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Original Research Article

The effect of previous and current COVID-19 infections on amniotic fluid index

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ABSTRACT

Background: COVID-19 infection had a multisystem effect. Although it does not cross the placenta, it can cause conformational changes that affect placental function, with the possibility of a change in amniotic fluid index and the development of oligohydramnios. The aim of the study is to estimate the effect of COVID-19 previous and current infections on the amniotic fluid index.

Methods: A prospective case-control study was conducted in a major maternity hospital from the 1st of April 2021 to the 1st of October 2021. 125-term pregnant ladies early in labor and had been diagnosed with COVID-19, either current or previous infection (according to serology testing IgG and IgM) were considered the case group, and 125-term pregnant ladies in labor but without COVID-19 infection as a control group. A transabdominal ultrasound was done to measure the amniotic fluid index for comparison between groups.

Results: Cases of previous infection had a reduced level of amniotic fluid index (mean 9.98 ± 4.93), which is statistically significantly lower than both the current infection and control, and the amniotic fluid index of the current infection was not different statistically from the control. Finally, it is 4.48 times more common to develop oligohydramnios if the patient had previous COVID 19 infection (odd ratio 4.48, 95% CI 10.87-1.85).

Conclusion: The previous COVID-19 infection is significantly associated with decreased AFI.

Keywords: SARS-CoV-2, Amniotic fluid index, Oligohydramnios, Serology testing, COVID-19

INTRODUCTION

SARS-CoV-2 is a highly contagious virus that can be transmitted through various means.^{1,2} The Changes that occur in pregnancy lead to increased oxygen consumption and decreased both functional residual capacity and chest compliance, making women more susceptible to respiratory pathogens and severe pneumonia.³ The centres for disease control and prevention (CDC) stated that pregnant women diagnosed with COVID-19 have a higher probability of requiring hospitalization, intensive care unit admission, and intubation.⁴ Several studies have demonstrated the impact of SARS-CoV-2 on placental histopathology in pregnant women who were infected with the virus during their third trimester. The placental

histopathology findings included chorioangioma, multifocal infarctions, and varying degrees of intervillous or subchorionic fibrin, which were associated with increased syncytial nodules.⁵ Additionally, in a group of seven patients, placental weight was found to be below the 5th percentile, and two of them had abnormal pathology results showing thrombotic vasculopathy with avascular fibrotic villi and/or placental infarct.⁶

In cases where the infection occurred at least one month before delivery, two out of three fetuses (33%) showed fetal growth restriction accompanied by oligohydramnios, which was found to be associated with the abnormal placentas mentioned earlier.⁷ In Zhu et al's retrospective study, it was discovered that cases of SARS-cov-2

infection were associated with abnormal levels of amniotic fluid.⁸ Oligohydramnios is a condition characterized by abnormally low volume of amniotic fluid, typically below 500 ml, occurring between the 32nd and 36th weeks of pregnancy, and is considered a serious condition for both the foetus and the mother.⁹

Ultrasound examination during the second or third trimester can diagnose oligohydramnios, which is characterized by an amniotic fluid index (AFI) below 5 cm or below the 5th percentile, and indicates a reduced volume of amniotic fluid.¹⁰ Is to estimate the effect of COVID-19 previous infection in the current pregnancy and current infection on amniotic fluid index.

METHODS

Study type

A prospective case control study conducted in Al-Elwiya Maternity Teaching Hospital during period extended for six months from 1st of April 2021 to the 1st of October 2021.

A one hundred and twenty-five pregnant ladies in early labor admitted to labor room or operative theater, who had been diagnosed with SARS-CoV-2 either current or previous infection (according to serology testing) and after obtaining full history and clinical examination, the patients interviewed with predesigned form that includes maternal age, gestational age, date of symptoms onset, parity, ultrasound estimation of amniotic fluid index, pregnancy outcome, serology results of mother on admission.

Other one hundred and twenty-five pregnant ladies with matched gestational age and in early labor, without SARS-CoV-2 infection (negative symptoms, negative ELISA and negative family history of infection) included to be control group for comparison purposes.

Inclusion criteria

Pregnant women (between 37 and 40 weeks) with SARS-CoV-2 infection confirmed by ELISA both current and previous infection, that were admitted for delivery. Cases with chronic diseases (diabetes, hypertension, etc), chronic drug use, birth defects, stillbirth, pregnancy induced conditions (preeclampsia, eclampsia, etc), and preterm cases.

AFI measurements

All cases were reviewed by same radiologist using the same ultrasound device (Philips HD11 XE Germany) the ultra-sonographic measurements were performed. Amniotic fluid index was calculated by measuring the maximum vertical diameter of 4 pocket, considering 5-25 cm as normal reference. A femur length was also being recorded.

Laboratory analysis

All cases had estimation of SARS-CoV-2 antibody titer using (Roche - cobas e 411 analyzer- Germany) at Al-Elwiya Maternity Teaching Hospital, main laboratory.

Patients with positive serology for IgG and negative serology for IgM had been considered as previous infection, while positive results for IgM, regardless IgG result, were considered active infection. Gestational age was calculated from last menstrual cycle or measurement of femur length of current ultrasounds or crown rump length from previous ultrasound in early pregnancy.

Ethical considerations were taken into account throughout the study. The study proposal was thoroughly reviewed and approved by the scientific and ethical committee of the Arabic Board of Obstetrics and Gynaecology, as well as the scientific committee of Al-Elwiya Maternity Teaching Hospital. Informed consent was obtained from each participant after providing a detailed explanation of the study's objectives, with a guarantee that the collected data would only be used for research purposes and would remain anonymous.

The data collected for the study was input into a Microsoft Excel worksheet and analysed using IBM-SPSS V26. Descriptive statistics, such as frequencies, means, and standard deviations, were presented in tabular form. The significance of categorical data was estimated using Chi-square and Fisher's exact tests, while non-parametric data was analysed using the student t-test and Mann-Whitney U test.

Based on the serology results, the participants were divided into three groups, group A (currently infected), group B (previously infected), and group C (control). The study aimed to estimate the effect of current and previous SARS-CoV-2 infection on AFI and compare the results to normal pregnant women without infection. Additionally, the study aimed to compare the effect of previous and current infection on AFI. A P value of less than 0.05 was considered significant.

RESULTS

A two hundred and fifty cases were enrolled in the study, of them 62 cases (24.80%) had previous COVID 19 infection and considered as group A, 63 cases (25.20%) had current infection and considered as group B and 125 cases (50%) were healthy pregnant women without COVID-19 infection and considered as the control group (group C).

Demographical data

The three groups were not different in regard to age, parity and gestational age. Amniotic fluid index of cases of previous infection had the lowest AFI (mean 9.98 ± 4.93) which is statistically significantly lower than both groups

B and C. while AFI of group B were not different statistically from group C. The incidence of cases of oligohydramnios was 11.6% in general and it was more in cases of Group A which is statistically significantly higher rate than both groups B and C, nevertheless incidence of

cases of oligohydramnios of group B were not different statistically from group C. Finally, it would be 4.48 time common to develop oligohydramnios if the patient had previous COVID-19 infection (odd ratio 4.48, 95% CI 10.87-1.85) (Table 1).

Table 1: Distribution of data according to the groups of the study.

Variables	Group A	Group B	Group C	P value*		
	n=62	n=63	n=125	P1	P2	P3
Maternal age (years) †	25.02±4.82 (19-46)	25.98±3.36 (18-32)	25.53±4.26 (17-42)	0.056	0.295	0.356
Parity†	3±2.2 (0-7)	2.97±2.29 (0-6)	3.1 ±2.26 (0-4)	0.887	0.798	0.681
Gestational age (weeks) †	37.67±1.75 (38.8-40)	37.93±1.72 (38.7-40)	37.46±1.67 (38.2-40)	0.425	0.44	0.072
Amniotic fluid index (cm) †	9.98±4.93 (2-19)	14.73 ±5.96 (3-25)	16.02±6.51 (3-27)	<0.001	<0.001	0.178
Oligohydramnios‡	Yes	16 (25.8)	4 (6.3)	0.003	0.001	0.546
	No	46 (74.2)	59 (93.7)			

*P1 represents the difference between group A and B; P2 represents the difference between group A and C; P3 represents the difference between group B and C. †Data presented in the form of mean±standard deviation (minimum to maximum). ‡ Data presented in the form of count (percentage).

DISCUSSION

Novel Coronavirus infection is an emerging, rapidly changing global health challenge affecting all health sectors.¹¹ There are many unknowns for pregnant women during COVID-19 pandemic, but still the risk factors for severe COVID-19 are similar in pregnancy to the general population. With Asymptomatic infection in pregnancy appears to be common, but is of uncertain clinical significance.¹²

Oligohydramnios, defined by ACOG guidelines as ultrasonographical measurable vertical pocket of amniotic fluid greater than 2 cm or an amniotic fluid index of 5 cm or less, requires (depending on the degree of oligohydramnios, the gestational age and the maternal clinical condition) delivery, or close maternal or fetal surveillance.¹³

Patients included in this study were those presented to our hospital for obstetrical causes, with mild to moderate COVID-19 symptoms, as cases of severe COVID-19 infection were not admitted in our hospital thus not included in this study.

In this study we found that previous infection (IgG positive) associated with decreased birth weight, while current infection does not have this effect, this suggesting a chronic pathological process leading to this effect, that as explained by Wong et al that IUGR, low birth weight and other complications, happened in cases of COVID-19 infected placentae which showed common histological features, that include maternal vascular mal-perfusion, inflammation and Fetal vascular mal-perfusion, a processes that are time consuming not expected to occur in acute settings.¹⁴ While Giuseppe et al, also found no

statistical significance between cases of acute infection and control in regards to birth weight.¹⁵ The mean amniotic fluid index was lower in cases of previous COVID-19 infections than current and control. To our knowledge this result was not investigated by other studies in literature to be compared with.

The rate of oligohydramnios was 25.80% in cases of previous infection a significantly higher rate than current infection and control, with odd ratio of 4.48. while current infection was not different statistically in term of the rate of oligohydramnios.

In study conducted by Patberg et al¹⁶ they found the rate of oligohydramnios to be 7.8% in cases of current COVID-19 infection and it is statistically different from control, this result explained by their inclusion of severe cases of COVID-19 infection which may have additional effect on the AFI and thus the rate of oligohydramnios. According to the study conducted by Elizabeth et al, there is a correlation between COVID-19 infection and an increase in placental histopathologic abnormalities, particularly vascular malperfusion. The study's findings were consistent among COVID-19 positive patients regardless of their symptoms.¹⁷ Prabhu et al conducted a comparable study and reported increased occurrence of fetal vascular malperfusion in individuals with covid-19 infection¹⁸ Although no abnormalities were observed in the placental histopathology in either case, the possibility of vascular malperfusion as a cause of oligohydramnios should be considered. Notably, oligohydramnios developed rapidly in both cases despite the absence of COVID-19 symptoms.

The recommendations based on the study include close observation of pregnant women with a history of COVID-

19 infection during pregnancy, more frequent follow-up visits for patients with a history of COVID-19 infection and oligohydramnios, primary prevention through distancing measures and pre-conceptual vaccination, and public education on social distancing and avoiding contact with known COVID-19 cases. The study also suggests the need for a more comprehensive study that includes severe cases of COVID-19 infection with longer follow-up periods and a detailed medical trial comparing the efficacy of RT-PCR and ELISA testing.

The limitations of the study were that severe cases were not included in our study (not managed in our hospital).

CONCLUSION

The previous COVID-19 infection is significantly associated with decreased AFI. These results support the need for additional attention to patients had COVID-19 infection during pregnancy.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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