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ASSOCIATION BETWEEN BIRTH DURING THE COVID- 19 PANDEMIC AND ANTHROPOMETRY OF INFANTS BETWEEN THE AGE OF 5-7 MONTHS WITH AND WITHOUT IN UTERO EXPOSURE TO MATERNAL SARS-COV-2 INFECTION

Medicine

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ABSTRACT

Background Over 200 million babies were born during the SARS-CoV-2 pandemic. Previous research suggests limited vertical transmission in infants of SARS-CoV-2-positive mothers. Maternal immune activation impacts fetal development via altered cytokine expression and placental inflammation. Studies indicate anthropometric changes in children born during the pandemic, noticeable at 6 months. Our hypothesis posits that maternal SARS-CoV-2 infection during pregnancy would be linked to delays in anthropometric measurements at 5-7 months of age. **Objectives** To evaluate the anthropometry of infants born during the COVID-19 pandemic between the ages of 5 and 7 months who were born to women who had COVID-19 during gestation and to women who did not have the infection throughout the gestation period. **Methodology** The cross-sectional descriptive study was conducted in tertiary care hospital between April 2021 and June 2021. The study comprised of infants between the age of 5-7 months who were born between October and December 2021, that is, during COVID-19 pandemic. A total of 127 out of 150 deliveries during October 2021 and December 2021 who were willing to participate in the study, of whom 75(59.06%) met our inclusion criteria and their children were assessed using anthropometry. **Results** After anthropometric assessment, data derived indicates that maximum number of infants had anthropometric values within -3SD to -2SD. **Conclusion** Our study suggests that infants aged 5-7 months born during the COVID-19 pandemic, with or without maternal SARS-CoV-2 exposure, experience significant delays in anthropometric measurements. More cohort studies are needed to assess long-term impacts and mitigation strategies.

KEYWORDS

INTRODUCTION

SARS-CoV-2, the virus causing COVID-19, emerged in Wuhan, China, in December 2019 [1,2]. Globally, by September 7, 2022, there were 603,711,760 cases, with 44,472,241 in India [3]. Over 200 million babies were born since the pandemic began, including 20 million in India during the first nine months [4,5]. Studies suggest low vertical transmission of the virus to infants [6-10] but note maternal immune activation's impact on fetal development [11-15].

Metz TD et al. report a direct link between infection severity and preterm delivery, with COVID-19 also associated with intrauterine growth issues [16]. Public health measures during the pandemic disrupted lives, causing stress and anxiety in pregnant and nursing women, and overburdened healthcare facilities, leading to a shortage of skilled birth attendants [17,18].

We proposed a hypothesis based on these studies that maternal SARS-CoV-2 infection during pregnancy would be linked to delays in social and motor development in the age group of 5-7 months.

AIM AND OBJECTIVES

Primary:

1. To evaluate the anthropometry of infants between the ages of 5 and 7 months who were born to women who had COVID-19 at the time of gestation during the COVID-19 pandemic.
2. To evaluate the anthropometry of infants at 6 months who were born to women who were not infected with COVID-19 at the time of gestation during the COVID-19 pandemic.

Secondary:

1. To assess the impact of the pandemic on anthropometry.
2. To determine the trimester in which the mother was infected.
3. To assess the relationship between trimester infected and its effect on the anthropometry of the child.

METHODOLOGY

1. Study Population

The study comprised mothers between the ages of 18 and 45 who had infants within 5-7 months of age who were admitted to our hospital's pediatric ward as inpatients or who had visited the pediatric outpatient department. The children were born between October and December 2021, that is, during COVID-19 pandemic. Only those who were willing to engage in the study were taken into consideration after the participants had been informed of its goal and methodology. The study excluded mother-child pairs who declined to participate in the study.
Sampling technique- Convenient sampling

2. Study Design

At our tertiary care hospital, a cross-sectional descriptive study was carried out between April 2021 and June 2021, two months after receiving approval from the institutional ethics committee. Women who had or had not been exposed to the SARS-CoV-2 virus during their pregnancies were approached, and questions regarding their age at conception, level of education, religion, mode of delivery, gestational age at delivery, sex of the infant, presence of comorbidities or any other illness during pregnancy, and history of vaccination were asked of them. The electronic health records of Thane Civil Hospital, where all of the Covid positive patients had been referred from our hospital, were used to gather the basic demographic information of SARS-CoV-2 positive mothers. SARS- CoV- 2 positivity status was determined based on laboratory polymerase chain reaction (PCR) results obtained at any time during pregnancy at any of the hospital network laboratories or external laboratories, which can be accessed through the official ICMR website using the person's mobile number. Based on the indicated gestational age in the EHR, the exposure trimester was calculated. Informed consent will be obtained before enrollment, and patients were informed of the study's purpose and methodology in a language they could comprehend.

Using an electronic weighing scale, an infantometer, and non-stretchable fibreglass tape, the following measurements were taken: weight, length, head, chest, and mid upper arm circumference and plotted on a WHO growth chart.

RESULTS

In Table 1, we present maternal characteristics. The study included 75

mother- child duo [23(32.43%) exposed, 52(67.57%) unexposed] with mean maternal age at delivery were 27 and 28 for unexposed and exposed groups, respectively. Among Covid-positive mothers, 1(4.35%) were affected in the first trimester, 5(21.74%) in the second trimester, and 17(73.91%) in the third trimester. Regarding SARS-CoV-2 unexposed participants, 24(46.15%) were unvaccinated, 15(28.85%) received the first dose, and 13(25%) completed both doses. Among Covid-19 exposed mothers, 21(91.30%) completed both vaccine doses, while 2 (8.70%) had one dose only. Religiously, 46(61.33%) identified as Hindu, 27(36%) as Muslim, and 2(2.66%) as Christian. Among SARS-CoV-2 positive cases, most had mild symptoms, 19(82.6%), while 4(17.4%) were asymptomatic.

Table 1 Maternal Characteristics

Maternal Characteristics		SARS CoV-2 unexposed	SARS CoV-2 exposed
No. Of Participants		52	23
Mean maternal age at delivery		27 yrs	28 yrs
Trimester Infected	1st trimester	NA	1 (4.35%)
	2nd trimester	NA	5 (21.74%)
	3rd trimester	NA	17 (73.91%)
COVID Vaccination	No doses taken	24 (46.15%)	0
	1st dose completed	15 (28.85%)	2 (8.70%)
	2nd dose completed	13 (25%)	21 (91.30%)
Religion	Hindu	27 (36%)	19 (25.33%)
	Muslim	23 (30.66%)	4 (5.34%)
	Christian	2 (2.66%)	0
	Others	0	0
Symptoms experienced	Asymptomatic	NA	4 (17.4%)
	Mild symptoms	NA	19 (82.6%)

In our study of 75 infants, 45(60%) were male and 30(40%) were female. Age distribution is shown in [Fig.1]: 17 23%) were 5 months old, 43(58%) were 6 months and 15(19%) were 7 months in age. Time of delivery is depicted in [Fig. 2]: 72(96%) were born at term, with 23(30.66%) from COVID-19-exposed mothers and 49(65.34%) from unexposed mothers. Additionally, 2(2.67%) were preterm, all from unexposed mothers, and 1(1.33%) were post-term, from unexposed mothers.

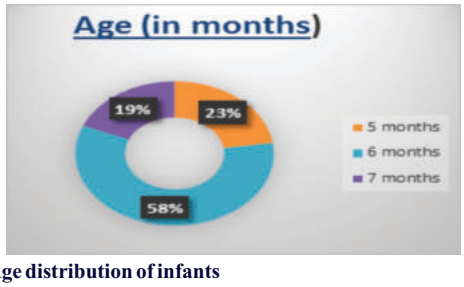

Fig. 1 Age distribution of infants

Fig. 2 Time of Delivery

In Table 2, we summarize infant characteristics. In terms of type of delivery, 51 (68%) [33 (44%) unexposed, 18 (24%) exposed] babies had normal delivery, while 24 (32%) [19 (25.33%) unexposed, 5 (6.67%) exposed] were delivered by c-section.

Table 2 Infant characteristics

Infant characteristics		Overall N=75	SARS-CoV-2 Unexposed N=52	SARS-CoV-2 Exposed N=23
Age	5 months	17 (22.67%)	16 (21.34%)	1 (1.33%)
	6 months	43 (57.33%)	21 (28%)	22 (29.33%)
	7 months	15 (20%)	15 (20%)	0 (0%)
Sex	Female	30 (40%)	19 (25.33%)	11 (14.67%)
	Male	45 (60%)	33 (44%)	12 (16%)
Type of delivery	Normal vaginal delivery	51 (68%)	33 (44%)	18 (24%)
	C section	24 (32%)	19 (25.33%)	5 (6.67%)
Delivery	Term	72 (96%)	49 (65.34%)	23 (30.66%)
	Pre term	2 (2.67%)	2 (2.67%)	0 (0%)
	Post term	1 (1.33%)	1 (1.33%)	0 (0%)

Anthropometric Measures for SARS-CoV-2 unexposed infants is given in [Table 3]. Under the height for age parameter in 5 month old infants, 2(3.85%) with <-3SD, 10(19.23%) within the range -2SD to -1SD and 4(7.69%) within the range of +1SD to +2SD. In 6 month old infants, 4(7.69%) with <-3SD, 16(30.77%) within the range of -2SD to -1SD and 2(3.85%) within the range of +1SD to +2SD. In 7 month old infants, 13(25%) within the range of -2SD to -1SD and 1(1.92%) within the range of +1SD to +2SD. Under the weight for age parameter in 5 month old infants, 5(9.62) were with <-3SD, 11(21.15%) within range of -2SD to -1SD. In 6 month old infants, 4(7.69%) were with <-3SD, 18 (34.62%) within range of -2SD to -1SD. In 7 month old infants, 7(13.46%) were with <-3SD, 7(13.46%) within the range of -2SD to -1SD. Under the mid upper arm circumference parameter in 5 month old infants, 2(3.85%) were with <-3SD, 13(25%) within the range of -2SD to -1SD and 1(1.92%) within the range of +1SD to+2SD. In 6 month old infants, 21(40.38%) within the range of -2SD to -1SD and 1(1.92%) within the range of +1SD to +2SD. In 7 month old infants, 2(3.85%) were with <-3SD, 12(23.08%) within the range of -2SD to-1SD. Under the parameter of head circumference in 5 month old infants, 16(30.77%) within the range of -2SD to -1SD. In 6 month old infants, 22(42.30%) within the range of -2SD to -1SD. In 7 month old infants, 12(23.07%) within the range of -2SD to -1SD, 2(3.84%) within the range of +1SD to +2SD. Under the parameter of BMI in 5 month old infants, 5(9.4%) with <-3SD, 11(21.15%) within the range of -2SD to -1SD. In 6 month old infants, 9(17.3%) with <-3SD, 12(23.08%) within the range of -2SD to -1SD. In 7 month old infants, 12(23.08%) with <-3SD, 2(3.85%) within the range of -2SD to -1SD. Within the context of anthropometry, maximum number of infants had anthropometric values within -2SD to -1SD (for unexposed height 73.04%, weight 67.3%, head circumference 94.21%, MUAC 86.47%, BMI 48.06%). for exposed height 100%, weight 100%, head circumference 100%, muac 100% BMI 100% - [Fig. 3])

Table 3 Anthropometric measures for SARS-CoV-2 unexposed

Anthropometric measures	Age	<-3 SD	-2 SD to -1 SD	+1 SD to +2 SD
Height for age	5 months	0 (0%)	1 (4.35%)	0 (0%)
	6 months	0 (0%)	22 (95.65%)	0 (0%)
	7 months	0 (0%)	0 (0%)	0 (0%)
Weight for age	5 months	0 (0%)	1 (4.35%)	0 (0%)
	6 months	0 (0%)	22 (95.65%)	0 (0%)
	7 months	0 (0%)	0 (0%)	0 (0%)
Mid-upper arm circumference	5 months	0 (0%)	1 (4.35%)	0 (0%)
	6 months	0 (0%)	22 (95.65%)	0 (0%)
	7 months	0 (0%)	0 (0%)	0 (0%)
Head circumference	5 months	0 (0%)	1 (4.35%)	0 (0%)
	6 months	0 (0%)	22 (95.65%)	0 (0%)
	7 months	0 (0%)	0 (0%)	0 (0%)
BMI	5 months	0 (0%)	1 (4.35%)	0 (0%)
	6 months	0 (0%)	22 (95.65%)	0 (0%)
	7 months	0 (0%)	0 (0%)	0 (0%)

The anthropometric measures for SARS-CoV-2 exposed is given in [Table 4]. Under the height for age parameter in 5 month old infants, (4.35%) within the range of -2SD to -1SD. In 6 month old infants, 22(95.65%) within the range of -2SD to -1SD. In 7 month old infants, there were no height for age measure values within the range of -2SD to -1SD. Under the weight for age parameter in 5 month old infants, 1(4.35%) within the range of -2SD to -1SD. In 6 month old infants, 22(95.65%) within the range of -2SD to -1SD. In 7 month old infants, there were no height for age measure values within the range of -2SD to -1SD. Under the mid upper arm circumference parameter in 5 month old infants, 1(4.35%) within the range of -2SD to -1SD. In 6 month old infants, 22(95.65%) within the range of -2SD to -1SD. In 7 month old infants, there were no height for age measure values within the range of -2SD to -1SD. Under the parameter of head circumference in 5 month old infants, 1(4.35%) within the range of -2SD to -1SD. In 6 month old infants, 22(95.65%) within the range of -2SD to -1SD. In 7 month old infants, there were no height for age measure values within the range of -2SD to -1SD. Under the parameter of BMI in 5 month old infants, 1(4.35%) within the range of -2SD to -1SD. In 6 month old infants, 22(95.65%) within the range of -2SD to -1SD. In 7 month old infants, there were no height for age measure values within the range of -2SD to -1SD. Within the context of anthropometry, maximum number of infants had anthropometric values within -2SD to -1SD (for exposed height 100%, weight 100%, head circumference 100%, muac 100% BMI 100% - [Fig. 4])

Table 4 Anthropometric measures for SARS-CoV-2 exposed

Anthropometric measures	Age	<-3 SD	-2 SD to -1 SD	+1 SD to +2 SD
Height for age	5 months	0 (0%)	1 (4.35%)	0 (0%)
	6 months	0 (0%)	22 (95.65%)	0 (0%)
	7 months	0 (0%)	0 (0%)	0 (0%)
Weight for age	5 months	0 (0%)	1 (4.35%)	0 (0%)
	6 months	0 (0%)	22 (95.65%)	0 (0%)
	7 months	0 (0%)	0 (0%)	0 (0%)
Mid-upper arm circumference	5 months	0 (0%)	1 (4.35%)	0 (0%)
	6 months	0 (0%)	22 (95.65%)	0 (0%)
	7 months	0 (0%)	0 (0%)	0 (0%)
Head circumference	5 months	0 (0%)	1 (4.35%)	0 (0%)
	6 months	0 (0%)	22 (95.65%)	0 (0%)
	7 months	0 (0%)	0 (0%)	0 (0%)
BMI	5 months	0 (0%)	1 (4.35%)	0 (0%)
	6 months	0 (0%)	22 (95.65%)	0 (0%)
	7 months	0 (0%)	0 (0%)	0 (0%)

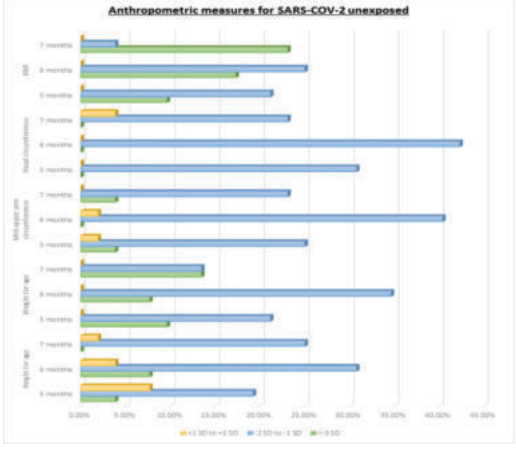

Fig. 3 Anthropometric values for SARS- CoV-2 unexposed infants

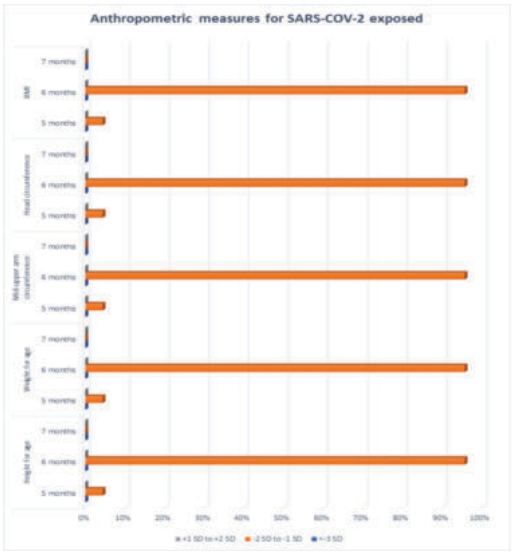

Fig. 4 Anthropometric values for SARS- CoV-2 exposed infants

DISCUSSION

A recent systematic study suggests limited evidence for SARS-CoV-2 vertical transmission [27]. An April 11, 2020 study observed higher IL-6 levels in pregnant women with SARS-CoV-2 compared to non-pregnant women, impacting fetal development [28]. Maternal immune activation may increase susceptibility to environmental exposures and epigenetic changes, potentially leading to disease-related symptoms [29].

Past experiences indicates that maternal infections during pregnancy are associated with adverse pregnancy outcomes, affecting fetal growth and development, potentially leading to intrauterine growth retardation, congenital anomalies, and impaired child development. COVID-19 presents with a range of symptoms across all age groups with varying severity. SARS-CoV-2, the virus causing COVID-19, has evolved into multiple variants and spread worldwide. COVID-19 affects pregnant women, leading to preterm deliveries and neonatal intensive care unit admissions. Further research is needed to understand the impact of intrauterine exposure to COVID-19 on neonatal growth and development. Inconsistent results in perinatal transmission studies may be due to virus variants and population immunization rates [30].

Beyond pediatric COVID-19 cases, the pandemic may have negative implications for child health. Diverted resources from maternal and child healthcare programs can harm prenatal and early childhood health. India, which had a pre-existing issue of child under nourishment, may experience setbacks due to the pandemic. In 2016, it was estimated that 36% of India's under-5 population was underweight, a decline from 43% in 1998–1999. However, the COVID-19 pandemic may reverse this progress [31].

In 118 low- and middle-income countries (LMICs), 253,500 infant deaths and 12,200 maternal deaths may have resulted from the pandemic's reduced access to antenatal and postnatal care, immunization, and preventive child healthcare during the six months beginning in May 2020, according to a modelling study by Roberton T et al [32].

In a study conducted by Nuzhat et al. [33] in Dhaka, Bangladesh, the health of 9,290 hospitalized under-5 children before and during the pandemic was compared, revealing worse health outcomes. These included a higher risk of dehydration, severe sepsis or septic shock, convulsions, hypernatremia, elevated creatinine levels, as well as an increase in stunting, wasting, and mortality in infants younger than six months.

Limitations

Our study faced certain limitations like smal overall sample size, significant difference between sample size of exposed and non-exposed infants, lack of representativeness of sample, lack of standardization in terms of geographic area, ethnic or sociocultural practices. There could be presence of counfounders and modifiers not

measured by us which could possibly be a source of bias. Hence further studies are warranted considering the above loopholes.

CONCLUSION

Our study's statistical evidence suggests that infants aged 5-7 months born during the COVID-19 pandemic, with or without in utero exposure to maternal SARS-CoV-2 infection, experience notable declines in anthropometric measurements. In utero exposure to COVID infection exacerbates these effects. This cross-sectional study in our tertiary hospital underscores the need for comprehensive multicentric research, encompassing diverse population subgroups based on race, geography, and other factors. Such research will enhance our understanding of its global impact and the lasting effects on children born during the COVID-19 pandemic. Future cohort studies should investigate its long-term impact on future generations' growth and development and identify necessary steps to mitigate potential consequences. These studies will also explore correlations between maternal disorders, aside from infections, and their impact on fetal development.

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