



Original Article

Neurodevelopmental Outcomes in Toddlers Born to Mothers Who Were Covid Positive in Their Antenatal Period

Dr. Adline Jenefa S¹, Dr Aazmi. M²

¹General surgery resident, Tirunelveli Medical College, Tirunelveli.

²Assistant Professor, Government Medical College, Tiruppur.

OPEN ACCESS

Corresponding Author:

Dr. Adline Jenefa S
General surgery resident,
Tirunelveli Medical College,
Tirunelveli.

Received: 01-04-2026

Accepted: 05-05-2026

Available online: 19-05-2026

ABSTRACT

Introduction: SARS-CoV-2, a single-stranded positive-sense RNA virus causing COVID-19 via respiratory droplets, led to global pulmonary and extrapulmonary (CNS, CVS, endocrine, dermatological, hematological) effects; pregnant individuals faced heightened risk due to pregnancy-related physiological/immunological changes, with rare vertical transmission but maternal immune activation (e.g., IL-6) potentially impairing fetal neurodevelopment [1,2,5-8], exacerbated by infants' immature immunity. Studies show mixed results—e.g., 3rd-trimester links [Ayed et al.], 1st/2nd-trimester risks [Edlow et al.], no infection association but pandemic effects [Shuffrey et al., Firestein, Rood, Munian], and 25% delay in full-term neonates [Shah et al.]—yet India's evidence remains unclear, mostly limited to <12-month-olds [2-4,6,8,9,12,13]. This study assesses neurodevelopment at 22 months using ASQ-3 in toddlers of COVID-exposed mothers, enabling early detection and interventions to enhance long-term quality of life.

Objectives: To estimate the prevalence of neurodevelopmental delay in toddlers born to SARS-CoV-2-exposed mothers and determine associated factors.

Methodology: This prospective cohort study, conducted over two months (Dec 15, 2023–Feb 15, 2024) in a South Indian district after Institutional Ethics Committee approval, enrolled 63 toddlers (21–23 months) born in 2021–2022 to RT-PCR-confirmed SARS-CoV-2-positive mothers (data from Deputy Director of Health Services); preterm infants were excluded to avoid prematurity confounding. Mothers were contacted via phone/Village Health Nurses and assessed at Health Sub-Centres on immunization days post-informed consent. Neurodevelopment was evaluated using ASQ-3 (22-month form) across five domains (communication, gross motor, fine motor, problem-solving, personal-social; each 0–60 score), defining delay as ≤ 2 SD below mean in ≥ 1 domain. Data from semi-structured questionnaires were analyzed in IBM SPSS v23: descriptives (mean \pm SD, frequencies/%), inferential tests (t-test, ANOVA), and Pearson correlations.

Results: Among 63 toddlers (55.6% male, 57.1% normal birth weight, 42.9% low birth weight), more than half (55.6%) were from nuclear families, with Hindus predominating (79.4%), and 55.6% of mothers were aged 20–25 years, mostly with primary or lower education (38.1% illiterate or primary), managed under home isolation (55.6%), vaccinated (58.7%), infected mainly in the third trimester (61.9%), and delivered vaginally (60.3%). Developmental delay affected 15.9% in problem solving, 12.7% in communication and personal social, 7.9% in fine motor, and 6.3% in gross motor, with significant inverse associations for gross motor with joint family, maternal age <20 years, and low birth weight; for fine motor with joint family, low maternal education, primigravida, NVD, and low birth weight; and for problem solving and personal social with joint family, low maternal education, maternal age <20 years, primigravida, home isolation, NVD, and low birth weight. Domain scores were strongly and positively correlated (all $P < 0.01$),

indicating that lower scores in one domain tended to accompany lower scores in others.

Conclusion: In conclusion, this study highlights a meaningful risk of developmental delay among toddlers exposed to SARS CoV 2 in utero, shaped not only by viral exposure but also by social and maternal factors. Strengthening and expanding the Rashtriya Bal Swasthya Karyakram to include targeted screening for children born to COVID positive mothers would support early detection, timely intervention, and improved long term neurodevelopment across the country.

Keywords: COVID-19, Neurodevelopmental Delay, In Utero SARS-CoV-2 Exposure, Ages and Stages Questionnaire-3 (ASQ-3), Toddler Development Assessment.

INTRODUCTION

SARS-CoV2, a single stranded positive sense RNA virus that caused COVID 19 had a huge impact globally. Covid was transmitted through respiratory droplets and it caused both pulmonary & extra – pulmonary (CNS, CVS, endocrine, dermatological, haematological) manifestations. Pregnant individuals were at increased risk for Covid because the physiological and immunological reactions that occurs during the pregnancy make them more susceptible for infections [1,2].

Even though vertical transmission is found to be rare [3,4], any maternal viral infection will lead to maternal immune activation via IL-6 release which might affect the neurodevelopment of the off-spring [1,2,5-8]. Also, the underdeveloped innate and adaptive immune system of the baby make them even more susceptible for infections [2].

Ayed et al. reported that third-trimester maternal COVID-19 exposure is associated with greater neurodevelopmental delay, whereas Edlow et al. found higher risk with first- and second-trimester exposure. In contrast, Shuffrey et al., along with Firestein, Rood, and Munian, observed no significant association between maternal COVID-19 infection and neurodevelopmental outcomes, suggesting that pandemic-related environmental factors may instead contribute to delays. Given that prematurity is a known risk factor and COVID-19 increases preterm births, Shah et al. specifically evaluated full-term neonates and reported neurodevelopmental delay in 25% at 16–18 months. Overall, evidence suggests that COVID-19 may influence neurodevelopment either directly or indirectly, regardless of gestational age at birth. Neurodevelopment was assessed using the Ages and Stages Questionnaire, 3rd edition (ASQ-3), at 22 months.

Especially in India, still there is no clear evidence regarding the association between maternal Covid exposure and neurodevelopmental outcome. Many studies were conducted globally among the age group less than 12 months [2-4,6,8,9,12,13] and there exists a disparity among those studies. But, Covid exerts some effect on neurodevelopmental outcome due to the maternal immune activation. Hence, a longer follow up is needed. This study is aimed at the neurodevelopmental outcome of the toddlers. If neurodevelopmental delays are detected early, early intervention methods can be opted and can be followed up at regular intervals to improve the future quality of the child's life.

Objectives:

- To estimate the prevalence of neurodevelopmental delay in toddlers with maternal exposure to SARS CoV-2
- To determine the factors associated with neurodevelopmental delay in toddlers with maternal exposure to SARS CoV-2

METHODOLOGY:

This prospective cohort study was conducted in a district of South India among toddlers aged 21–23 months who were born during 2021 and 2022 to mothers with documented SARS-CoV-2 infection during pregnancy. All eligible toddlers in the locality with a history of maternal COVID-19 exposure during the specified period were included. Ethical clearance was obtained from the Institutional Ethics Committee, and the study was conducted over two months from December 15, 2023 to February 15, 2024. Inclusion criteria comprised toddlers born to mothers diagnosed with COVID-19 by RT-PCR testing of nasopharyngeal and/or oropharyngeal swabs at any point during pregnancy in recognized hospital network laboratories, while preterm infants were excluded to eliminate the confounding effect of prematurity on neurodevelopmental outcomes. Data regarding COVID-19 positive mothers were obtained from the Deputy Director of Health Services office. Mothers were contacted via telephone or through Village Health Nurses and were requested to bring their children to the nearest Health Sub Centre, where assessments were conducted on weekly immunization days. After obtaining informed written consent from the primary caregiver, data were collected using a semi-structured questionnaire and the Ages and Stages Questionnaire, 3rd edition (ASQ-3) for 22 months, under the supervision of a medical officer. The ASQ-3 evaluates five developmental domains—communication, gross motor, fine motor, problem solving, and personal-social skills—each consisting of six items with scores ranging from 0 to 60. Developmental delay was defined as a score ≤ 2 standard deviations below the population mean in one or more domains, while scores > 2 standard deviations were considered normal. Data were entered into Microsoft Excel and analyzed using IBM SPSS version 23. Descriptive statistics were used to summarize baseline characteristics, with continuous variables expressed as mean \pm standard deviation and

categorical variables as frequencies and percentages. Inferential statistics, including independent t-test and ANOVA, were applied to assess associations between domain scores and relevant variables, while Pearson correlation analysis was used to evaluate relationships across developmental domains.

RESULTS:

Demographic profile:

More than half of the toddlers (55.6%) belonged to nuclear families, while 44.4% were from joint families. The majority of study subjects were Hindus (79.4%), followed by Christians (14.3%) and Muslims (6.3%).

Mothers of toddlers:

The majority of mothers were aged 20–25 years (58.7%), with ages ranging from 17 to 33 years, and only 7.9% were above 30 years. Most had primary education (38.1%), while 22.2% were illiterate, and a small proportion had higher education. More than half of the mothers (55.6%) were managed under home isolation during COVID-19, and 58.7% were vaccinated. Infection occurred predominantly in the third trimester (61.9%), followed by the second trimester (36.5%), with very few cases in the first trimester. Slightly more than half were multigravida (50.8%), and the majority (74.6%) were in the low-risk category. Most deliveries were by normal vaginal delivery (60.3%), while 39.7% underwent LSCS.

Toddlers:

Among the 63 toddlers, 55.6% were males and 44.4% were females. More than half (57.1%) had normal birth weight, while 42.9% were of low birth weight.

Developmental Domains:

Developmental delay was observed in 12.7% of toddlers in the communication domain and 12.7% in the personal-social domain. Delay in fine motor and gross motor domains was seen in 7.9% and 6.3% respectively, with gross motor being the least affected. The highest proportion of delay was noted in the problem-solving domain (15.9%), while the majority of toddlers in all domains were developmentally appropriate for age.

Factors associated with developmental delay:

Table 1: Association of mean scores with mother and toddler variables:

| Characteristic | Communication | Gross Motor | Fine Motor | Problem Solving | Personal Social |
|-----------------------------|---------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Mother | | | | | |
| Joint Family | T= 2.598 Sig=0.170 | T= 3.204 Sig=0.033 | T= 2.676 Sig=0.024 | T= 3.213 Sig=0.000 | T= 2.997 Sig=0.000 |
| Primary and below education | T= -2.466 Sig=0.332 | T= -1.558 Sig=0.101 | T= -3.027 Sig=0.005 | T= -1.970 Sig=0.001 | T= -2.751 Sig=0.000 |
| <20 years of age | T= -4.625 Sig=0.181 | T= -2.814 Sig=0.007 | T= -4.305 Sig=0.189 | T= -4.380 Sig=0.654 | T= -3.771 Sig=0.005 |
| Primigravida | T= -1.495 Sig=0.099 | T= 2.133 Sig=0.156 | T= 1.745 Sig=0.043 | T= 1.884 Sig=0.000 | T= 1.898 Sig=0.001 |
| No high risk | T= 0.147 Sig=0.427 | T= 2.266 Sig=0.227 | T= -0.239 Sig=0.860 | T= -0.344 Sig=0.178 | T= -0.603 Sig=0.089 |
| Home Isolation | T= 1.210 Sig=0.095 | T= 1.067 Sig=0.060 | T= 1.776 Sig=0.115 | T= 1.815 Sig=0.012 | T= 1.223 Sig=0.013 |
| No Vaccination for Covid | T= -0.057 Sig=0.952 | T= 0.939 Sig=0.939 | T= 0.192 Sig=0.208 | T= 0.038 Sig=0.080 | T= 0.147 Sig=0.058 |
| NVD | T= -3.430 Sig=0.107 | T= -2.150 Sig=0.274 | T= -2.862 Sig=0.018 | T= -3.032 Sig=0.001 | T= -2.345 Sig=0.001 |
| Muslim | F=0.104 Sig=0.901 | F=1.215 Sig=0.304 | F=0.853 Sig=0.431 | F=0.423 Sig=0.657 | F=0.866 Sig=0.426 |
| II Trimester | F=1.509 Sig=0.229 | F=0.158 Sig=0.854 | F=0.736 Sig=0.483 | F=1.982 Sig=0.147 | F=0.096 Sig=0.909 |
| Toddler | | | | | |
| Male baby | T= -1.796 Sig=0.529 | T= -0.552 Sig=0.598 | T= -0.804 Sig=0.739 | T=0.756 Sig=0.368 | T= -0.395 Sig=0.974 |
| LBW | T= -3.984 Sig=0.138 | T= -2.868 Sig=0.035 | T= -3.130 Sig=0.036 | T= -3.472 Sig=0.000 | T= -2.519 Sig=0.000 |

Independent t-tests revealed no significant associations between communication delay and any variables (family type, maternal age/education, gravida, COVID treatment place/vaccination, high-risk status, baby gender, low birth weight).

Significant associations emerged for gross motor delay with joint family, maternal age <20 years, and low birth weight; fine motor delay with joint family, maternal education <primary school, primigravida, normal vaginal delivery, and low birth weight; and problem-solving/personal-social delays with joint family, maternal education <primary school, age <20 years, primigravida, COVID treatment place, normal vaginal delivery, and low birth weight. ANOVA showed no significant links between trimester of infection/religion and domain mean scores. (Table 1)

Table 2. Correlation between scores among the domains

| | | TSC | TSGM | TSFM | TSPOS | TSPES |
|-------------------------|--------------|---------|---------|---------|---------|---------|
| Communication (TSC) | Correlation | 1 | 0.457** | 0.665** | 0.662** | 0.636** |
| | Significance | | 0.000 | 0.000 | 0.000 | 0.000 |
| Gross motor (TSGM) | Correlation | 0.457** | 1 | 0.537** | 0.612** | 0.649** |
| | Significance | 0.000 | | 0.000 | 0.000 | 0.000 |
| Fine motor (TSFM) | Correlation | 0.665** | 0.537** | 1 | 0.778** | 0.706** |
| | Significance | 0.000 | 0.000 | | 0.000 | 0.000 |
| Problem solving (TSPOS) | Correlation | 0.662** | 0.612** | 0.778** | 1 | 0.845** |
| | Significance | 0.000 | 0.000 | 0.000 | | 0.000 |
| Personal social (TSPES) | Correlation | 0.636** | 0.649** | 0.706** | 0.845** | 1 |
| | Significance | 0.000 | 0.000 | 0.000 | 0.000 | |

** . Correlation is significant at the 0.01 level (2-tailed)

For a decrease in the value of one domain, there is also decrease in the value of another domain and vice versa. The correlation is statistically significant (P<0.05) (Table 2).

DISCUSSION:

In this study of 63 toddlers (21-23 months), 12/63 (19%) had developmental delay, including 9 with global delay and 2 across all 5 domains; domain-specific rates were communication (8/63, 12.7%), gross motor (4/63, 6.3%), fine motor (5/63, 7.9%), problem-solving (10/63, 15.9%), and personal-social (8/63, 12.7%), aligning with Shuffrey et al. (20%) and Ayed et al. (10%). Delays were highest in communication, problem-solving, and personal-social domains, consistent with Hessami et al. and others, though fine motor was commonest elsewhere. Significant associations included joint vs. nuclear family, maternal education (primary or below), and young maternal age (<20 years); primigravida, non-high-risk mothers, home isolation, unvaccinated status, NVD, 2nd-trimester infection, male sex, and LBW also showed higher delays (non-significant except family/education), with explanations tied to care, inexperience, exposure, and biology—mirroring some studies despite conflicting reports of no COVID-exposure link [3-6,9,10,14,16].

CONCLUSION:

In conclusion, significant developmental delay affects 12/63 (19%) toddlers of SARS-CoV-2-exposed mothers, with 9 global cases and 2 across all 5 domains (communication 12.7%, gross motor 6.3%, fine motor 7.9%, problem-solving 15.9%, personal-social 12.7%); delays were highest in communication, problem-solving, and personal-social domains, linked to in utero exposure and risk factors like joint family upbringing, young/low-education/primigravida mothers, home isolation, LBW, and NVD. Extending the Rashtriya Bal Swasthya Karyakram (RBSK, launched 2013 by MoHFW-NHM for 4 Ds screening) to targeted post-pandemic checks for these children would enable early detection and interventions nationwide.

Acknowledgement: Sponsored by ICMR.

REFERENCES:

1. Moore KM, Suthar MS. Comprehensive analysis of covid-19 during pregnancy. *Biochemical and Biophysical Research Communications*. 2021;538:180–6. Doi:10.1016/j.bbrc.2020.12.064
2. Ayed M, Embaireeg A, Kartam M, More K, Alqallaf M, AlNafisi A, et al. Neurodevelopmental outcomes of infants born to mothers with SARS-COV-2 infections during pregnancy: A national prospective study in Kuwait. *BMC Pediatrics*. 2022;22(1). Doi:10.1186/s12887-022-03359-2
3. Firestein MR, Shuffrey LC, Hu Y, Kyle M, Hussain M, Bianco C, et al. Assessment of neurodevelopment in infants with and without exposure to asymptomatic or mild maternal SARS-COV-2 infection during pregnancy. *JAMA Network Open*. 2023;6(4). Doi:10.1001/jamanetworkopen.2023.7396
4. Rood M, ten Kate L, Boeddha NP, van 't Kruijs K. Clinical characteristics, transmission rate and outcome of neonates born to covid-19-positive mothers: A prospective case series from a resource-limited setting. *Pediatric Infectious Disease Journal*. 2022;42(1):35–42. Doi:10.1097/inf.0000000000003758
5. Hessami K, Norooznejhad AH, Monteiro S, Barrozo ER, Abdolmaleki AS, Arian SE, et al. Covid-19 pandemic and infant neurodevelopmental impairment. *JAMA Network Open*. 2022;5(10). Doi:10.1001/jamanetworkopen.2022.38941

6. 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 Network Open*. 2022;5(6). Doi:10.1001/jamanetworkopen.2022.15787
7. Brum AC, Vain NE. Impact of perinatal covid on fetal and neonatal brain and neurodevelopmental outcomes. *Seminars in Fetal and Neonatal Medicine*. 2023;28(2):101427. Doi:10.1016/j.siny.2023.101427
8. Shuffrey LC, Firestein MR, Kyle MH, Fields A, Alcántara C, Amso D, et al. Association of birth during the COVID-19 pandemic with neurodevelopmental status at 6 months in infants with and without in utero exposure to maternal SARS-COV-2 infection. *JAMA Pediatrics*. 2022;176(6). Doi:10.1001/jamapediatrics.2021.5563
9. Munian D, Das R, Hazra A, Ray S. Outcome of neonates born to covid-positive women at 6 months of age. *Indian Pediatrics*. 2021;58(9):853–6. Doi:10.1007/s13312-021-2308-1
10. Shah AV, Howell HB, Kazmi SH, Zaccario M, Sklamberg FE, Groth T, Martindale P, Dreyer B, Verma S. 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 May;43(5):659-663. doi: 10.1038/s41372-023-01642-3. Epub 2023 Mar 17. PMID: 36932135; PMCID: PMC10020764
11. Mulkey SB, Williams ME, Jadeed N, Zhang A, Israel S, DeBiasi RL. Neurodevelopment in infants with antenatal or early neonatal exposure to SARS-COV-2. *Early Human Development*. 2022;175:105694. Doi:10.1016/j.earlhumdev.2022.105694
12. Martenot A, Labbassi I, Delfils-Stern A, Deruelle P, Kuhn P. Medical and neurodevelopmental outcomes at 10 months of age in infants born at 34 weeks plus to mothers with covid-19. *Acta Paediatrica*. 2022;112(2):296–7. Doi:10.1111/apa.16570
13. Pinheiro GS, de Souza RC, de Oliveira Azevedo VM, Guimarães NS, Pires LG, Lemos SM, et al. Effects of intrauterine exposure to SARS-COV-2 on infants' development: A rapid review and meta-analysis. *European Journal of Pediatrics*. 2023;182(5):2041–55. Doi:10.1007/s00431-023-04910-8
14. Metz TD. Is it exposure to the pandemic or to maternal SARS-COV-2 infection that is adversely affecting early childhood neurodevelopment? *JAMA Network Open*. 2022;5(6). Doi:10.1001/jamanetworkopen.2022.15793
15. Edlow AG, Castro VM, Shook LL, Haneuse S, Kaimal AJ, Perlis RH. Sex-specific neurodevelopmental outcomes among offspring of mothers with SARS-COV-2 infection during pregnancy. *JAMA Network Open*. 2023;6(3). Doi:10.1001/jamanetworkopen.2023.4415
16. Wu T, Chen L, Wang Y, Shi H, Niu J, Yin X, Li M, Tan C, Jiang H, Zheng D, Wei Y, Zhao Y, Wang X, Qiao J. Effects of SARS-CoV-2 Infection During Late Pregnancy on Early Childhood Development: A Prospective Cohort Study. *Front Pediatr*. 2021 Nov 23;9:750012. doi: 10.3389/fped.2021.750012. PMID: 34888266; PMCI