Maternal and neonatal outcomes in COVID-19 infected pregnancies: a prospective cohort study

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Abstract

Background: Despite the large number of pregnant women with the coronavirus disease 2019 (COVID-19), there is not enough analytical study to compare maternal and fetal consequences of COVID-19 infected with non-infected pregnancies. This cohort study aimed to compare maternal and fetal consequences of COVID-19 infected with non-infected pregnancies.

Methods: We included pregnant women with and without COVID-19 who were admitted to Arash Hospital in Tehran, Iran from March 1 to Sep 1, 2020. Clinical features, treatments, and maternal and fetal outcomes were assessed.

Results: One hundred and ninety-nine women enrolled, including 66 COVID-19 infected and 133 non-infected pregnant women prospectively. Caesarean Section (CS) was carried out in total 105 women (52.76%). A significant difference was found in term of delivery type between COVID-19 infected and non-infected pregnant women (aRR: 1.31, 95%CI: 1.04, 1.65, p= 0.024). No significant association was found between COVID-19 infection and preterm birth (PB) (aRR: 1.16, 95%CI: 0.54, 2.48, p= 0.689), low birth weight (LBW) (aRR: 1.13, 95%CI: 0.55, 2.31, p= 0.723), gestational diabetes (GDM) (aRR: 1.67, 95%CI: 0.81, 3.42, p= 0.160), preeclampsia (aRR: 2.02, 95%CI: 0.42, 6.78, p= 0.315), intrauterine growth restriction (IUGR) (aRR: 0.16, 95%CI: 0.02, 1.86, p= 0.145), preterm rupture of membrane (PROM) (aRR: 0.19, 95%CI: 0.02, 2.20, p= 0.186), stillbirth (aRR: 1.41, 95%CI: 0.08, 18.37, p= 0.614), postpartum haemorrhage (aRR: 1.84, 95%CI: 0.39, 8.63, p= 0.185), neonatal intensive care unit (NICU) admission (aRR: 1.84, 95%CI: 0.77, 4.39, p= 0.168), neonatal sepsis (aRR: 0.84, 95%CI: 0.48, 1.48, p= 0.568). The percentage of patients (4/66, 6.06%) being admitted to the ICU was significantly higher than the control group (0%) (p< 0.001).

Conclusion: Basically, although pregnancy and neonatal outcomes were not significantly different, the need for ICU care for pregnant women with COVID-19 was significantly higher compared with those without COVID-19.

Keywords: pregnancy, COVID-19, neonatal, perinatal, miscarriage, preterm birth

Introduction

In recent months and during the rapid outbreak of COVID-19 all around the world, many pregnant women, like other people, are infected with the virus. Nevertheless, no enough data is available on the clinical characteristics, manifestations, outcomes, and complications of this virus in pregnancy. Physiological respiratory and non-respiratory changes during pregnancy may predispose pregnant women to COVID-19 infection and worsen outcomes.[1] Some physiological changes in pregnancy include decreased lung volume and functional residual volumes due to diaphragmatic elevations, airway edema, increased oxygen consumption, hyper coagulation state, and altered cell immunity. It seems that these physiological changes may potentially lead to severe pulmonary infectious diseases during pregnancy. In previous pandemics such as H1N1, pregnancy increased susceptibility to serious illness and higher mortality rates than the general population.[2] A 2009 study found that women with H1N1 were four times more likely to be hospitalized[3] and also maternal mortality rate from the severe acute respiratory syndrome (SARS) virus has been reported about 25%.[4] Despite this background, the majority of reported cases of COVID-19 infection in pregnancy have been classified as mild features of the disease and not more severe than general population.[5,6] Most previous studies on the virus during pregnancy have been in the form of retrospective studies, case reports and case series. In fact, available evidence on the effects of the virus on pregnant women is still insufficient and inconclusive and there is no consensus between the experts about the virus and pregnancy and also many questions have remained unanswered and need to be investigated. A recent study has described the characteristics of COVID-19 infected pregnant and non-pregnant women in reproductive age in United States.[6] Although the study has some limitation, in any case, infecting a large number of pregnant women in a short period of time in this study indicates the importance of more detail studies in this field around the world to obtain strong scientific evidence for the proper and adequate management of these pregnancies. Since COVID-19 pandemic, a number of articles have been published about this virus and pregnancy mostly associated with China. At a time that the virus is spreading swiftly around the globe, there is an inevitably urgent need for some well-designed studies in different countries based on diverse nationalities in order to be able to deal with the virus in pregnant women based on strong and solid scientific evidence. Really as far as we know there are very few prospective cohort studies in this area, so we decided to design a prospective cohort study to compare maternal and fetal consequences of COVID-19 infected pregnancy with non-infected pregnancy.

Methods

Study design and participants

This study is a prospective cohort study conducted in Arash women's hospital, a university hospital affiliated with Tehran University of Medical Sciences. This study has been approved by the Ethics Committee of Tehran University of Medical Sciences. The ethical code is IR.TUMS.VCR.REC.1398.1057. Written informed consent was obtained from all participants for the publication of individual data from before enrolment when data were collected prospectively. In this study, all pregnant women who were hospitalized in Arash Hospital from March 1 to Sep 1, 2020 were evaluated in terms of inclusion and exclusion criteria. Inclusion criteria were all pregnant women who had been hospitalized in our hospital during the study period and were willing to participate in the study. Based on the presence or absence of clinical signs or symptoms of COVID-19 infection, women were divided into two general categories: one group whose participants had clinical signs and symptoms of the virus and the other group who did not show any clinical signs and symptoms. Clinical symptoms have included fever, dry cough, progressive cough, tachypnea, shortness of breath, diarrhea, anosmia, decreased oxygen saturation and fatigue. Reverse transcriptase–polymerase chain reaction (RT-PCR) for COVID-19 nucleic acid (COVID-19 RT-PCR) test of nasopharyngeal swabs and chest computed tomography (CT) scan were performed for the women with clinical symptoms. Women with positive COVID-19 RT-PCR test were classified as infected group. In cases with negative COVID-19 RT-PCR test, if they had very typical clinical symptoms verified by an infectious disease specialist, considering the false negative probability of COVID-19 RT-PCR test and high diagnostic sensitivity of CT scan finding[7], positive findings of CT scan have been considered as a criterion utilized as a tool to confirm the infection. These findings in chest CT scan included ground-glass opacity, consolidation, reticulation/thickened interlobular septa and nodules.[7] Women with negative results of both CT scan and COVID-19 RT-PCR test who had typical clinical symptoms or had laboratory findings including: leukocytosis (white blood cell (WBC) count$>11\times10^9$/L), lymphopenia (lymphocyte count$<1.0\times10^9$/L), thrombocytopenia, increased C-reactive protein (CRP) ($\geq$10 mg/L) were excluded from the study. Another exclusion criteria for the infected group was positive CT scan finding in women with mild or transient symptoms in the absence of typical clinical symptoms. Women who did not have any clinical signs or symptom of infection were considered as a control group. In our hospital, universal screening is

not performed for all inpatients and since some of affected people may be asymptomatic[8], in order to minimize the presence of asymptomatic individuals in the control group as much as possible, we used precise exclusion criteria. So exclusion criteria for control group included: a history of any suspicious symptoms of the virus over the past two weeks, contact with COVID-19 virus infected or suspected individuals within the last 14 days, any suspicious clinical symptoms of the virus over the last two weeks in their family members, attendance in crowded areas such as shopping malls and parties and also travelling over the past 14 days, going to hospitals or clinics for any reason within the last 14 days except for the time of current hospitalization. All pregnant women who were hospitalized during the study period were screened according to the above inclusion and exclusion criteria.

Procedures

Patients were treated according to the protocols of the World Health Organization (WHO). All other management and procedures in two groups were performed based on obstetrics indications and our hospital protocols. Given the lack of strong evidence to perform CS in women infected by the virus, our hospital's protocol was choosing delivery method based on other obstetrics indications. So we didn't impose CS on women because of coronavirus infection. It's worth mentioning that, in our hospital, women give birth in separate rooms during childbirth, and during this epidemic, we have decided to avoid using common tools such as birth balls as much as possible and also doctors, residents, and midwives who take care of each patient are specific for the same patient and do not take care of different patients at the same time as well as use of complete personal protective equipment. Babies born to infected mothers underwent early cord clamping and early temporary separation from their mothers immediately after birth and COVID-19 RT-PCR test was done via their nasopharyngeal and throat within the same hour after birth.

Data Collection

Demographic data and clinical features regarding symptoms, comorbidities, laboratory and radiological findings on admission and prenatal and neonatal outcomes were retrieved from medical records and reviewed and analyzed. A trained team of researchers reviewed and retrieved data from each patient.

Statistical Analysis

Continuous variables were described by mean ± standard deviation (SD) or median (interquartile range (IQR)), considering the normality. Categorical variables were described by counts and percentages (%). Prenatal and neonatal outcomes were compared using the Chi-square test for categorical variables, and Student's t-test for continuous variables. We estimated the risk ratios (RRs) and 95% CIs for categorical adverse pregnancy and neonatal outcomes using Modified poisson regression model. Also a linear mixed effects model was used to analyse changes in continuous pregnancy and neonatal outcomes. The models were adjusted for the following potential confounders: body mass index (BMI), maternal age, previous delivery type, gestational age, previous pregnancy problems and pre-existing medical problems. We adjust the variables based on a minimal sufficient set obtained from a causal diagram. Statistical analyses were performed on Stata 16.0 (Stata Corp, College Station, TX, USA). All statistical tests were two-tailed at the significance level of $P < 0.05$.

Results

During the study period, 665 pregnant women have been admitted to our hospital with complaints of respiratory problems and were evaluated by an infectious disease specialist. Among them, 244 people were suspected of being infected with COVID-19 virus and underwent diagnostic evaluation that 109 of them have been hospitalized and among them, according to inclusion and exclusion criteria, 66 women were included. During this time, among non-infected women who were hospitalized in our hospital, according to some detailed eligibility criteria, 133 pregnant women entered into the study as a control group.

Clinical and laboratory findings of infection in COVID-19 infected pregnant women

Forty three COVID-19 infected cases were delivered, 21 women continued their pregnancy by the end of study and two women aborted. As illustrated in Table 1, fatigue (51/66, 77.27%) was the most frequently observed symptom, followed by fever (39/66, 59.09%), dry cough (31/66, 46.96%), dyspnea (27/66, 40.90%), and myalgia (16/66, 24.24%). A total of 15 (22.72%) patients had decreased oxygen saturation. The most frequent abnormality in laboratory tests included: raised CRP (42/66, 63.63%), leukocytosis (43/66, 65.15%), and lymphopenia (46/66,

69.70%). Four COVID-19 infected pregnant women (6.06%) were admitted to intensive care unit (ICU), none of which required intubation and invasive ventilation (Table 1). There was no ICU admission in control women. The percentage of patients being admitted to the ICU was significantly higher than the control group (p< 0.001). Overall, oxygen therapy, lopinavir/ritonavir and chloroquine therapy were administered in (15/66, 22.72%), (45/66, 68.18%) and (47/66, 71.21%) of patients, respectively. There were no complications such as acute respiratory distress syndrome, acute respiratory system injury, acute kidney injury or septic shock in the patients.

Clinical characteristics and pregnancy outcomes in two groups

Age range of participants was 15 to 46 years, the mean age was 30.97 years (SD= 6.38) in COVID-19 infected cases, and 28.79 (SD= 6.42) in the control group (p=0.024). Among all participants, 167 (83.75%) of women were in the third trimester of pregnancy that 49 (29.34%) and 118 (70.66%) of them were in infected and control groups respectively. Interestingly, the infected group had a lower gestational age [32.64 (9.68)] in comparison with controls [36.57 (5.30)] (p< 0.001). There were no differences between groups regarding clinical characteristics, past medical and obstetric history except hyperemesis gravidarum (p< 0.001) (Table 2). Furthermore, infected women had almost the same frequency of pre-existing medical problems (17/66, 25.75%) compared to control group (38/133, 28.57%) (p= 0.675). It should be noted that since hypothyroidism was common in two groups, especially in the control group, we did not classify hypothyroidism with other underlying diseases in the same category to prevent its confounding effect. The unadjusted and adjusted estimates for total maternal and neonatal outcomes are presented in Table 3 and 4. CS was carried out in total 105 women (52.76%). The unadjusted result showed significantly higher frequency of CS in COVID-19 infected cases compared with controls (RR: 1.54, 95%CI: 1.04, 2.27, p= 0.030), similarly after adjusting for potential confounders, a significant difference was found in term of delivery type between infected and non-infected women (aRR: 1.31, 95%CI: 1.04, 1.65, p= 0.024). Pregnant women with COVID-19 had almost the same frequency of PB compared to pregnant women without infection (RR: 1.64, 95%CI: 0.98, 2.74, p= 0.064), after adjusting for potential confounders, no significant difference was found in term of PB between two groups (aRR: 1.16, 95%CI: 0.54, 2.48, p= 0.689). In addition, no significant association was found between COVID-19 infection

and GDM, preeclampsia, IUGR, PROM, stillbirth, postpartum haemorrhage and postpartum infection.

Furthermore, there were no significant differences between groups in terms of essential neonatal outcomes including LBW, NICU admission, neonatal sepsis, APGAR score at one and five minutes (Tables 3 and 4). In our study, only one infant had a positive COVID-19 RT-PCR test after birth, and the other infants had negative results. Considering this issue that the baby was completely isolated and separated from the mother immediately after birth, there is a possibility of vertical transmission in this baby, but anyway, since we did not examine the umbilical cord blood and amniotic fluid in terms of virus culture, we cannot definitively claim that there has been a vertical transmission in this baby. The infected women were asked about travel history. It should be noted that during COVID-19 pandemic, there were two public holidays in Iran, which during the first holiday, none of women traveled but three of infected women had a history of travelling during the second holiday.

Discussion

In this prospective cohort study we compared pregnancy outcomes in symptomatic women infected by COVID-19 virus with non-infected pregnant women. We have tried to address some issues including: the severity of COVID-19 virus infection in pregnancy, the risk of virus infection with pregnancy progress, the virus impact on pregnancy outcomes, delivery type, the possibility of vertical transmission and neonatal consequences.

A review reported the estimated reproduction number for COVID-19 around 3.28.[9] According to an article from Iran[10], the reproduction number during the first week of outbreak was 4.86 that was relatively high. After implementing heavy restrictions (such as closing schools, universities, governmental departments and many businesses, banning intercity and inter-provincial travel, restricting religious gatherings) reproduction number declined to 1 on 4, April 2020. Accordingly, after mid-April 2020, government offices and low-risk businesses reopened and travel was permitted. At the same time, unfortunately, the second peak of COVID-19 outbreak in Iran started again with more intensity than before. Traveling is one of the most important factors in the spread of the virus.[11] During the pandemic, there were two public holidays in Iran, one from March 19 to March 24, 2020 (Persian New Year) which was during travel ban and the other

from May 2 to May 5, 2020 in which travelling was given permission. During the first holiday, none of our infected women traveled but three of them had a history of travelling during the second holiday. Given precise exclusion criteria including travel history for our control group, we couldn't compare infected women with control group according to travel history. Some studies to date have shown that COVID-19 infection is probably not more severe in pregnant women.[6,12-14] Recently, Center for Disease Control and Prevention in the United States has reported the characteristics of 91,412 women in reproductive age who were infected by COVID-19 virus including 8,207 pregnant women.[6] However, their report has some limitations and drawbacks including the following: Clinical sign and symptoms were recorded for only 65% of pregnant women and 90% of non-pregnant women. Although the prevalence of hospitalization in pregnant women was reported to be higher than non-pregnant women, it is not clear whether the hospitalization was due to COVID-19 infection or other complications of pregnancy. Another limitation of their report is that neither gestational age at the time of infection nor pregnancy outcomes were recorded. However, according to their report, the prevalence of shortness of breath and cough in pregnant and non-pregnant women was equal and headache, muscle pain, diarrhea, fever and chills were even less common in pregnant women. Malavik Probho et al.[15] in a prospective cohort study on pregnancy >20 gestational weeks have evaluated all symptomatic and asymptomatic COVID-19 positive women. In their study, only pregnant women who had referred for delivery were examined, while in our study, pregnant women in all gestational age and also the consequences of continuing pregnancy after recovery were examined. Since they had universally performed screening for all patients, they divided individuals based on a positive virus test. So, even though they studied 70 people, only 15 of them were symptomatic, while in our study, all of 64 cases were symptomatic. One of the merits of their study is that they examined the pathology of placenta in infected pregnancy which is appreciated and we suggest more research in this field in the future. They had no maternal death and also no women required mechanical ventilation.[15] Likewise, during our study, four women were admitted in ICU but none of them required intubation and invasive ventilation. Given all of them were in the third trimester of pregnancy and also all had hypoxia, they were taken to the ICU for close monitoring. We also did not have any critically-ill cases that required mechanical ventilation. However, it should be noted that the absence of a critically-ill patient in our study cannot be generalized to all pregnancies.

In late February 2020, a very ill 22-year-old pregnant woman with no underlying disease who had been infected by COVID-19 virus was referred to our hospital at 37 gestational weeks because of fever and severe shortness of breathing that had started ten days earlier. She developed lymphopenia, thrombocytopenia and low O_2 saturation (60%) and unfortunately died within seven hours of admission. Since this happened before the beginning of our cohort study, we did not include her in this study. Recently, Hantoushzade et al. has reported nine pregnant women with severe COVID-19 disease which seven of them died.[16] Their study is a multidisciplinary study that has selected highly ill patients from different centers across Iran, alongside non-random selection bias. However, since no cases of COVID-19 death have been reported in pregnancy so far, their study could make an important change in available evidence about the manifestation of the virus in pregnancy. Most of the COVID-19 infected pregnant women that have been reported so far were in the third and late second trimesters.[13,16,17] In our study, 88.75% of those surveyed were in the third trimester of pregnancy. Really, the possibility of picking up infected women based on careful examination and history at earlier ages of pregnancy is lower because of the less routine prenatal visits in first and second trimesters. On the other hand, given the general policies around the world regarding home quarantine during a virus pandemic, pregnant women may not go to medical centers even if there are mild symptoms. So we believe that previous reports including our study might be influenced by these factors and the higher average gestational age in our patients should be interpreted with caution.

In our study, there was no increase in adverse pregnancy outcomes including PB, GDM, preeclampsia, IUGR, PROM, stillbirth, postpartum haemorrhage and postpartum infection. Most previous studies including a review article[18] had also the same results. Since in most previous studies no comparison has been made between infected and non-infected individuals due to their methodology, it isn't possible to give a definite opinion about the effect of this virus on pregnancy outcomes based on the available data and more prospective studies are needed. Our results showed that CS frequency was different in the studied groups and also in the majority of previous studies, it was higher in infected people.[13,15,18-21] Among mentioned studies, only one study was performed as a prospective cohort[15] in which, the occurrence of CS was significantly higher in infected women whose result should be interpreted with caution because some important confounding factors including chronic hypertension, overweight and pre-gestational diabetes were significantly higher among infected people in their study, which have not been

adjusted in analysis and accordingly, their results can be influenced. On the other hand, in their study, there was no discrepancy between groups in terms of the cause of CS.[15] In a review study, fetal distress was reported to be the most common cause of CS in infected women.[19] However, in our study, the most common cause of CS was a history of previous CS.

In our study, only one infant had a positive COVID-19 RT-PCR test after birth that it cannot be definitively related to vertical transmission. Although no decisive vertical transmission of the virus has been reported so far, there are a few reports of COVID-19 viral pneumonia in three infants,[22] elevated SARS-COV-2 IgM and IgG levels in two hours after birth in a newborn[23] and a newborn whose nasopharyngeal culture was positive for COVID-19 virus 16 hours after birth.[24] Since several factors may play some roles in the vertical transmission, we recommend culture of amniotic fluid, umbilical cord blood and neonatal nasopharyngeal swab at the time of delivery in order to accurately determine the vertical transmission. Several studies have reported neonatal complications in some of their neonates,[13,22,25] whereas in some other studies, no neonatal complication has been observed.[16,26] The prevalence of neonatal complications was not different between groups in our study. Nevertheless, we have the impression that maternal condition during peak of the disease may lead to severe transient placental insufficiency. We suggest evaluating uterine and umbilical vessels Doppler at the onset and peak of the disease and also after the mother's recovery and comparing them with neonatal outcomes in future studies. One of the strengths of our study is that it was designed as a prospective cohort study, while most of the previous studies were case reports and series and a few studies had a case-control design. The other strength of our study was that we didn't consider only women who had positive COVID-19 RT-PCR test as an infected group, but given the probability of false negative results in the virus RT-PCR, those who had positive CT scan findings in the presence of very typical clinical symptoms were also considered as an infected people, so in this way, we tried not to ignore the infected women as much as possible. As we explained in the method section, one of the strengths of our study was choosing very precise exclusion criteria for two groups, especially for the control group. One of the limitations of our study is that there is no universal screening for all pregnant women in our hospital, so it is highly likely for some asymptomatic infected women to be found among non-infected group. To overcome this limitation, we have made our best effort to select non-infected women very meticulously as we described in the method section. However, it is possible that some asymptomatic women have been misclassified.

Another limitation of the study was the short duration of the study and small sample size. Although the sample size of our study is higher than most of previous studies on COVID-19, but for rare pregnancy outcomes the small sample size leads to a wide confidence interval.

Conclusion

We found no differences between COVID-19 infected and non-infected pregnant women according to maternal and neonatal outcomes except delivery type. Unfortunately, there is still not enough evidence about COVID-19 virus in pregnancy. Given the effect of many potential factors, such as the severity of maternal infection, the time interval between the onset of symptoms and childbirth, the adequacy of the placental blood supply, the findings provide a rationale for conducting further cohort studies aimed at evaluating the association between COVID-19 infection and prenatal and neonatal outcomes considering aforementioned factors.

Authors' Contributions

All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. MS, RP, RH, and TS were responsible for study concept and design. RP, MS, TS, LH, AM, MR, AA, AS, and GR were responsible for the acquisition, analysis, or interpretation of data. MS, RP, TS and RH were responsible for drafting the manuscript. MS was responsible for statistical analysis.

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Conflict of interest

We declare no competing interests.

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Table 1. Sign and symptoms, treatment and clinical features of overall 64 COVID-19 infected pregnant women.

Signs and symptoms	Overall (n= 66)
Fever	39 (59.09)
Fatigue	51 (77.27)
Dry cough	31 (46.96)
Myalgia	16 (24.24)
Dyspnea	27 (40.90)
Pharyngalgia	6 (9.09)
Tachycardia	5 (7.57)
Tachypnea	3 (4.62)
Haemoptysis	4 (6.06)
Headache	3 (4.54)
Anosmia	5 (7.57)
Vomiting	7 (10.60)
Diarrhea	5 (7.57)
Dysgeusia	3 (4.54)
Heart rate, median (IQR), bpm	94 (101-86)
Respiratory rate, median (IQR)	18 (18-16)
Arterial pressure, median (IQR), mm Hg	110.7 (120.7-102.7)
White blood cell count, $\times 10^9$/L	
4400 – 11000	23 (34.85)
11001 – 21610	43 (65.15)
Lymphocyte count, $\times 10^9$/L	
200 – 1000	46 (69.70)
1001 – 7000	20 (30.30)
C-reactive protein (mg/L)	
0.5 – 10	24 (36.37)
10 – 116	42 (63.63)

Treatments	
ICU admission	4 (6.06)
High-flow nasal cannula oxygen therapy	15 (22.72)
Chloroquine	45 (68.18)
Lopinavir/ritonavir	47 (71.21)
Oseltamivir	27 (40.90)

Table 2 Clinical characteristics of COVID-19 infected and control groups.

	Non infected pregnant women (n=133)	Infected pregnant women (n=66)	P-Value‡
Age (year)*	28.79 (6.42)	30.97(6.38)	0.024
BMI (kg/m2)*	29.58 (5.09)	29.45 (4.23)	0.858
Gestational age *	36.57 (5.30)	32.64 (9.68)	<0.001
Gravidity*	2.21 (1.07)	2.20 (1.22)	0.952
Parity*	0.93 (0.91)	1.13 (0.86)	0.138
Comorbidities†	38 (28.57)	17 (25.75)	0.675
History of previous CS†	38 (28.57)	28 (42.42)	0.050
Hyperemesis gravidarum†	12 (9.02)	15 (22.72)	<0.001

BMI: body mass index; CS: cesarean section

*: Values given as mean ± SD (standard deviation)

†: Values given as number (percentage)

‡ Continuous variables compared with independent t-test, categorical variables compared with chi-square test or Fisher exact test.

Table 3: Association between maternal infection and maternal and neonatal outcomes.

Pregnancy outcome	Crude RR (95% CI)	P-Value	Adjusted RR (95% CI) †	P-Value*
Caesarean section	1.54 (1.04, 2.27)	0.030	1.31 (1.04, 1.65)	0.024
Gestational diabetes	1.40 (0.66, 2.99)	0.376	1.67 (0.81, 3.42)	0.160
Preeclampsia	2.95 (0.86, 10.11)	0.070	2.02 (0.42, 6.78)	0.315
PROM	0.21 (0.02, 1.69)	0.104	0.19 (0.02, 2.20)	0.186
IUGR	0.21 (0.02, 1.69)	0.104	0.16 (0.02, 1.86)	0.145
Stillbirth	0.97 (0.09, 10.58)	0.985	1.41 (0.08, 18.37)	0.614
Polyhydramnios	0.64 (0.02, 16.15)	0.792	1.68 (0.21, 11.48)	0.725
Oligohydramnios	0.98 (0.09, 10.66)	0.990	2.45 (0.45, 18.12)	0.515
Hyperemesis gravidarum	0.84 (0.58, 1.23)	0.383	0.89 (0.62, 1.27)	0.529
Postpartum haemorrhage	1.49 (0.45, 4.85)	0.507	1.84 (0.39, 8.63)	0.185
Postpartum infection	1.09 (0.31, 3.94)	0.886	0.89 (0.19, 4.15)	0.883
Preterm birth	1.64 (0.98, 2.74)	0.064	1.16 (0.54, 2.48)	0.689
Low birth weight	1.58 (0.73, 3.39)	0.245	1.13 (0.55, 2.31)	0.723
NICU admission	1.94 (0.81, 4.62)	0.131	1.84 (0.77, 4.39)	0.168

Neonatal sepsis	0.95 (0.56, 1.59)	0.848	0.84 (0.48, 1.48)	0.568

IUGR: intrauterine growth restriction, PROM: premature rupture of membranes.

†Risk ratio estimated directly from Modified poisson regression or Firth penalized likelihood method considering rarity of outcome. The final multivariable models were adjusted for the following risk factors: gestational age, parity, body mass index, maternal age, previous caesarean section, previous pregnancy problems, pre-existing medical problems, and mode of delivery.

*Significant at P value <0.05.

Table 4: Association between maternal infection and neonatal outcomes.

Pregnancy outcome	Crude MD (95% CI)	P-Value	Adjusted MD (95% CI) †	P-Value*
Neonate weight	-193.36 (-440.88, 54.15)	0.124	-99.64 (-283.74, 84.44)	0.289
Neonate height	81.04 (-7.53, 169.63)	0.072	90.81 (-1.56, 183.20)	0.054
APGAR min1	-0.48 (-1.20, 0.22)	0.178	-0.18 (-0.68, 0.31)	0.463
APGAR min5	-0.56 (-1.31, 0.18)	0.136	-0.11 (-0.31, 0.09)	0.285

†Mean difference estimated directly from linear mixed-effects model. The final multivariable models were adjusted for the following risk factors: gestational age, parity, body mass index, maternal age, previous caesarean section, previous pregnancy problems, pre-existing medical problems, and mode of delivery.

*Significant at P value <0.05.