



Assessment of severity and feto-maternal outcomes among COVID-19 infected pregnant females hospitalized at tertiary care center in western Nepal

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Objective: There is a paucity of data assessing the severity of coronavirus disease 2019 (COVID-19) infection and feto-maternal outcomes in pregnant women in Nepal, especially during the third wave of the pandemic with the Delta variant. This study aimed to severity as well as maternal-fetal outcomes among pregnant women with COVID-19 infection.

Methods: In this cross-sectional study carried out amongst COVID-19 positive pregnant women visiting our institution for 6 months from January through June 2022, data surrounding COVID-19 severity and fetal outcomes were collected in a structured questionnaire. Disease severity was categorized based on the NIH (National Institutes of Health) severity classification. Descriptive statistics were used to describe the outcomes.

Results: A total of 105 pregnant females infected with COVID-19 during the third wave were included in our study. The participants ranged from 16 through 40 years, mean gestational age being 36.6 weeks. Most of the women (40.55%) belonged to Brahmin and Chhetri ethnic backgrounds. About half (48.55%) of females were asymptomatic and four patients had severe disease requiring intensive care management. Only 13 pregnant females underwent vaccination. Of the 91 females that underwent delivery at our center, 77 (84.62%) were term. The rate of cesarean delivery was slightly higher (51.65%) than normal delivery. None of the babies born to COVID-19 positive pregnant females tested positive for COVID-19 and there were no stillbirths or any congenital anomalies. The majority of babies (68.14%) had normal fetal weight.

Conclusion: Severe COVID-19 infection and adverse maternal-fetal outcomes during the third wave of COVID-19 infection with the Delta variant in Nepal were less than in other regions of the world despite low rates of vaccination.

Keywords: COVID-19, Delta virus, fetal outcomes, maternal outcomes, Nepal, severity

Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), resulted in a global pandemic^[1]. As of August 2023, there have been over 700 million confirmed cases of COVID-19 globally, including nearly 7 million deaths^[2]. According to the WHO, more than 1 million

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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HIGHLIGHTS

- Coronavirus disease 2019 (COVID-19) has adverse impact on pregnancy and pregnancy outcomes.
- There is evidence gap about pregnancy outcomes during the pandemic in Nepal.
- Severe COVID-19 infection and adverse maternal-fetal outcomes during the third wave of COVID-19 infection with the Delta variant in Nepal was less than other regions.
- Vaccination was poorly achieved within the pregnant population.

confirmed cases of COVID-19 and over 12 000 deaths have been reported so far from Nepal^[3].

Till date, vaccination has been the only effective measure to curb and prevent COVID-19 infection. Several clinical trials have been conducted to find out the safe and effective treatment of COVID-19, including drugs like ivermectin, chloroquine, interferons, steroids as well as a myriad of other antiviral drugs and therapies^[4,5]. However, the safety and efficacy of these medications during pregnancy is not yet well established.

There is conflicting evidence regarding the impact of COVID-19 on pregnancy and neonatal outcomes. Pregnancy itself is an immunocompromised state and the normal physiologic changes in pregnancy increase the risk of morbidity and mortality related

to respiratory illnesses. There is extensive evidence to support the fact that COVID-19 positive pregnant females had higher rates of hospitalization, ICU admission, and need for mechanical ventilation than the normal population^[6]. However, there is a vast heterogeneity in maternal-fetal outcomes based on geographic and socio-economic variation. There are very few studies from Nepal that have tried to explore this area of clinical importance.

Thus, we conducted this study intending to assess the severity as well as maternal-fetal outcomes among pregnant women with COVID-19 infection admitted to our teaching hospital, which serves as a major referral center in western Nepal.

Materials and methods

This was a descriptive cross-sectional study carried out amongst COVID-19 positive pregnant women visiting our institution from January to June, 2022. The inclusion criteria included: (1) all pregnant females who required admission to our facility throughout the study duration, (2) those who had positive test results for SARS-CoV-2, and (3) those who consented to their participation in the study. We excluded all the cases that: (1) tested negative for SARS-CoV-2, (2) patients that had non-obstetric medical-surgical comorbidities, and (3) those who did not consent to their participation in our study.

We classified COVID-19 illness categories based on the NIH (National Institutes of Health) guidelines:^[7]

- asymptomatic infection- individuals who test positive for SARS-CoV-2 using a virologic test but have no symptoms consistent with COVID-19;
- mild illness- individuals who have any of the various signs and symptoms of COVID-19 (e.g. fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but do not have shortness of breath, dyspnea, or abnormal chest imaging;
- moderate illness- individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation measured by pulse oximetry (SpO₂) \geq 94% on room air at sea level;
- severe illness- individuals who have SpO₂ $<$ 94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO₂/FiO₂) $<$ 300 mmHg, a respiratory rate $>$ 30 breaths/min, or lung infiltrates $>$ 50%; and
- critical illness- individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

Ethical approval for the study was obtained from the Institutional Review Committee of GMCTH (Ref 130/078/079). All the participants were informed about the study by the researchers themselves, which comprised of the residents and faculties within the Department of Obstetrics, GMCTH, and informed consent was obtained. The anonymity of the study participants was maintained throughout. Our manuscript was reported in line with the Strengthening the reporting of cohort, cross-sectional and case-control studies in surgery (STROCSS) criteria^[8].

For the enrolled patients, data was collected in a standardized questionnaire. The findings were entered into Microsoft Excel-13. After data cleaning, it was imported and analyzed by using Statistical Package for Social Sciences 25 (SPSS Science Inc.). Descriptive statistics were used for reporting proportions.

Results

A total of 105 COVID-19 positive pregnant women were included in the final analysis. Ninety-one (86.67%) pregnant females underwent institutional delivery at our center, and 14 were those who had pregnancy-related complications requiring hospital admission. The participants' age ranged from 16 to 40 years, mean age being 26.12 ± 5.61 years. The mean gestational age of the study participants was 36.6 weeks and varied from 12.5 weeks to 41.6 weeks. Only 13 (12.38%) pregnant females underwent vaccination. The ethnic distribution and COVID-19 severity in our study are summarized in Tables 1 and 2, respectively.

About four-fifths (82.83%) of the pregnant females in our study were asymptomatic or only mildly symptomatic. Fourteen pregnant females were moderately symptomatic in our cohort and only 4 (3.4%) pregnant females had severe COVID-19 requiring ICU admission. Fortunately, none had critical illness in our study population.

The distribution of COVID-19 spectrum and ethnicity is illustrated in Table 3. Dalits, who are the socio-economically backward group within Nepal, had a comparatively higher occurrence of severe COVID-19 in our study.

Of the 91 COVID-19 positive pregnant females who underwent institutional delivery at our center- 77 (84.62%) were term pregnancies and 14 (15.38%) were preterm deliveries. Mode of delivery was by lower segment cesarean section in slightly over half, 47 (51.65%) cases (Table 3), and all cases that were subject to surgical intervention were purely due to fetomaternal indications rather than COVID itself (Table 4).

None of the neonates tested positive for COVID-19. Neonatal intensive care unit (NICU) admission was required for 40 babies, 21 of which had meconium aspiration and 19 had early onset neonatal sepsis. None of the babies had any congenital anomaly, nor were there any intrauterine fetal deaths or stillbirths. The majority of the babies born to COVID-19 positive mothers had normal fetal weight (62, 68.14%), while low and very-low birth weights were found in 20 and nine babies, respectively.

Discussion

In our study, we describe the findings for a total of 105 pregnant females infected with COVID-19 during the third wave of COVID in Nepal. The participants ranged from 16 through 40 years, mean gestational age being 36.6 weeks, the majority of whom delivered at our center (91, 86.67%). Most of the pregnant families belonged to Brahmin and Chhetri ethnic backgrounds (43, 40.55%). About half (51, 48.55%) of females were asymptomatic while mild and moderate disease was found in 36

Table 1
Ethnicity of the study participants

Ethnic distribution	Frequency (%)
Brahmin & Chhetri	43 (40.55)
Dalit	28 (26.66)
Janajati	20 (19.04)
Newar	6 (5.71)
Muslim	5 (4.76)
Others	3 (2.85)

Table 2
Spectrum of COVID-19 illness severity

COVID severity	Frequency (N= 105) (%)
Asymptomatic	51 (48.55)
Mild	36 (34.28)
Moderate	14 (13.33)
Severe	4 (3.4)
Critical	- (-)

(34.28%) and 14 (13.33%), respectively. Only four patients had severe disease requiring intensive care management. Of the 91 mothers that underwent delivery at our center, 77 (84.62%) were term pregnancies and the rate of cesarean delivery was slightly higher than normal delivery (47, 51.65% vs 44, 48.35%). None of the babies born to COVID-positive pregnant females tested positive for COVID-19 and nor were there any stillbirths or any congenital anomalies. Forty babies required NICU admission. The majority of the babies had normal fetal weight (62, 68.14%).

There is a paucity of data in terms of COVID-19 disease severity and pregnancy outcomes in the Nepalese population, especially with the Delta variant infection. In the study by Thapa *et al.*^[9] from Kathmandu, which included 52 pregnant females during the first wave, more than 90% of pregnant females were asymptomatic and none had moderate, severe, or critical infection. This is in contrast to our study in which more than half of the study participants had symptomatic infection and a few even required intensive care support. One plausible explanation for this can be the surge of the delta variant during the third wave, which was more virulent than the initial strains of the virus and was associated with higher risk of severe maternal illness, placental dysfunction, and fetal compromise^[10]. There is good evidence to suggest that racial and ethnic minority groups have a higher risk of symptomatic as well as severe COVID-19 infection and deaths^[11]. In our study, there was a higher incidence of severe COVID-19 in Dalit community, the ethnically marginalized community in western Nepal, and this is in line with the known information.

Synthesis of the existing evidence in reviews, meta-analyses, and large-scale studies suggest that neonates born to COVID-19 positive pregnant mothers have a higher risk of preterm delivery, cesarean birth, and increased risk of maternal morbidity and mortality, but the frequency of miscarriage and congenital anomalies were similar to noninfected pregnant females^[12-14]. In our cohort, the majority of females (nearly 85%) were term and

Table 3
Distribution of COVID-19 severity in terms of ethnic groups

Ethnicity	Clinical severity					Total
	Asymptomatic	Mild	Moderate	Severe	Critical	
Brahmin & Chhetri	22	12	8	1	-	43
Dalit	13	11	1	3	-	28
Newar	4	2	-	-	-	6
Janajati	17	8	1	-	-	20
Muslim	1	1	3	-	-	5
Others	-	2	1	-	-	3
Total	51	36	14	4	-	105

Table 4
Mode of delivery

Modality	Frequency (%)
LSCS	47 (51.65)
Normal delivery	44 (48.35)
Total	91 (100)

the rates of cesarean were slightly higher than normal delivery. There were no miscarriages or congenital anomalies in our study population. Other studies from Nepal during the pandemic time also had similar findings^[15].

Mother-to-child transmission of COVID-19 is rare and the overall reported rate of congenital infection is about two percent^[16]. None of the studies from Nepal report congenital infection, and neither did us in our study. The majority of children born to COVID-19 positive pregnant women had normal birth weight. Low and very low birth weight babies were frequently found in preterm pregnancies and this may be due to their prematurity rather than COVID infection per se. The severity of COVID-19 infection and adverse feto-maternal outcomes was less during the delta virus surge in Nepal. This may be explained by the fact that the circulating virus strain was less virulent and use of certain medications like ivermectin might have had some protective effect.

Unfortunately, only 13 pregnant females in our study received any vaccination against the virus. There is a low rate of vaccine acceptance among pregnant women in Nepal, and this might be attributed to difficulty in access due to lockdown, delayed rollout of vaccines for the pregnant population as well as increased hesitancy owing to the concern for the safety and efficacy of the vaccines and decreased public awareness^[17,18].

Our study is an important one to fill in the knowledge gap of pregnancy outcomes and disease severity among pregnant COVID-19 positive pregnant women. However, our study had some limitations, one major limitation being the exclusion of pregnant females who had nonobstetric medical and surgical illnesses. There is strong data to suggest that pre-existing comorbidities strongly correlate with the severity of maternal COVID-19 infection and adverse pregnancy outcomes. The exclusion of such patients makes our data less definitive. Because ours is a single-center study, the data we obtained might not be generalizable to other regions. We recommend other researchers to address these aspects in further studies. We also recommend the stakeholders to address the issue of vaccine hesitancy among the pregnant population as well as to provide timely awareness to the high-risk group since it is related to both maternal as well as fetal life. Nonetheless, we provide important information regarding maternal COVID-19 infection during the surge of the Delta virus strain in Nepal.

Conclusion

Severe COVID-19 infection and adverse maternal-fetal outcomes during the third wave of COVID-19 infection with the Delta variant in Nepal were less than in other regions of the world despite low rates of vaccination.

Ethical approval

Ethical approval for this study was provided by the Institutional Review Committee of Gandaki Medical College (Ref 130/078/079).

Consent

Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

C.P. and M.K.: were involved in the conceptualization of the study; C.P., M.K., and S.C.: were involved in the data analysis. All authors were involved in the design of the study, data collection, literature review, writing and editing of the manuscript, and approved the final version of the manuscript.

Conflicts of interest disclosure

There are no conflicts of interest.

Registration of research studies

1. Name of the registry: Research Registry.
2. Unique identifying number or registration ID: research-registry9522.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): <https://www.researchregistry.com/register-now#user-researchregistry/registerresearchdetails/650467b177ea570027811bad/>.

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Data availability statement

Data is available from the corresponding author upon reasonable request.

Provenance and peer review

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