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Developmental outcome of babies born to mother infected with Coronavirus-19 during pregnancy

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Abstract

Introduction: Developmental effect on children of mothers who had corona virus during pregnancy is unknown. This study aims to determine developmental outcomes of these babies after infancy.

Method: This is an observational study carried out from 1 Oct 2020 to 31 Dec 2020. All the babies born from the mother who were tested positive for coronavirus anytime during pregnancy were included. Controls were those babies whose mothers were PCR negative prior to delivery. All the children were assessed for development at 12 months of age. They were screened using BRIGANCE III and ages and stages questionnaires (ASQ) for development profile in all domains. The total score obtained in the test was compared against the normative value for that age and sex.

Result: During the study period 1967 babies were delivered. Among them, 48(2.44%) babies were born from mothers who were tested positive for COVID-19. Out of these 12 children returned for development assessment. Out of 12 cases two (16.6%) and among controls three (25%) failed the BRIGANCE III screening. ASQ showed that among all the cases who failed developmental screening test, in both groups, were below cut off score in communication domain.

Conclusion: There is no difference in the developmental outcome of children who were born from a mother who contracted COVID-19 during pregnancy as compared to those born from mothers who had no evidence of that infection.

Keywords: ASQ, Brigrance, COVID-19, Development



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Introduction

COVID-19 is disease caused by SARS-CoV-2, was announced as a global pandemic by World Health Organization (WHO) on 11 Mar 2020.¹ Latest data from WHO showed that there are more than 760 million confirmed cases of COVID-19 and more than 6.9 million deaths.²

Here in Southeast Asia, there are reports of 31 million confirmed COVID-19 cases and more than 400 thousand related deaths. A recent data from Nepal has shown that 1003450 cumulative confirmed cases are reported and 12031 cumulative deaths.³

Viral and bacterial infections during pregnancy have been associated with an array of adverse pregnancy outcomes, including spontaneous abortion, premature birth, stillbirth, intrauterine growth restriction, and fetal neurological defects.⁴⁻⁷ Recent studies have shown that SARS-CoV-2 vertical transmission is rare. Even though there is less chance of vertical transmission or a direct effect of the virus on the fetus, the impact of gestational infections can still be devastating to growing fetus.^{8,9} This is possibly mediated by Maternal Immune Activation (MIA) and other inflammatory processes.¹⁰ The mother's immune responses to a pathogen and health rather than the ensuing disease itself may be responsible for the abnormalities in fetal brain development.¹¹ There are studies that has shown that several viral infections during pregnancy can potentially lead to neurodevelopmental problems like autism spectrum disorder.¹²⁻¹⁵

Developmental outcomes of such babies born are largely unknown. Thus, this study aims to see if there are any developmental problems in children born to mothers with COVID-19 infection during pregnancy.

Method

This is an observational study carried out from 1 Oct 2020 to 31 Dec 2020. Ethical approval was obtained from institutional review committee (IRC) of Patan Academy of Health Sciences (PAHS) (Ref. drs2110191571) prior to inception of the study. All the babies born from mothers who were tested positive for coronavirus (via PCR) anytime during pregnancy, during this study period, were identified and included in the study after taking written consent, and the contact information including impatient number of the mother and baby were recorded. The nature of the study was communicated to the parents. All the newborn and maternal events and details were recorded in a proforma. All the babies were

asked to follow up after 1 year (preferably at 1 year scheduled vaccination or other well baby visits) for developmental assessment. When the parents failed to attend at the stipulated time, they were called in their recorded mobile number during working hours. The cases were excluded from the study if they did not come for a visit even after 3 attempts calls in different days. Controls were also identified at 1:1 ratio. Controls were those children who were born at Patan Hospital and their mother had no reported history of SARS CoV2 infection during pregnancy. The records were obtained from mothers' files. The controls were taken consecutively who attended the last day of the week (Fridays) at the pediatric referral clinic at Patan Hospital. All the children, cases and controls, were screened using BRIGANCE III after a written consent. Those children who failed in the screening test were administered Ages and Stages Questionnaires (ASQ) to identify the domains of development that were affected. ASQ looks at gross motor (GM), fine motor (FM), problem solving, communication and personal-social domains. For premature babies (<37 weeks), age was corrected for prematurity. The total score obtained in the test was compared against the normative value for that age and sex.

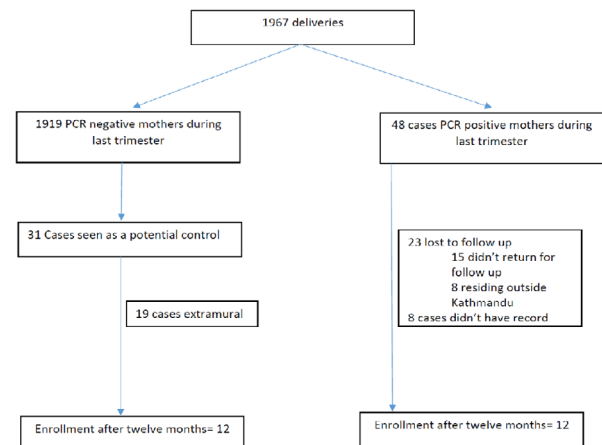


Figure 1. Consort diagram of cases and control involved in the study

Data was entered in excel and imported to Statistical Package for Social Sciences (SPSS).

Result

During the study, 1,967 babies were delivered, with 48(2.44%) born to mothers who tested positive for COVID-19. Out of these, only 12 returned for developmental assessment; 23 were lost to follow-up, 15 lived outside Kathmandu Valley, and eight cases had untraceable patient files. All 12 babies from Polymerase Chain Reaction (PCR) positive mothers tested negative.

There were no differences in baseline characteristics between the cases and controls, Table 1. Three (25%) deliveries among cases and four (33.33%) deliveries among control groups were born vaginally. Developmental screening using the BRIGANCE III test showed that two (16.67%) of cases and three (25%) of controls failed. Additionally, both cases and controls scored below the cutoff in the communication domain on the Ages and Stages Questionnaires, (ASQ), indicating developmental concerns in this area, Figure 2-6.

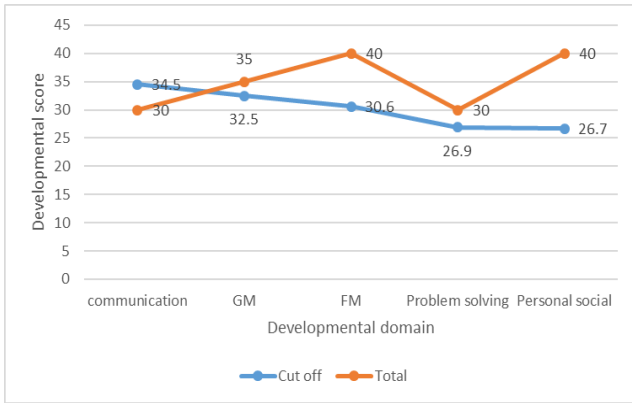


Figure 2. Case who failed ages and stages questionnaire (ASQ)

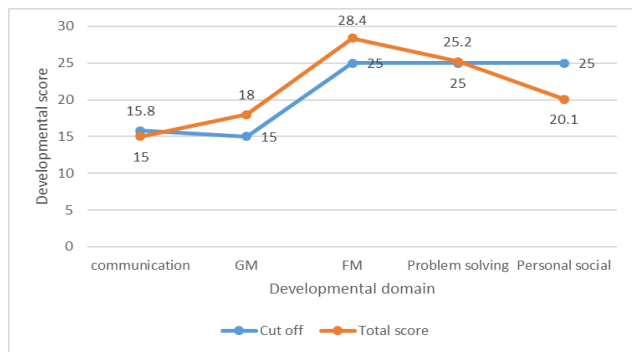


Figure 3. Case who failed ages and stages questionnaire (ASQ)

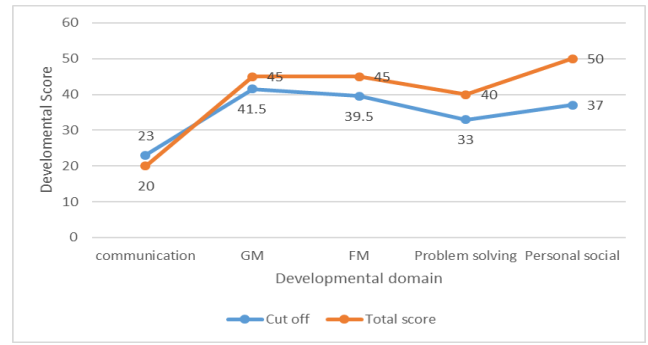


Figure 4. Control who failed ages and stages questionnaire (ASQ)

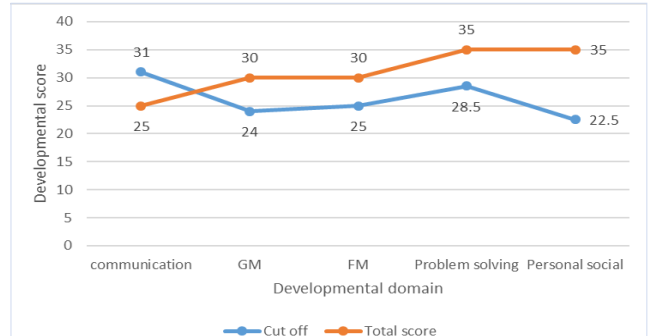


Figure 5. Control who failed ages and stages questionnaire (ASQ)

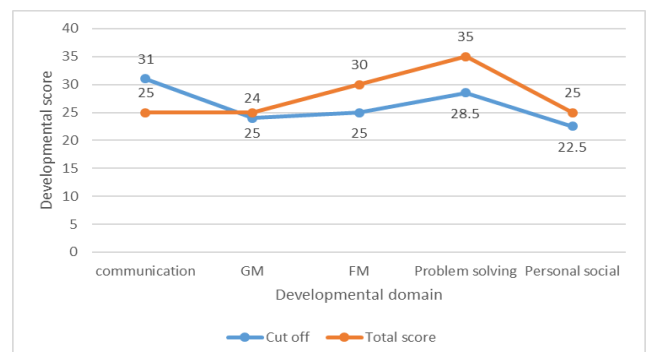


Figure 6. Control who failed ages and stages questionnaire (ASQ)

Table 1. Baseline characteristics of cases and controls (N=24)

Variables	Cases	Control
Age	16.08±3.35	15.50±2.11
Sex		
Male	7(58.33%)	9(75%)
Female	5(41.67%)	3(25%)
Mode of delivery		
Normal	3(25%)	4(33.33%)
C-section	9(75%)	8(66.67%)
Gestation (weeks)	36.16±3.61	37.75±1.60
Birth weight (gm)	2739.91±866.33	2807.50±384.43
Current weight (Kg)	10.54±1.37	9.50±1.55
Current length (Inch)	76.29±2.83	77.55±4.86
Head circumference (cm)	44.50±2.77	45.79±1.92

Table 2. Comparison of different development domains as screened by BRIGANCE III

Variables	Cases (mean±SD)	Control (mean±SD)
Receptive language-general	6.00±1.53	5.50±1.31
Receptive Language Body Parts	7.16±5.68	2.83±3.45
Identifies Pictures	4.66±3.33	4.16±2.88
Receptive Language Animal Sounds	4.50±3.42	3.00±2.76
Gross Motor Skills	7.25±2.09	5.83±1.80
Fine Motor Skills	6.33±1.49	6.00±1.59
Expressive Language General	5.08±1.97	4.41±1.56
Expressive Language Naming Object	1.41±1.67	1.08±1.37
Expressive Language Phrase	0.25±0.58	0.12±0.43
Self Help Skills	6.58±1.16	6.25±0.96
Social And Emotional Skills	8.50±2.19	7.08±2.15

Table 3. Brigance III screening test comparison among case and control groups

	Cases	Control	Total
Fail	2	3	5
Pass	10	9	19

Discussion

This is a prospective study which looked at the effect of COVID-19 on children born to mothers who had COVID-19 anytime during the last trimester of pregnancy. Out of total deliveries 48(2.44%) mothers contracted SARS-CoV-2. Most of the pregnant mothers gave birth by Cesarean- section (C-section). The C-section rate among cases in our study population was nine (75%) and eight (66%) in the control group. This is comparable to other studies as well. There are studies that have shown that there are higher rates of cesarean birth in pregnant ladies with COVID-19. A systematic review and meta-analysis showed that 56.9% of the pregnant mothers underwent C-section.¹⁶ A similar study also showed C-section rate as high as 87.6%.¹⁷ A systematic review of 39 studies showed that 52.3% to 95.8% of the deliveries were via C-section.¹⁸ This high proportion of C-section might be because the fear of potential transmission of the coronavirus to the newborn. Also, the background C-section rate for the institute might be high. None of the newborns delivered in our study tested positive by Reverse Transcriptase (RT) PCR. Which was similar to finding of study done in Wuhan Maternal and Child Health Hospital, China.¹⁹

Developmental screening was done using BRIGANCE III. It gave a cumulative score which was then tallied in the reference range for that age. Two (16.67%) of the cases and three (25%) of controls failed this. Among the cases and controls who failed the BRIGANCE screening, ages and stages questionnaires (ASQ) were administered to identify the domains of development that are affected. Among the two failed cases in our

study, one child was below the cut off score for both the communication and personal social domains and the other was delayed in the communication domain only. Among the control group, three (25%) failed and all of them are below cut off for communication domain and age appropriate in other domains. However, a study done in 2020 in maternal and child health hospital in Hubei province in China showed that babies of mothers with SARS-CoV-2 infection during pregnancy scored less in all the domains. However, it was statistically different in fine motor skills ($p=0.031$).¹⁹ Although there is no plausible reason as to why there is a low score in communication skills in our study, it might be the reflection of increasing social communication difficulties and symptoms related to autism spectrum disorder in children. Another reason for delay in language and communication skills in children who are born to mothers with SARS-CoV-2 infection might be due to increased separation of children in early days due to fear of viral transmission.

Developmental outcome of 255 infants who were born to mothers with SARS Cov2 infection was assessed at 6 months of age at Columbia University Irving Medical Center in New York. ASQ administered and there was no statistical difference noted in developmental outcome in these babies.²⁰ A similar study done in China in 2020 also showed that SARS-CoV-2 infection during late pregnancy did not increase the risk of developmental difficulties at 3 month of age.²¹

There are some limitations of this study. This study has a small sample size as the dropout rate was high. Many children did not come for follow up despite frequent calls, some were residing outside Kathmandu Valley. Similarly, it was difficult to ascertain previous SARS-CoV-2 infection among mothers of children who were selected as controls because some infection might have gone unnoticed.

Conclusion

SARS Cov 2 infection in that occurs late doesn't affect the development of infants. However, this study needs to be validated by a study including larger sample size.

Conflict of Interest

None

Funding

None

Author Contribution

Concept, design, planning: ARO; Literature review: ARO, BB; Data collection: ARO, BB; Data analysis: ARO, BB; Draft manuscript: ARO, BB; Revision of draft: ARO, BB; Final manuscript: ARO; Accountability of the work: ARO, BB.

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