Maternal and Perinatal Outcomes of COVID-19 at Paropakar Maternity and Women's Hospital, Nepal: A Retrospective Cohort Study

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Abstract

Background: COVID-19 infection has emerged as a major public health crisis with impact on health systems. COVID-19 during pregnancy has direct implications on the pregnancy outcomes, maternal complications, and neonatal outcomes. There have been few studies comparing direct maternal and perinatal outcomes in a cohort of exposed and non-exposed mothers in Low- and Middle-Income Countries (LMICs). The purpose of this study was to provide a description of the features of COVID-19 infection during pregnancy and compare the outcomes among an exposed and unexposed group of women at a tertiary women's hospital.

Methods: A retrospective cohort study was conducted at the Paropakar Maternity and Women's Hospital (PMWH), Kathmandu Nepal. The exposed group were the mothers with COVID-19 infection during pregnancy and the unexposed group were the mother without COVID-19 infection. Information on 610 pregnant women who visited the hospital between 26 August 2020 and 21 February 2021 were retrieved from the hospital among which 118 women were tested positive for COVID-19 and 492 women were COVID-19 negative. Chi square test was used to assess the association of the COVID-19 status of the mother with pregnancy outcomes, maternal complications, and neonatal complications with $p < 0.05$ considered as statistically significant.

Findings: Of 610 pregnant women in the study sample, majority of the women in both the cohort were of age 20 - 35 years and from Janajati ethnicity, however higher percentage of COVID-19 positive mother visited PMWH from outside of Kathmandu valley. The study identified association between COVID-19 status of the mother with pregnancy outcomes ($p < 0.001$), hypertensive disorders ($p = 0.017$), and early neonatal death ($p = 0.005$).

Conclusion: The study has identified association between COVID-19 status of mother and pregnancy outcomes, maternal complication (hypertensive disorder), and neonatal complication (early neonatal death). A national obstetric surveillance system and registry should be developed to collect and analyse information about complications of pregnancy during pandemics and other public health crises.

Keywords: _Cohort; Complications; COVID-19; Maternal; Neonatal; Outcomes; Pregnancy; Retrospective_

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Introduction

COVID-19 infection has emerged as a global health crisis, having a profound impact on health systems and on pregnancy outcomes. By 21 February 2021, SARS-CoV-2 had infected 273,431 people in Nepal with 2,993 deaths [1]. A nation-wide lockdown was imposed throughout Nepal from 24 March for 4 months which was prolonged in many parts of the country. Lockdown and other restrictions resulted in major disruptions of health service availability and utilization throughout the most of 2020.

Pregnancy is a unique physiological condition which may have sudden emergencies that needs to be tackled in time for favourable outcomes. When infected with COVID-19, pregnant women are considered a high-risk group compared to non-pregnant women as pregnant women are reported to have an increased risk of maternal admission in intensive care unit (ICU), invasive ventilation and maternal death [2-6] along with increased risk of preterm birth [4,7], stillbirths [5-8] and neonatal deaths [8]. COVID 19 infection is identified to have increased the risk of preeclampsia/ eclampsia and delivery by Caesarean Section [5,7,9] while some studies from High Income Countries (HIC) reported fewer adverse outcomes [6,9].

Majority of studies on direct impact of COVID-19 in pregnancy outcomes, maternal complications, and neonatal complications are from High Income Countries (HIC) with limited data on the direct impact of COVID-19 from Low- and Middle-Income Countries (LMIC) in South Asia. With this background, the present study aimed to assess the direct impact of COVID -19 infection in cohorts of exposed and unexposed Nepalese women and their neonates during pregnancy and the post-partum period.

Methods

Study setting

The study was conducted at Paropakar Maternity and Women's Hospital (PMWH), a public sector hospital. PMWH is the largest women's hospital in Nepal, with 415 beds and is the only dedicated maternity hospital in the country. This hospital caters to more than 200,000 outpatients and 28,000 in-patients with over 20,000 births annually and receives referrals from all across Nepal. Due to its high case load, PMWH is expected to have managed the largest proportion of COVID-19 positive pregnancies in Nepal and was therefore selected as the study site.

During the year before the COVID-19 pandemic, PMWH had 22147 deliveries with 21.9% foetal adverse outcomes and 6.9% maternal adverse maternal outcomes. The total maternal and infant adverse outcomes was 28.8% [10]. At the time of the study Kathmandu was the epicentre of the pandemic and reporting more than 60% of cases diagnosed throughout the country. PMWH established additional facilities for COVID-19 patients - a 150-bedded isolation centre for women and a dedicated delivery unit for COVID-19 infected women.

The study is based on the World Health Organization WHO/HRP 2020 standard research protocol, for investigating outcomes of pregnant or recently pregnant women infected with COVID-19 (exposed) compared to pregnant or recently pregnant women not infected with COVID-19 [11]. The protocol was modified for application to the Nepalese context with universal testing of pregnant women for COVID-19 and antibody testing of pregnant women and neonatal testing not offered. Testing with reverse transcriptase polymerase chain reaction (RT-PCR), was offered based on national criteria for triage, i.e. being symptomatic, having history of contact, coming from a hotspot, and travel history [12,13].

Pregnant or recently pregnant women who were triaged, underwent testing and those with a positive RT-PCR, were included in the "exposed" group and pregnant or recently pregnant women who did not have symptoms or history suggesting need for triage and COVID-19 testing constituted the "unexposed" group [12].

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Study design

The study was a retrospective cohort study of maternal and neonatal outcomes among women "exposed" to COVID-19, and an "unexposed" group, admitted to Paropakar Maternity and Women's Hospital (PMWH). The study was approved by the Institutional Review Board of the hospital. Pregnant women at any stage in pregnancy and up to 6 weeks post-partum were included in the study.

The sample size estimate was based on 80% statistical power and type 1 error at 5% level. The sample size selected is expected to have the outcome of interest among the COVID-19 exposed and also the effect size (ES). Assuming 28.8% of the COVID-19 unexposed population experience an adverse pregnancy outcome, based on an analysis of PMWH data for 2018/19, in order to detect at least 30% increased risk of adverse pregnancy/neonatal outcome due to being exposed to COVID-19 (i.e. risk ratio (RR) = 1.30) initial sample size per group is 253 (total: 506). As the number of exposed at PMWH was 118, a ratio of exposed to unexposed of 1: 4 was taken to enhance precision, giving a sample size of 472 for unexposed group. However, information of 492 mothers from unexposed group were used for calculation.

Being a retrospective study, the study variables were selected from the registers and case records based on documentation and its importance. The variables consisted of pregnancy outcomes-mode of delivery, maternal complications- gestational diabetes and hypertension, anaemia, haemorrhage and pre-term labour, abortion complications, and foetal outcomes- stillbirths, early neonatal deaths, and low birth weight.

Data collection and management

610 pregnant women admitted to the hospital between 26 August 2020 and 21 February 2021, were the study subjects, among which 118 women were exposed and 492 unexposed. Data was obtained from a retrospective review of the registry and case records of women who were admitted to PMWH. Random numbers were applied to the inpatient obstetric admissions at PMWH to select the unexposed cohort.

Women who were pregnant and tested positive for COVID-19 were admitted to PMWH and managed according to national guidelines [12-14]. All women hospitalized at PMWH consisted of asymptomatic/pre-symptomatic/mild COVID-19 infection as defined in the national guidelines, i.e. haemodynamically stable, SpO_2 > 93% in room air, and no respiratory distress [14]. All patients who tested positive by RT-PCR were delivered in a COVID-19 dedicated labour and delivery ward and operation theatre. COVID-19 was not considered an indication for Caesarean section. Breast feeding was encouraged in all exposed and unexposed mothers.

Statistical analysis

The data for the study was collected from the PMWH registry and entered in Epidata version 3.1. All data was analysed using StataCorp LLC version 15.0. The Chi square test was used to assess the association between COVID 19 status in women with their pregnancy outcomes, maternal complications, and neonatal complications. A p-value of less than 0.05 was considered statistically significant.

Results

Among the women included in the study, 570 women had delivery at PMWH (96 exposed and 474 unexposed), 7 women had abortion complications (6 exposed and 1 unexposed), 2 women were post-abortal/post-partum (1 exposed and 1 unexposed) and 31 women remained undelivered (15 exposed and 16 unexposed) during the study period.

Table 1 depicts the background characteristics of the exposed and unexposed pregnant women. Majority of the women were from 20-35 years age group (90.8%) in both the exposed (94.1%) and unexposed group (90.0%). Majority of the women were from Janajati (48.7%) in both exposed (49.2%) and unexposed group (48.6%). However, more exposed women were from outside of Kathmandu valley (60.2%) than unexposed women (31.9%).

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	Unexposed		Exposed		Total	
	No.	%	No.	%	No.	%
Age (Years)						
< 20	34	6.9	4	3.4	38	6.2
20 - 35	443	90.0	111	94.1	554	90.8
> 35	15	3.1	3	2.5	18	3.0
Caste/Ethnicity						
Brahmin/ Chhetri	163	33.1	45	38.1	208	34.1
Janajati	239	48.6	58	49.2	297	48.7
Others*	90	18.3	15	12.7	105	17.2
Place of residence						
Kathmandu valley	335	68.1	47	39.8	382	62.6
Outside of Kathmandu valley	157	31.9	71	60.2	228	37.4
Total	492	100	118	100	610	100

***Table 1:** Background characteristics.*

*Others includes Dalits, Madhesis, unidentified castes.

There was significant association (p < 0.001) between the COVID-19 status and pregnancy outcomes (Table 2). In addition, significant association was identified among COVID-19 status and maternal complication of hypertensive disorders (p = 0.017) but not with other maternal complications like diabetes, anaemia, antepartum and postpartum haemorrhage, pre-term labour, and others (Table 3). Moreover, significant association was identified among COVID-19 status and early neonatal death (p = 0.005) but not with low birth weight (Table 4).

Discussion and Conclusion

This study conducted during the first wave of the pandemic, shows that 118 pregnant women admitted to PMWH with positive RT-PCR, had a mild disease, as defined in the national guidelines [14]. Even though women admitted to PMWH had asymptomatic or mild disease, other feto-maternal adverse outcomes were noted to be disproportionately severe. The lack of women needing intensive care among the

	Unexposed		Exposed		Total		p-value
	No.	%	No.	%	No.	%	
Abortion	1	0.2	6	5.1	7	1.1	
Normal vaginal delivery	297	60.4	52	44.1	349	57.2	
Vacuum/ forceps delivery	8	1.6	0	0.0	8	1.3	
Caesarean section delivery	168	34.1	43	36.4	211	34.6	< 0.001
Pregnancy continued	16	3.3	15	12.7	31	5.1	
Missing data	2	0.4	2	1.7	4	0.7	
Total	492	100.0	118	100.0	610	100.0	

***Table 2:** Pregnancy outcomes.*

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	Unexposed		Exposed		Total		p-value
	No.	%	No.	%	No.	%	
Diabetes in pregnancy	6	1.2	1	0.9	7	1.2	0.733
Hypertensive disorders	12	2.4	8	6.8	20	3.3	0.017
Anaemia*	44	8.9	11	9.3	55	9.0	0.897
Haemorrhage-antepartum and postpartum	8	1.6	3	2.5	11	1.8	0.502
Pre-term labour	40	8.1	12	10.2	52	8.5	0.476
Women with any complications	105	21.3	28	23.7	133	21.8	0.573
Total	492		118		610		

Table 3: *Maternal complications.*

*Hb ≤11 g/dl.

	Unexposed		Exposed		Total		p-value
	No.	%	No.	%	No.	%	
Early neonatal Deaths	12	2.53	8	8.33	20	3.5	0.005
Low birth weight*	61	12.9	14	14.4	75	13.1	0.650
Total live births	474		97		570		

Table 4: *Neonatal outcomes.*

exposed cohort at PMWH contrasts with high occurrence of women needing intensive care in high income countries (HIC) [15,16]. Some of the reasons for this high rate of progression to severe disease in HIC were explained by the fact that 70% of the women in HIC were overweight or obese, 40% were 35 years or over and a third had pre-existing morbidities. While BMI has not been recorded in this study, the mean BMI among Nepalese women aged 15 - 49 is 22 kg/m^2, well within the normal range for South Asian women, and only 22% are overweight or obese [17]. Further pregnancies occur at a younger age in Nepal, with 70% women in the COVID-19 cohort and 68% women in the unexposed group being in the age group of 21 - 30 years. With changes in lifestyle, non-communicable diseases are becoming more common in Nepal, but have not reached the high levels prevailing in HICs.

In this study, the proportion of women with hypertensive disorders and diabetes was 7.7% in the exposed group and 3.6% in the unexposed group which is much lower than in HIC. The general prevalence of hypertension at a population level in Nepal is reported to be 9.4% and 2.5% for hyperglycaemia (≥ 126 mg/dl) in the age group 15 - 24 years [18]. These factors, could in part, explain the absence of severe and critical cases in this study cohort.

The cause for the high proportion of abortion complications at PMWH and the high neonatal mortality are uncertain. Many other studies from HICs report no increase in abortion [19,20] or neonatal deaths [16,20-22]. The PMWH findings of adverse pregnancy and infant outcomes must be considered along with the high numbers of COVID-19 positive women who travelled, sometimes from distant districts, to access services at PMWH, with delay in reaching the treating institution. At health facilities in LICs, including PMWH, the additional constraints posed by limited staffing and lack of PPE could also have contributed to adverse outcomes.

During the study period, the proportion of women delivered by Caesarean Section (CS) in the exposed group was not significantly higher than in the unexposed group. The mean CS rate for both groups was 37% which is slightly higher than the CS rate in the preceding

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year at PMWH. Increase in Caesarean births has been reported in many studies [5,8,15], while some have reported no significant difference [4,6,23]. There was no significant increase in maternal complications in the exposed cohort in this study which is similar to findings from other studies [16,24].

This study identified significant association between COVID-19 status and pregnancy outcomes. There was association among COVID-19 status and hypertensive disorders but not with other maternal complications like diabetes, anaemia, antepartum and postpartum haemorrhage, pre-term labour, and others in this study. Association was identified between COVID-19 status and early neonatal death but not with low birth weight in this study. A systemic review has identified association of COVID-19 with increased risk of preeclampsia, gestational diabetes, preterm birth, stillbirth, and low birth weight [25]. A study in United States has also identified association of COVID-19 pandemic with increase in pregnancy-related complications and maternal deaths during delivery hospitalization [26]. However, a multi-country study in LMICs has identified no increase in the stillbirth, neonatal mortality, maternal mortality, low birthweight, or preterm birth rates during the COVID-19 period compared with the previous year.

Strengths and Weaknesses

This study was conducted in a public sector women's hospital with the objective of generating local context specific data. As this is a retrospective study, the conclusions drawn are based on data that was available at the PMWH records, which may not be adequate for drawing unbiased conclusions. This study did not have the power to detect differences in individual adverse outcomes, thus conclusions drawn from these comparisons may not be generalizable.

Research Implications

The study has identified an association of COVID-19 status with pregnancy outcomes, maternal complications, and neonatal outcomes; however, a causal inference could not be made. Thus, there is clearly a need for population-based data from Nepal, with national and regional surveillance and research, to provide the evidence for effective and cost-effective planning of health services during pandemics and other health crises.

Competing Interest

Authors do have any competing interest to declare.

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