$) females in the control group. The mean age of the mothers was 28.48 ± 5.74 (min: 17-max: 40) years in the study group and 29.18 ± 6.02 (min: 17-max: 39) years in the control group ($p=0.596$). The median week of birth was 39 weeks in both groups (min: 37-max: 42+1 weeks in the study group, min: 37-max: 41+1 weeks in the control group) ($p=0.518$). The mean birth weight was $3,227.38 \pm 446.76$ g in the study group and $3,262.50 \pm 382.96$ g in the control group ($p=0.707$). In the study group, 25.0% of mothers contracted COVID-19 in the first trimester, 30.0% in the second trimester, and 45.0% in the third trimester. A comparison of the remaining demographic characteristics between the study and control groups is presented in **Table 1**.

Table 1. Comparison of the demographic characteristics of the study and control groups

		Study group		Control group		p*
		n	%	n	%	
Maternal comorbidity	Present	6	15.0	2	5.0	0.136
	Absent	34	85.0	38	95.0	
Follow-up during pregnancy	Present	37	92.5	36	90.0	0.692
	Absent	3	7.5	4	10.0	
Number of pregnancies	One	12	30.0	14	35.0	0.358
	Two	17	42.5	11	27.5	
	Three or more	11	27.5	15	37.5	
Number of living children	One	14	35.0	16	40.0	0.072
	Two	19	47.5	10	25.0	
	Three or more	7	17.5	14	35.0	
Miscarriage or stillbirth	None	31	77.5	34	85.0	0.541
	One	6	15.0	5	12.5	
	Two	3	7.5	1	2.5	
Mode of delivery	Cesarean section	18	45.0	18	45.0	1.000
	Normal vaginal	22	55.0	22	55.0	
Status of receiving breast milk	Regular	39	97.5	36	90.0	0.166
	Irregular	1	2.5	4	10.0	
Formula use	Present	8	20.0	16	40.0	0.051
	Absent	32	80.0	24	60.0	
Vitamin D supplementation	Regular	40	100.0	39	97.5	0.314
	Irregular	0	0.0	1	2.5	
Iron supplementation	Regular	33	82.5	34	85.0	0.762
	Irregular	7	17.5	6	15.0	

*Chi-square test

The first-month HC was determined to be at or below 3p in four (16.7%) and two (7.7 %) infants in the study and control groups, respectively ($p=0.295$). No significant differences

were detected in the first-month BW, BL, and HC percentile comparisons between the two groups ($p > 0.05$). At the sixth-month follow-up, 6 (22.2%) infants in the study group and one (3.6%) infant in the control group had an HC below 3p, indicating a statistically significant difference ($p < 0.045$). However, the length and weight percentiles of the two groups evaluated at the sixth month did not differ significantly ($p > 0.05$). At the ninth month, there were no significant differences between the two groups in terms of BW, BL, or HC percentiles ($p > 0.05$) (**Table 2 and Figure**).

Table 2. Comparison of the study and control groups according to whether their head circumference, length, and weight were within the normal percentile range at the first, sixth, and ninth-month follow-up visits

		Group				p*
		Study		Control		
		n	%	n	%	
First-month head circumference	Non-normal	4	16.7	2	7.7	0.295
	Normal	20	83.3	24	92.3	
First-month length	Non-normal	0	0.0	0	0.0	-
	Normal	19	100.0	18	100.0	
First-month weight	Non-normal	1	3.8	0	0.0	0.520
	Normal	25	96.2	24	100.0	
Sixth-month head circumference	Non-normal	6	22.2	1	3.6	0.045
	Normal	21	77.8	27	96.4	
Sixth-month length	Non-normal	4	14.8	4	14.3	0.626
	Normal	23	85.2	24	85.7	
Sixth-month weight	Non-normal	2	7.1	1	3.7	0.514
	Normal	26	92.9	26	96.3	
Ninth-month head circumference	Non-normal	3	14.3	2	6.3	0.304
	Normal	18	85.7	30	93.8	
Ninth-month length	Non-normal	3	14.3	4	12.5	0.580
	Normal	18	85.7	28	87.5	
Ninth-month weight	Non-normal	1	4.8	1	3.1	0.640
	Normal	20	95.2	31	96.9	
*Pearson's Chi-square test; Fisher's exact test was used where appropriate						

*Pearson's Chi-square test; Fisher's exact test was used where appropriate

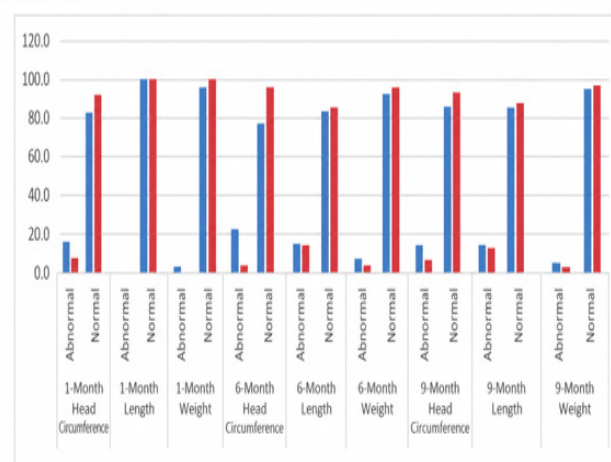


Figure. Distribution of the study and control groups according to whether their head circumference, length, and weight were within the normal percentile range at the first, sixth, and ninth months

Given that the physical examination and laboratory testing of infants with a low first-month percentile yielded normal results, only HC was checked and continued to be followed

up. At the sixth month, three of the six infants whose HC percentile was not normal had no other remarkable physical examination findings. Microcephaly screening and developmental tests of these infants were normal, and their HC values were within the normal range in subsequent measurements. The remaining three infants did not attend subsequent follow-up appointments. According to the sixth-month measurements, the BL percentile was 3p or below in four infants in each group. The BW assessment undertaken at the sixth month revealed that two infants in the study group and one infant in the control group had values outside the normal range. These infants were followed up in terms of both BL and BW.

At the ninth-month follow-up, values in or below 3p were detected in the HC measurements of three infants in the study group and two infants in the control group, in the BL measurements of three infants in the study group and four infants in the control group, and in the BW measurements of one infant in each group. One infant in the study group had both HC and BL values at or below 3p. The patient was followed up, and her progress was within normal limits. Her laboratory and developmental test results were normal. It was observed that one of the other two infants with a low HC showed normal values during the follow-up, whereas the remaining infant did not attend the subsequent follow-up appointments. Of the other two babies in the study group whose BL values were at or below 3p, one was observed to have a normal length during the follow-up, while the other did not attend the subsequent follow-up appointments. It was observed that the infants in the study group who had a low BW achieved a normal weight by the 18th month after following dietary recommendations. In the control group, one infant had both HC and BL values at the 3p limit, but these values increased to normal levels in subsequent follow-up visits. One infant with BW and BL values $\leq 3p$ was referred to an endocrinologist, but did not attend follow-up visits. The other patient with a low HC had normal HC measurements during subsequent follow-ups. The remaining two infants with a low BL in the control group achieved BL values within normal limits by the 15th-month of follow-up.

Upon comparison of the first-, sixth-, and ninth-month HC, BL, and BW percentiles according to gender, we determined that the HC of 96.4% of the male and 77.3% of the female infants were within normal limits at the first month ($p=0.051$). No statistically significant gender-related differences were found in the BL and BW percentiles evaluated at the first month or the HC, BL, and BW percentiles evaluated at the sixth and ninth months ($p>0.05$ for all). The comparison of the HC, BL, and BW percentiles of the infants in the study group according to the trimester of maternal COVID-19 revealed that the infants born to mothers who contracted COVID-19 during the second trimester had higher rates of HC measurements below 3p at all three follow-up evaluations; however, a statistical comparison could not be made (Table 3).

To observe the effect of SARS-CoV-2 infection during pregnancy on the neurodevelopment of infants, we used the results of the DDST-II, a test routinely performed at the well-child polyclinic of our hospital. DDST-II revealed that the neurodevelopment of 39 infants in each group was consistent

Table 3. Evaluation of whether the percentiles of the study group were within the normal range according to the trimester during which mothers had COVID-19

		Trimester of maternal COVID-19					
		First		Second		Third	
		n	%	n	%	n	%
First-month head circumference	Non-normal	1	16.7	2	22.2	1	11.1
	Normal	5	83.3	7	77.8	8	88.9
First-month length	Non-normal	0	0.0	0	0.0	0	0.0
	Normal	5	100.0	7	100.0	7	100.0
First-month weight	Non-normal	0	0.0	0	0.0	1	10.0
	Normal	6	100.0	10	100.0	9	90.0
Sixth-month head circumference	Non-normal	1	20.0	3	30.0	2	16.7
	Normal	4	80.0	7	70.0	10	83.3
Sixth-month length	Non-normal	2	40.0	1	9.1	1	9.1
	Normal	3	60.0	10	90.9	10	90.9
Sixth-month weight	Non-normal	1	20.0	1	9.1	0	0.0
	Normal	4	80.0	10	90.9	12	100.0
Ninth-month head circumference	Non-normal	0	0.0	2	28.6	1	14.3
	Normal	7	100.0	5	71.4	6	85.7
Ninth-month length	Non-normal	0	0.0	1	14.3	2	28.6
	Normal	7	100.0	6	85.7	5	71.4
Ninth-month weight	Non-normal	1	14.3	0	0.0	0	0.0
	Normal	6	85.7	7	100.0	7	100.0

COVID-19: Coronavirus disease 2019

with their age, while the results were suspicious in one infant in the study group and abnormal in one infant in the control group. The infant with a suspicious result in the study group had problems with gross motor skills, and his mother contracted COVID-19 during the second trimester (sixth month) of pregnancy. The infant with abnormal results in the control group had issues with language development.

DISCUSSION

In this study, we aimed to evaluate the effect of SARS-CoV-2 during pregnancy on the growth and development of infants in the first year after birth using anthropometric measurements and the DDST-II. At the sixth month, the HC values of six babies (22.2%) in the study group and one infant (3.6%) in the control group were found to be at or below 3p ($p<0.045$). The neurodevelopment of 39 infants in each group was consistent with their age according to the DDST-II, while one infant in the study group had a suspicious result and one infant in the control group had an abnormal result.

It has been reported that SARS-CoV-2 infection during pregnancy is associated with increased maternal death, maternal and neonatal morbidity, preterm birth, and an increased rate of cesarean deliveries.¹⁸ SARS-CoV-2 infection during pregnancy increases the risk of preeclampsia, eclampsia, and hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome.²³ During the study period, 140 infants born to mothers who contracted SARS-CoV-2 during pregnancy were followed up. None of the mothers had a history of severe COVID-19 infection or related hospitalization. The final study group consisted of 40 infants

after excluding nine premature births, three low-birth-weight infants, five NICU admissions, and other cases that were lost to follow-up.

In two separate studies examining the pregnancy outcomes of females with and without a history of SARS-CoV-2 infection during pregnancy, the BW values of the infants were compared between the two groups, and no significant difference was detected.^{24,25} Similarly, in our study, there was no significant difference between the infants in the study and control groups in terms of their BW.

In a cohort study investigating the clinical course of SARS-CoV-2 infection and its impact on pregnant females, Şahin et al.²⁶ found that 44.7% of 533 pregnant females were infected in the third trimester, 30.9% in the second trimester, and 24.4% in the first trimester. In another study evaluating the effects of SARS-CoV-2 during and after pregnancy, Lokken et al.²⁷ reported that the majority of females contracted SARS-CoV-2 in the third trimester of pregnancy (56.3%), followed by the second trimester (27.9%) and the first trimester (15.8%). Similarly, in our study, 25.0% of mothers with a history of COVID-19 during pregnancy contracted the disease in the first trimester, 30% in the second trimester, and 45% in the third trimester.

There is no evidence supporting the idea that cesarean delivery prevents vertical transmission of COVID-19.²⁸ Mirbeyk et al.²⁹ conducted a systematic review of pregnant females with COVID-19 and their newborns and found a high rate of cesarean delivery (86%). A medical specialty thesis conducted in Türkiye to compare COVID-19-positive pregnant females at birth with non-COVID pregnant females in terms of maternal, neonatal, and perinatal outcomes showed a high rate of cesarean delivery (46 of 50 births) but noted no significant difference when compared with the control group.³⁰ Similarly, upon examining the modes of delivery among the pregnant females in our study and control groups, we observed that 45% of the females underwent cesarean sections, while 55% underwent normal vaginal delivery. There was no significant difference between the study and control groups in terms of the mode of delivery. However, as our study did not investigate whether COVID-19 was present at the time of birth, we were unable to determine the impact of this factor on the mode of delivery.

The optimal course of action for maintaining the health of a newborn is for a mother with suspected or diagnosed COVID-19 to breastfeed her infant and continue the normal process.³¹ A multicenter study conducted by the Turkish Neonatology Association on 125 newborns born to females infected with COVID-19 revealed that the rates of formula use (56.8%) and expressed breast milk use (36%) were higher than the rate of breast milk feeding.³² In our cohort, 97.5% of the infants in the study group and 90% of those in the control group received breast milk regularly for six months. The absence of a significant difference between the two groups and the high rate of infants regularly fed breast milk can be attributed to mothers being informed about the benefits of breastfeeding.

In a study conducted in South India on postpartum breastfeeding, the Breastfeeding Self-Efficacy Scale Short

Form (BSEF-SF) was administered to 63 COVID-19-positive and 63 COVID-19-negative mothers, and the scores were significantly lower in the former. In addition, the rate of mothers with above-average BSES-SF scores was significantly higher among those who received postpartum breastfeeding recommendations.³³

TORCH (intrauterine) infections are a risk factor for hearing impairment in newborns. At our hospital, auditory brainstem response (ABR) screening is performed on all healthy term babies who have not been admitted to the NICU. In our cohort, no infant from either group failed the hearing test. In a retrospective cohort study, Oskovi-Kaplan et al.³⁴ examined the hearing screening results of infants born to mothers who contracted COVID-19 during pregnancy and found no statistically significant difference between the COVID-19 and control groups in the risk of hearing loss. In another study, Alan et al.³⁵ compared the hearing screening results of infants born to pregnant females who tested positive and negative for SARS-CoV-2 during pregnancy. According to the ABR test results, the newborns in the COVID-19 group were more likely to have a “refer” result bilaterally than those in the control group. These discrepancies in the findings of previous studies concerning the effect of COVID-19 on hearing underscore the need for further research.

According to the first-month HC measurements, four infants (16.7%) in our study group and two (7.7%) in our control group had values outside the normal range ($p>0.05$). In addition, one infant in the study group had a BW in the low percentile group. At the sixth month, the HC percentile was evaluated to be within the normal range in six infants (22.2%) in the study group and one infant (3.6%) in the control group, indicating a statistically significant difference ($p=0.045$). Three infants with low HC measurements achieved normal HC values during follow-up, while the remaining three infants did not attend subsequent follow-up appointments. At the ninth-month follow-up of the infants, no significant difference was observed between the two groups in relation to the HC, BL, or BW measurements.

Zeng et al.³⁶ conducted a study in China and found that all physical growth parameters, including BW, BL, and HC, were above 3p in 72 newborns exposed to SARS-CoV-2. In a study from the USA, Schuh et al. included 33 infants born to mothers with SARS-CoV-2 infection and reported BW, BL, and WC measurements taken at the first postnatal visit, as well as at two, four, and six months. The authors stated that the infants had a normal distribution in terms of the Z-scores and growth rates of these measurements.³⁷ A common result obtained from these studies is the absence of short-term negative effects of intrauterine COVID-19 exposure on infants' physical growth. In addition, in the above-mentioned study, Schuh et al.³⁷ evaluated 15 newborns neurodevelopmentally using the Ages & Stages Questionnaires®, Third Edition (ASQ-3) and found the development of the infants to be appropriate for their age. According to the results of the DDST-II, which was conducted to observe the effect of SARS-CoV-2 infection during pregnancy on the neurodevelopment of the infants in our cohort, neurodevelopment was consistent with chronological age in 39 infants in each group. However, one infant in the study group had a suspicious result and one infant in the control group had an abnormal result.

A study comparing infants born to 222 mothers infected with SARS-CoV-2 and 7,550 mothers in the control (uninfected) group during the same period revealed a higher rate of neurodevelopmental diseases among infants born to infected mothers. The authors also noted a higher risk among those exposed to maternal infection in the third trimester.¹⁸ In another study, Pinheiro et al.¹⁷ did not find evidence of a higher neurodevelopmental delay in infants exposed to intrauterine SARS-CoV-2 compared to unexposed infants, but did show that the fine motor and problem-solving skills of infants with SARS-CoV-2 exposure were negatively affected, and they had lower scores in fine motor skills. In the current study, infants with suspicious DDST-II results in the study group had problems related to gross motor skills, while infants with abnormal DDST-II results in the control group had problems with language development. We also determined that the mother of the infant with a neurodevelopmentally suspicious result contracted COVID-19 in the second trimester (sixth month) of pregnancy.

Shah et al.¹⁶ administered the ASQ-3 to term infants born to pregnant females with SARS-CoV-2 to screen for neurodevelopmental delays. The ASQ-3 is a screening tool used to assess neurodevelopment in five specific domains: communication, fine motor, gross motor, problem solving, and personal-social skills. In the literature on the ASQ-3 developmental screening of healthy term infants without intrauterine COVID-19 exposure, 12.6-13.6% of infants have been reported to have delays in at least one developmental domain.³⁸ In contrast, Shah et al.¹⁶ determined that 24% of the infants were below the cut-off value, and 29% were near the cut-off value in at least one developmental domain, indicating a percentage increase in neurodevelopmental delay in infants with intrauterine COVID-19 exposure.

Limitations

This study had several limitations. First, its retrospective, single-center design limits the generalizability of the findings and may have introduced selection bias, as infants with incomplete medical records or loss to follow-up were excluded from the study. In addition, because this was a retrospective study based on available medical records, no a priori sample size calculations were performed. Second, the relatively small sample size, particularly after stratification according to the trimester of maternal infection, may have reduced the statistical power to detect subtle differences between groups and precluded multivariable analyses to adjust for potential confounders. Third, important confounding variables, including socioeconomic status, parental education, postnatal home environment, early developmental stimulation, nutritional factors, and maternal comorbidities, were not systematically available and, therefore, could not be accounted for in the analyses. These factors may independently influence infant growth and neurodevelopment and should be considered when interpreting our findings. Fourth, neurodevelopment was assessed using the DDST-II, which is a developmental screening tool rather than a diagnostic assessment, and may be less sensitive than comprehensive instruments such as the Ages and Stages Questionnaire, Third Edition (ASQ-3), or the Bayley Scales of Infant and Toddler Development, for detecting subtle developmental deficits, particularly in fine motor and problem-solving domains. Fifth, the follow-up period was limited to the first year of life and may not have been

sufficient to identify neurodevelopmental or growth abnormalities that emerge later in the childhood. Finally, detailed information regarding the severity of maternal COVID-19, viral load, and treatment during pregnancy was not systematically available, preventing the evaluation of possible dose-response or severity-related associations with infant outcomes.

CONCLUSION

In this retrospective case-control study, maternal COVID-19 infection during pregnancy was not associated with significant differences in birth weight, gestational age, or overall neurodevelopment during the first year of life compared to unexposed infants. A significantly higher rate of HC below the third percentile was observed in the study group at six months, although this difference was not sustained at nine months and did not correspond to abnormal neurodevelopmental screening results in the affected infants. These findings are reassuring but should be interpreted with caution, given the limited sample size and short follow-up duration. Larger prospective multicenter studies with extended follow-up and more comprehensive neurodevelopmental assessment tools are needed to clarify the long-term impact of prenatal SARS-CoV-2 exposure on childhood growth and development and to determine whether the transient HC findings observed here reflect a true biological effect or a chance finding.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was approved by the Ethics Committee of Ankara Training and Research Hospital, University of Health Sciences (Date: 07.09.2022, Decision No: E-22-1072).

Informed Consent

This retrospective study used pre-existing anonymized patient data. No additional intervention was performed, and there was no direct patient contact. The study was approved by the Ethics Committee, and the requirement for written informed consent was waived by the ethics committee.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

The authors received no financial support for the conduct or publication of this research.

Author Contributions

Concept: AET, HEY, DK; Design: RS, DK, ÖB; Data Collection: HEY, AT, DK; Data Analysis: AET, AT, RS; Interpretation of Data: HEY, ÖB, AT; Drafting of the Manuscript: AET, DK; Critical Revision: AT, RS.

REFERENCES

1. Republic of Türkiye Ministry of Health. COVID-19 Information Platform. Accessed October 7, 2022. <https://covid19.saglik.gov.tr>
2. Al Riyami N, Sheik S. COVID-19 and pregnancy: a narrative review of maternal and perinatal outcomes. *Sultan Qaboos Univ Med J*. 2022; 22(2):167-178. doi:10.18295/squmj.8.2021.120

3. De Rose DU, Piersigilli F, Ronchetti MP, et al. Novel coronavirus disease (COVID-19) in newborns and infants: what we know so far. *Ital J Pediatr.* 2020;46(1):56. doi:10.1186/s13052-020-0820-x
4. Khalil A, von Dadelszen P, Draycott T, Ugwumadu A, O'Brien P, Magee L. Change in the incidence of stillbirth and preterm delivery during the COVID-19 pandemic. *JAMA.* 2020. doi:10.1001/jama.2020.12746
5. Mlakar J, Korva M, Tul N, et al. Zika virus associated with microcephaly. *N Engl J Med.* 2016;374(10):951-958. doi:10.1056/NEJMoa1600651
6. Cheeran MC, Lokensgard JR, Schleiss MR. Neuropathogenesis of congenital cytomegalovirus infection: disease mechanisms and prospects for intervention. *Clin Microbiol Rev.* 2009;22(1):99-126. doi:10.1128/CMR.00023-0
7. Al-Haddad BJS, Jacobsson B, Chabra S, et al. Long-term risk of neuropsychiatric disease after exposure to infection in utero. *JAMA Psychiatry.* 2019;76(6):594-602. doi:10.1001/jamapsychiatry.2019.0029
8. Cordeiro CN, Tsimis M, Burd I. Infections and brain development. *Obstet Gynecol Surv.* 2015;70(10):644-655. doi:10.1097/OGX.0000000000000236
9. Yockey LJ, Lucas C, Iwasaki A. Contributions of maternal and fetal antiviral immunity in congenital disease. *Science.* 2020;368(6491):608-612. doi:10.1126/science.aaz1960
10. Zerbo O, Qian Y, Yoshida C, Grether JK, Van de Water J, Croen LA. Maternal infection during pregnancy and autism spectrum disorders. *J Autism Dev Disord.* 2015;45(12):4015-4025. doi:10.1007/s10803-013-2016-3
11. Adams Waldorf KM, McAdams RM. Influence of infection during pregnancy on fetal development. *Reproduction.* 2013;146(5):R151-R162. doi:10.1530/REP-13-0232
12. Francis F, Bhat V, Mondal N, et al. Fetal inflammatory response syndrome (FIRS) and outcome of preterm neonates - a prospective analytical study. *J Matern Fetal Neonatal Med.* 2019;32(3):488-492. doi:10.1080/14767058.2017.1384458
13. Juan J, Gil MM, Rong Z, Zhang Y, Yang H, Poon LC. Effect of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcome: systematic review. *Ultrasound Obstet Gynecol.* 2020;56(1):15-27. doi:10.1002/uog.22088
14. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ.* 2020;370:m3320. doi:10.1136/bmj.m3320
15. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: a systematic review of 108 pregnancies. *Acta Obstet Gynecol Scand.* 2020;99(7):823-829. doi:10.1111/aogs.13867
16. Shah AV, Howell HB, Kazmi SH, et al. Developmental screening of full-term infants at 16 to 18 months of age after in-utero exposure to maternal SARS-CoV-2 infection. *J Perinatol.* 2023;43(5):659-663. doi:10.1038/s41372-023-01642-3
17. Pinheiro GSMA, de Souza RC, de Oliveira Azevedo VMG, et al. Effects of intrauterine exposure to SARS-CoV-2 on infants' development: a rapid review and meta-analysis. *Eur J Pediatr.* 2023;182(5):2041-2055. doi:10.1007/s00431-023-04910-8
18. Edlow AG, Castro VM, Shook LL, Kaimal AJ, Perlis RH. Neurodevelopmental outcomes at 1 year in infants of mothers who tested positive for SARS-CoV-2 during pregnancy. *JAMA Netw Open.* 2022;5(6):e2215787. doi:10.1001/jamanetworkopen.2022.15787
19. Shook LL, Sullivan EL, Lo JO, Perlis RH, Edlow AG. COVID-19 in pregnancy: implications for fetal brain development. *Trends Mol Med.* 2022;28(4):319-330. doi:10.1016/j.molmed.2022.02.004
20. McCarthy J, Liu D, Kaskel F. The need for life-course study of children born to mothers with prior COVID-19 infection. *JAMA Pediatr.* 2021;175(11):1097-1098. doi:10.1001/jamapediatrics.2021.2423
21. Gökçay G. Çocuk sağlığı izlemi. In: Neyzi O, Ertuğrul T, Darendeliler F, eds. *Pediatric. 5th ed.* Nobel Tıp Kitabevleri; 2020:37-43.
22. Yalaz K, Anlar B. Denver II Gelişimsel Tarama Testi: Türk Çocuklarına Uyarlanması ve Standardizasyonu. *Gelişimsel Çocuk Nörolojisi Derneği.* Accessed December 10, 2022.
23. Smith ER, Oakley E, Grandner GW, et al. Adverse maternal, fetal, and newborn outcomes among pregnant women with SARS-CoV-2 infection: an individual participant data meta-analysis. *BMJ Glob Health.* 2023;8(1):e009495. doi:10.1136/bmjgh-2022-009495
24. Liao J, He X, Gong Q, Yang L, Zhou C, Li J. Analysis of vaginal delivery outcomes among pregnant women in Wuhan, China during the COVID-19 pandemic. *Int J Gynaecol Obstet.* 2020;150(1):53-57. doi:10.1002/ijgo.13188
25. Zhang L, Jiang Y, Wei M, et al. Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province. *Zhonghua Fu Chan Ke Za Zhi.* 2020;55(3):166-171. doi:10.3760/cma.j.cn112141-20200218-00111
26. Sahin D, Tanacan A, Erol SA, et al. Updated experience of a tertiary pandemic center on 533 pregnant women with COVID-19 infection: a prospective cohort study from Turkey. *Int J Gynaecol Obstet.* 2021;152(3):328-334. doi:10.1002/ijgo.13460
27. Lokken EM, Huebner EM, Taylor GG, et al. Disease severity, pregnancy outcomes, and maternal deaths among pregnant patients with severe acute respiratory syndrome coronavirus 2 infection in Washington State. *Am J Obstet Gynecol.* 2021;225(1):77.e1-77.e14. doi:10.1016/j.ajog.2020.12.1221
28. World Health Organization. Breastfeeding during COVID-19: Scientific brief. Published June 23, 2020. Accessed January 3, 2023. https://apps.who.int/iris/bitstream/handle/10665/332639/WHO-2019-nCoV-Sci_Brief-Breastfeeding-2020.1-eng.pdf
29. Mirbeyk M, Saghazadeh A, Rezaei N. A systematic review of pregnant women with COVID-19 and their neonates. *Arch Gynecol Obstet.* 2021;304(1):5-38. doi:10.1007/s00404-021-06049-z
30. Ferlibaş E. Doğum esnasında COVID-19 pozitif gebeler ile COVID dışı gebelerin maternal, neonatal ve perinatal sonuçlar açısından karşılaştırılması [master's thesis]. [Necmettin Erbakan Üniversitesi, Meram Tıp Fakültesi]; 2021.
31. Yılmaz E, Çağlayan N, Yazıcı S. COVID-19 pandemisinin gebelik, doğum ve doğum sonrası döneme etkileri ve sürecin yönetimi. *Van Sag Bil Derg.* 2020;13:92-99.
32. Oncel MY, Akın IM, Kanburoglu MK, et al. A multicenter study on epidemiological and clinical characteristics of 125 newborns born to women infected with COVID-19 by Turkish Neonatal Society. *Eur J Pediatr.* 2021;180(3):733-742. doi:10.1007/s00431-020-03767-5
33. Nismath S, Rao SS, Addala S, Ravikiran SR, Kamath N. Breastfeeding self-efficacy in COVID-19 positive postpartum mothers in a community maternal facility in South India: a case control study. *Ethiop J Health Sci.* 2023;33(1):13-20. doi:10.4314/ejhs.v33i1.3
34. Oskovi-Kaplan ZA, Ozgu-Erdinc AS, Buyuk GN, et al. Newborn hearing screening results of infants born to mothers who had COVID-19 disease during pregnancy: a retrospective cohort study. *Ear Hear.* 2022;43(1):41-44. doi:10.1097/AUD.0000000000001167
35. Alan MA, Alan C. Hearing screening outcomes in neonates of SARS-CoV-2 positive pregnant women. *Int J Pediatr Otorhinolaryngol.* 2021;146:110754. doi:10.1016/j.ijporl.2021.110754
36. Zeng LK, Zhu HP, Xiao TT, et al. Short-term developmental outcomes in neonates born to mothers with COVID-19 from Wuhan, China. *World J Pediatr.* 2021;17(3):253-262. doi:10.1007/s12519-021-00426-z
37. Schuh TL, Mithal LB, Naureckas S, Miller ES, Garfield CF, Shah MD. Outcomes from birth to 6 months of publicly insured infants born to mothers with severe acute respiratory syndrome coronavirus 2 infection in the United States. *J Perinat Med.* 2021;50(3):334-342. doi:10.1515/jpm-2021-0251
38. Agarwal PK, Xie H, Sathyapalan Rema AS, et al. Evaluation of the Ages and Stages Questionnaire (ASQ 3) as a developmental screener at 9, 18, and 24 months. *Early Hum Dev.* 2020;147:105081. doi:10.1016/j.earlhumdev.2020.105081

Hazal Eryılmaz Yıldır

Graduated from the Faculty of Medicine at Namık Kemal University, Türkiye. She completed her residency in Pediatrics at Ankara Training and Research Hospital, where she received comprehensive training in general pediatrics, neonatology, pediatric emergency medicine, pediatric intensive care, and preventive child health. Following the completion of her pediatric residency, Dr. Eryılmaz relocated to Belgium. She is currently preparing to complete the professional registration and licensing process required to practice medicine in Belgium and has not yet commenced clinical practice there.

