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Original Article (Pages: 17558-17571)

Comparing the Growth and Development of Six Months Infants between the Mothers With/Without Covid-19 during Their Pregnancy

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Abstract

Background: Viral infection during pregnancy induces pro-inflammatory cytokines and increases the level of IL-6, which as a measure of the inflammation of the mother's immune system is effective on the development of the brain of the fetus and increases the rate of mental disorders of the fetus. The possible effect of the mother's COVID-19 on children, if any, is still unknown. Therefore, this study was conducted with the aim of investigating and comparing the consequences of neurodevelopment and growth at the age of 6 months in infants among mothers with/without exposure to COVID-19 during pregnancy in Birjand, 2021.

Methods: A total of 161 pregnant women with PCR-positive coronavirus and 181 pregnant women without infection were selected by simple random sampling. Demographic characteristics including age, occupation, education, gender, nationality, sex of babies, along with data related to the neurodevelopmental status of infants by the use of ASQ questionnaire were extracted and entered into SPSS 16 software. For descriptive statistics, Mean, standard deviation, and frequency distribution tables were used, and inferential analyses were conducted by the use of Chi-square, t-test, and analysis of variance at a significance level of less than 0.05. The disturbance was equal / lower than 1 SD in each of ASQ-3 score domains.

Results: In this cohort study, demographic characteristics in the exposed and unexposed groups were not significantly different. There was no statistically significant difference between the average score of the ASQ_3 questionnaires as well as the average score in the areas of communication, gross motor, fine motor, problem-solving, and social personality among infants born from mothers with and without COVID-19. Also, there was no significant difference in the incidence of disorders in different fields of neurodevelopment, except for the field of establishing communication between the two groups of exposed and unexposed. On the other hand, cesarean delivery was significantly higher in pregnant mothers with COVID-19 during pregnancy. However, there was no significant relationship between the incidence of COVID-19 and the rate of premature delivery, and low birth weight neonates. In addition, the severity and time of the corona infection during pregnancy did not have any significant effect on the neurodevelopment of infants with intrauterine exposure to COVID-19.

Conclusion: According to the results of the study, infection with COVID-19 does not increase the incidence of developmental disorders in 6-month-old infants. Furthermore, it does not increase low

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Received date: Dec.24,2022; Accepted date: Apr.13,2023

birth weight and premature delivery. Due to the limitations of the study, it is suggested to conduct a study with a larger number of pregnant mothers with a severe form of the disease, especially in the first trimester of pregnancy, and to follow up with the babies at an older age.

Key Words: ASQ-3 questionnaire, COVID-19, Frequency, Growth and Development, Infant, Neurodevelopment, Pregnancy.

* Please cite this article as: Namakin K, Saadatinasab Z, Salehiniya H, Zardast AH. Comparing the Growth and Development of Six Months Infants between the Mothers With/Without Covid-19 during Their Pregnancy. Int J Pediatr 2023; 11 (04):17558-17571. DOI: **10.22038/ijp.2023.69768.5148**

1- INTRODUCTION

After the detection of the first case of COVID-19 in 2019 in Wuhan, China, and its global spread, the World Health Organization (WHO) declared a public health emergency and then a pandemic in March 2020 (1). The transmission rate of SARS-COV-2 is similar to SARS-COV (0.03) around 2-3% and the mortality rate is 2% and much lower than SARS-COV (9.6%) (2, 3).

Pregnancy is a special situation in which various immunological-endocrine mechanisms under the influence of progesterone occur to protect the fetus from immune activation and expulsion. The predominant physiological changes, while favorable for the fetus, make the mother sensitive to infectious pathogens and make pregnancy challenging during COVID-19. The possible effect of mothers' infection with COVID-19 on children, if any, is still unknown. However, the profound activation of the immune system, even in the absence of placental infection, the developing fetal brain may be affected due to maternal and placental inflammation and changes in cytokine expression during the significant period of development (4, 5).

On the other hand, as intrauterine viral infection induces pro-inflammatory cytokines (6), pregnant women with COVID-19 infection have a higher level of interleukin 6 (IL-6) than non-pregnant women. Interleukin 6, as a measure of the inflammation of the mother's immune system, affects the mutual relationship between the fetus and the placenta, and consequently, the brain development of the fetus and increases the risk of psychological disorders in the child. On the other hand, interleukin 6 has a negative effect on the child's cognitive status at the age of 12 months, which indicates the effect of maternal inflammation in causing neurodevelopmental disorders (7). Also, the mother's psychosocial stress can increase inflammation and change hormones related to the hypothalamus-pituitary-adrenal axis and affect the etiopathogenesis of the child's neurodevelopmental disorders (8).

Mode of delivery, low birth weight, preterm delivery, cesarean section, adverse pregnancy outcomes, and vertical transmission have been reported as the consequences of a pregnant mother contracting a COVID-19 infection (9). Maternal health problems, such as vitamin D deficiency, increase preterm delivery in COVID-19-positive patients (10, 11). Pregnant women are at a higher risk for severe complications from COVID-19 and are more likely to be mechanically ventilated and hospitalized in the intensive care unit (ICU) than non-pregnant women, and are exposed to severe complications and mortality from viral infections (12).

Furthermore, viral infections during the entire period of pregnancy can lead to various pregnancy complications such as maternal death, pregnancy loss, and premature birth. Fetal and neonatal abnormalities related to viral infections during pregnancy, especially those causing vertical transmission, can cause IUGR,

stillbirth, microcephaly, movement disorders, and other neurodevelopmental disorders (13-16). In addition, children who are exposed to maternal infectious diseases during pregnancy also face lifelong health problems (16). Furthermore, the stress of worry and anxiety during pregnancy is often associated with intrauterine growth restriction or preterm delivery (17). With the spread of the COVID-19 pandemic, the number of infected pregnant women has increased; thus, concern has increased for mothers and their infants (18).

Considering all the mentioned cases and the newness of this disease, this study was designed with the aim of investigating the consequences of exposure with COVID-19 during pregnancy and its effects on fetal neurodevelopment. Through identifying these factors and taking effective measures, the complications and difficulties of this risky situation on the health of the mother and fetus may be reduced.

2- MATERIALS AND METHODS

2-1. Design and population

This study was conducted using a retrospective cohort method with the population of pregnant women living in Birjand during the second half of 2020 and 2021. Pregnant mothers who were infected with COVID-19 during pregnancy and whose infection was confirmed by PCR test were included in the study along with their infants as the exposure group (exposed). Also, pregnant mothers who did not have symptoms of Covid-19 and positive PCR test during pregnancy and their infants were considered as the non-infected group (non-exposed).

2-2. Inclusion and exclusion criteria

Pregnant mothers without uncontrolled underlying disease, including untreated hypothyroidism, untreated high blood pressure, etc., were included in the study. Infants with underlying diseases such as, perinatal asphyxia, confirmed sepsis like symptoms, viral disease in pregnancy (toxoplasmosis, rubella, cytomegalovirus, herpes and other agents (TORCH)), as well as critically ill and intubated infants in NICU were excluded from the study.

2-3. Sampling

Based on the study of Shuffrey et al. (11), with the prevalence of disorder in two groups of 5 and 14% respectively, and considering the study power of 80% and the confidence limit of 95%, the sample size in each group was 166 people.

The list of live births in 2021 and the status of the mother's infected or not with COVID-19 was extracted from the Sib system of Birjand health center. Then random sampling was done until the required sample size was reached based on the inclusion and exclusion criteria of the study.

2-4. Data collection tool

The required data was collected by basic information checklist and ASQ questionnaire. Basic information of babies and expectant mothers included age, education, mother's occupation, time of mother’s exposure to COVID-19, type of delivery, gestational age at delivery, COVID-19 treatment, gender of the infant, weight of the infant, etc. The ASQ-3 standard questionnaire was used to examine the neurodevelopmental status of infants; and the validity and reliability of this instrument has been confirmed in various studies (19, 20). Its reliability estimates ranged from 0.78 to 0.95 by Cronbach’s alpha (21).

The ASQ questionnaire examines the development process in five areas of fine movements, gross movements, problem solving, communication and personal-social areas. It contains 30 questions in the 5 developmental areas:

a) The field of communication: what the child understands from the conversation of the people around him and what he can express, such as humming, making noises from the mouth, listening and understanding the meaning of what is said, and expressing words and sentences.

b) The Field of gross movements: movements and coordination between the large muscles of the body, such as the movements of the trunk, arms and legs.

c) The field of fine movements: movements and coordination between small muscles of the body, such as fine movements of hands and fingers.

d) Problem solving field: child's learning and playing with toys

e) Personal-social field: Establishing the type of relationships and the type of interaction between the child and his toys, other children and adults, in individual games, collective games, and cooperation with others (social work).

The answer "yes" to each question gets 10 points, the answer "sometimes" gets 5 points and the answer "not yet" gets 0 points. The cut-off points for each age are recorded in two columns "one standard deviation below the mean" and "two standard deviations below the mean". After summarizing the scores in each developmental area and comparing them with the cut-off points of the desired age group, a decision is made regarding appropriate measures (need for referral, need for practice and re-examination and acceptable) (22, 23). In this study, a score of equal to/ lower than 1 SD was considered a disorder.

2-5. Study implementation method

After obtaining initial permits to start the work, the list of live births and their mothers and the status of mothers with COVID-19 was extracted from the electronic health file in the Integrated Health System of Birjand health center, known as SIB.

More information about mother's symptoms during the time of COVID-19 exposure during pregnancy and, the time of COVID-19 exposure during pregnancy, was asked in the form of oral questions, in phone calls to the mothers. Information about weight, type of delivery, etc. was extracted from the infant's file at the time of birth.

In mothers who were infected with COVID-19 in the last month of pregnancy and before labor, 48 hours after giving birth, the status of COVID-19 infection of the infant was determined by performing a PCR test for the infant in order to determine the complications in these children. The infection could be caused by the infants' direct contact with the virus or due to the disorders caused by the mother's infection during pregnancy and the intrauterine exposure of the infant to COVID-19. Then, at the age of six months, the ASQ questionnaire was completed in comprehensive health centers by healthcare workers.

2-6. Ethical considerations

This study was approved by the Ethics Committee of Birjand University of Medical Sciences with the code of ethics IR.BUMS.REC.1401.102. In addition, Verbal consent was obtained from the mothers before the start of the study and they were assured that the information would be published anonymously.

2-7. Data analysis

Data analysis was done using SPSS 16 software and describing qualitative data were described as numbers and percentages and quantitative data as means and standard deviations. Inferential data analysis was performed using Chi-square, Independent t-test, and One-way ANOVA statistical tests at a significance level of less than 0.05.

3- RESULTS

Among the 342 participants, 161 were in the exposed group (pregnant mothers infected with COVID-19 during pregnancy) and 181 were in the non-exposed group (pregnant mothers were not infected with COVID-19 during pregnancy).

According to group matching in terms of age, the average age in the exposed group was 29.34±5.22 and in the non-exposed group, it was 29.96±5.76. In terms of other basic information such as occupation (p=0.759), education (p=0.831), Iranian/non-Iranian citizenship (p=0.821), birth of a male infant (p=0.293), and underlying diseases, there was not any statistically significant difference between two groups. More details are presented in **Table 1**.

For 8 babies, due to the mother's infection with corona in the days leading up to delivery, PCR test was performed in the first 48 hours of birth, and the results were negative.

Table-1: Comparison of demographic and basic information of participants by group

Characteristic			Group		P-value
			Exposed (161)	Non-exposed (181)	
Age(year) (±μ SD)			29.34± 5.22	29.96± 5.76	0.300*
Job (number (%))		Housewife	136 (84.5%)	156 (86.2%)	0.759**
		Employee	25 (15.5%)	25 (13.8%)	
Education (No (%))		Illiterate and primary school	9 (5.6%)	13 (7.2%)	0.831**
		Secondary and high school	66 (41/0%)	72 (39.8%)	
		University	86 (53.4%)	96 (53.0%)	
Citizenship (No (%))		Iranian	158 (98.1%)	177 (97.8%)	0.821**
		Non-Iranian	3 (1.9%)	4 (2.2%)	
Infant’s gender (No (%))		Girl	63 (39.1%)	81 (44.8%)	0.293**
		Boy	98 (60.9%)	100 (55.2%)	
Underlying disease history (No (%))	Diabetes	Non-Diabetes	144 (89.4%)	158 (87.3%)	0.807**
		Gestational Diabetes	16 (9.9%)	22 (12.2%)	
		Chronic Diabetes	1 (0.6%)	1 (0.6%)	
	Hypertension	Yes	3 (1.9%)	3 (1.9%)	0.885**
		No	158 (98.1%)	178 (98.3%)	
	Hypothyroid	Yes	26 (16.1%)	36 (19.9%)	0.370**
		No	135 (83.9%)	145 (80.1%)	
Inflectional disease history during pregnancy (No (%))		Yes	0 (0.0%)	0 (0.0)	-
		No	161 (100.0%)	181 (100.0%)	

* t-test, **chi- square

Based on the results of the statistical analyses, 6.8% of pregnant women in the exposed group and 6.1% in the non-exposed group had premature birth (before the 37th week of pregnancy), not showing a significant difference (p=0.776). Also, 6.8% of the pregnant mothers in the exposed group and 1.6% in the non-exposed group had an infant weighing less than 2500 grams, which was not statistically significant (p=0.470). A total of 50.3% in the exposed group, and 39.2% in the non-exposed group had cesarean delivery, which was statistically significant

(p=0.039) and a higher percentage of pregnant mothers who were infected with COVID-19 during pregnancy compared to mothers who were not infected during pregnancy, experienced cesarean delivery (**Table 2**).

Table-2: Comparison of the frequency of premature delivery, low birth weight, and type of delivery in exposed and unexposed groups

Characteristic		Group		* P-value
		Exposed (161)	Non-exposed (181)	
Gestational age at delivery	Before 37 Weeks (preterm delivery)	11 (6.8%)	11 (6.1%)	0.776
	≥37 weeks	150 (93.2%)	170 (93.9%)	
Weight of infants at delivery time (M±SD)	Less than 2500 grams	13 (8.1%)	11 (6.1%)	0.470
	≥2500 grams	148 (91.9%)	170 (93.9%)	
Type of delivery (Number (%))	NVD	80 (49.7%)	110 (60.8%)	0.039
	C/S	81 (50.3%)	71 (39.2%)	

*chi- square

Among the participants, 0.6% of the infants born to mothers with COVID-19 during pregnancy had communication disorders, while in infants whose mothers were not infected with COVID-19 during pregnancy, this rate was 4.4%, which was significantly higher (p=0.028).

In the field of gross motor, 1.2% of infants born to mothers in the affected group had disorders while the percentage was 1.7% in the non-exposed group and this difference was not statistically significant (p=0.749).

In the field of fine motor, 5% of the infants born to mothers in the affected group were impaired and this was 2.8% in the non-exposed group, which were not significantly different (p=0.287).

In the field of solving the problem, 0.6% of the infants born to the mothers of the affected group had disorders. This rate was 1.7% in the non-exposed group and this difference was not statistically significant (p=0.374).

In the field of fine motor, 1.2% of infants born to mothers in the affected group had disorders. This rate was 2.2% in the non-exposed group which was not statistically significant (p=0.496).

Therefore, it can be concluded that the mother's infection with COVID-19 during pregnancy does not significantly cause disorders in the infant regarding the different fields of the ASQ questionnaire (except the communication field). 4.4% of non-exposed neonates showed disorder in the communication field, while this rate was 0.6% in the exposed group. The summary of the results is given in **Table 3**.

The average score of the communication field in infants born to mothers with and without COVID-19 during pregnancy was 55.99±5.30 and 54.94±6.35, respectively. This score difference was not statistically significant (p=0.100).

In the field of gross motor, the average score in infants born to mothers with COVID-19 in pregnancy was 53.56±7.96 and in infants born to non-infected mothers was 53.40±7.74. Therefore, no significant difference was observed between the two groups (p=0.850).

Table-3: Comparison of the frequency of disorders in the ASQ questionnaire by field in the exposed and unexposed groups

Disorders		Group		*P-value
		Exposed (161)	Non-exposed (181)	
Disorder in field of Communication	yes	1 (0.6%)	8 (4.4%)	0.028
	no	160 (99.4%)	173 (95.6%)	
Disorder in field of gross motor	yes	2 (1.2%)	3 (1.7%)	0.749
	no	159 (98.8%)	178 (98.3%)	
Disorder in field of fine motor	yes	8 (5.0%)	5 (2.8%)	0.287
	no	153 (95.0%)	176 (97.2%)	
Disorder in field of solving problems	yes	1 (0.6%)	3 (1.7%)	0.374
	no	160 (99.4%)	178 (98.3%)	
Disorder in Social-personal field	yes	2 (1.2%)	4 (2.2%)	0.496
	no	159 (98.8%)	177 (97.8%)	

*chi- square

In the field of fine motor, the average score in infants born to mothers with and without COVID-19 during pregnancy was 58.12±4.20 and 57.58±4.30, respectively; but this score difference was not statistically significant (p=0.100).

Although in terms of solving the problem, the average score in infants born to mothers infected with COVID-19 during pregnancy was higher than the average score in infants born to non-infected mothers (57.57 ± 4.30 and 56.93 ± 5.15, respectively); however this difference was not significantly different (p=0.213).

Also, the average score of personal social field in infants born to mothers infected with COVID-19 in pregnancy was higher than the average score in infants born to non-infected mothers (56.11 ± 5.91 and 55.55 ± 6.38, respectively), which was not statistically significant (p=0.406).

In general, no significant difference was observed (p=0.324) between the average score of ASQ in infants born to exposed mothers (281.36 ± 20.39) and the average score of infants born to non-exposed mothers (279.14 ± 21.06).

Therefore, it can be concluded that the mother's infection with COVID-19 during pregnancy does not have a significant effect on the average total score and the score of the different areas of ASQ questionnaire of infants. Summary of the results is given in **Table 4**.

Table-4: Comparison of the average scores in ASQ questionnaire fields in the exposed and non-exposed groups

ASQ Neurodevelopmental Fields	Group		*P-value
	Exposed (161) (Mean ±SD)	Non-exposed (181) (Mean ±SD)	
Communication field	55.99± 5.30	54.94± 6.35	0.100
Gross movement field	53.56± 7.96	53.40± 7.74	0.850
Fine movement filed	58.12± 4.20	57.58± 4.30	0.648
Problem solving field	57.57± 4.30	56.93± 5.15	0.213
Social-personal field	56.11± 5.91	55.55± 6.38	0.403
Total score	281.36± 20.39	279.14± 21.06	0.324

*t-test

143 pregnant mothers who were infected with COVID-19 during pregnancy received the necessary treatments on an outpatient basis, while 18 were admitted to internal wards or ICU. The average score of ASQ in infants whose mothers were treated on an outpatient basis during pregnancy due to COVID-19 infection was higher than that of infants whose mothers were hospitalized due to COVID-19 infection (281.49 ± 20.67 vs. 280.28 ± 18.51), but this observed difference was not statistically significant (p=0.812). (**Table 5**)

Therefore, it can be said that the severity of COVID-19 infection during pregnancy does not affect the average ASQ score of infants.

A total of 124 pregnant mothers were infected with COVID-19 during 0 to 14 weeks of pregnancy, 57 during 14 to 28 weeks of pregnancy and 75 after 28 weeks of pregnancy. The average score of ASQ in infants whose mothers were infected with COVID-19 in the period of 0 to 14 weeks of pregnancy (286.58±15.44) was higher than that of the infants whose mothers were infected with COVID-19 in the 14 to 28 weeks of pregnancy (280.96±20.78) and infants whose mothers were infected with COVID-19 after the 28th week of pregnancy (279.82±21.39), but this difference was not statistically significant (p=0.363) (**Table 5**). Therefore, it can be said that the time of getting infected with COVID-19 during pregnancy does not affect the average ASQ score of infants.

Table-5: Comparison of ASQ average scores in infants of the exposed mothers, based on severity and time of infection

Covid 19 infection		Number (%)	ASQ score (Mean ±SD)	Test statistics	*P-value
Severity of infection	Outpatient treatment	143 (88.8%)	281.49± 20.67	0.238	0.812*
	hospitalization	18 (11.2%)	280.28± 18.51		
Time of infection	0-14 gestational weeks	24 (14.9%)	286.58± 15.44	1.019	0.363**
	14-28 gestational weeks	57 (35.4%)	280.96± 20.78		
	28 w to end of pregnancy	75 (46.6%)	279.82 ± 21.39		

*t-test, ** One-way ANOVA

4- DISCUSSION

This cohort study aimed at investigating and comparing the outcomes of growth and development at the age of six months in infants of mothers with/without COVID-19 during pregnancy during 1400, in Birjand, using the ASQ questionnaire. According to the results, cesarean delivery was significantly higher in pregnant mothers affected with COVID-19 during their pregnancy (60.8% vs. 39.2%, p=0.039). This result is consistent with that of the study by Piekos et al. (2022) (24), while in the study of Capretti et al. (2022) (25) and Zlatkin et al. (2020) (26), the cesarean rate did not differ between women with and without infection. Risk factors for cesarean section in mothers with COVID-19, older age and higher rate of comorbidities, in vitro fertilization and multiple pregnancies have been reported (27). Due to the possibility of vertical transmission of infection from mother to fetus during pregnancy or during childbirth, reported as 39.6% (28), prevention or fear of infection transmission to the fetus can be considered as one of the reasons for the high rate of

cesarean delivery in mothers with COVID-19 (29).

According to the results of the current study, the rate of infection with COVID-19 does not increase the rate of premature delivery (p=0.568). The results of previous studies have been different regarding the difference in the rate of cesarean delivery in pregnant mothers infected with COVID-19 (25, 26, 30-33). In the study by Capretti et al. (2022) (25), Zlatkin et al. (2020) (26) and Yang et al. (2020) (34) preterm delivery rates between women with and without COVID-19 was not significant. In contrast, in the study by McClymont et al. (2022) (33), the risk of preterm delivery was significantly higher among pregnancies with COVID-19 (11.05% vs. 6.76%; relative risk, 1.63 [95% CI, 1.52-1.76]).

In the present study, there was no statistically significant difference in having low birth weight newborns (less than 2500 grams) between the two groups of pregnant mothers with or without COVID-19 during pregnancy. This is in agreement with the study by Yang et al. (2020) in China, finding no statistical difference in low birth weight between mothers with and without COVID-19 (34). But in the study by Piekos et al. (2022), pregnant mothers with COVID-19 had babies with lower birth weights; especially in case of infection in the third trimester of pregnancy (24). It seems that having a moderate or severe form of COVID-19 and increasing the birth rate will increase the risk of premature birth and low birth weight (35).

In this study, it was observed that the mother's infection with COVID-19 during pregnancy has no significant effect on the neurodevelopment of infants, and the average score of the ASQ fields, except for the field of communication.

Shuffrey et al. (2022) also did not report significant differences in different domains of ASQ_3 in infants with and without maternal infection with COVID-19 at six months (11). In another study, it was shown that the experience of the 2020 pandemic was associated with a higher risk of delays in fine motor and communication domains at one year of age. The relationship between pandemic experience and communication delay at one year of age only existed in first-born children, and no relationship was observed in any fields at six months (36). Munian et al. (2021) also reported no significant difference in terms of neurodevelopment and re-hospitalization in early infancy between infected/uninfected children of COVID-19-positive mothers (37). While it was reported that infection in the third trimester of pregnancy is associated with more diagnosis of neurodevelopmental disorders (4). In addition, in a national study in Kuwait, 3.3 % delay in communication, 27% delay in gross motor, 40% delay in fine motor, 10% delay in problem solving and 30% delay in personal social field were found. In that study, the mother's gestational age in infants with developmental delay was different from infants without developmental delay. Developmental delay was more common in babies born to infected mothers in the first and second trimester of pregnancy than in babies born to mothers with COVID-19 in the third trimester. Also, the probability of developmental delay in gestational ages less than 31 weeks was higher than that in gestational ages above 31 weeks (6).

A study in China also reported that infants of mothers with COVID-19 during pregnancy had lower scores in communication, gross motor, fine motor, problem solving, and personal-social fields. However only the range of fine motion was statistically significant (P = 0.031) (38).

In the present study, there was no correlation between the severity of the

disease and the time of the mother's COVID-19 infection and the occurrence of neurodevelopmental disorders in infants up to 6 months of age. The results of the current study are consistent with the results of the study of Shuffrey et al. (2022) (11), but considering that one of the causes of the disorder in the neurodevelopment of the newborn is the level of interleukin 6 intake (39-41), finding no relationship between the mother's infection and the newborn's disruption in this study can be attributed to the high proportion of mild form of infection among the pregnant mothers under study (88.9%) (11); and, the amount of interleukin 6 was not investigated in this study.

Nonetheless, it seems that the COVID-19 infection, like other infectious diseases (measles and rubella) in the first trimester of pregnancy, should have a greater effect on the neurodevelopment of the infant (42-44).

Moreover, it seems that the low number of infections in the first trimester of pregnancy (14.9%) might have also affected the findings regarding the insignificant relationship between the time of mother's infection with COVID-19 disease and neurodevelopmental disorder in this study.

5- CONCLUSION

According to the results of the study, infection with COVID-19 does not increase the incidence of developmental disorders in 6-month-old infants. Also, it does not increase low birth weight and premature delivery. But the rate of cesarean delivery increases significantly.

6- LIMITATIONS OF THE STUDY

Considering the limited number of mothers and infants participating in the study and the time of the ASQ-3 screening test, it would be possible to achieve more reliable and accurate results, if the study was conducted with a larger number of pregnant mothers and infants. Regarding the manifestation of some neurological disorders at an older age, it is suggested that ASQ-3 growth and development assessment tests be conducted at the age of one year and older. In addition, in several studies, low birth weight has been investigated as an independent risk factor (45, 46), which in this study due to the small number of samples, it was not possible to divide the participants into more groups for comparisons.

Also, considering that the ASQ questionnaire is completed by the child's mother or nurse, one of the most important limitations of this study is the accuracy of the information provided, especially, due to the doubts of the mothers while completing the questionnaire.

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