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Clinical Profile, Disease Severity and Perinatal Outcomes of Laboratory-confirmed COVID-19 among Pregnant Women Delivering in a Tertiary Care Centre

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ABSTRACT

Background: Pregnant women and their fetuses represent a high-risk population during coronavirus disease 2019 (COVID-19) pandemic. During pregnancy, body undergoes significant physiologic, mechanical, and immunologic alterations which increases susceptibility to infections. Thus pregnant women are at an increased risk for severe illness from COVID-19. This study explored the clinical profile, disease severity, and perinatal outcomes of pregnant women with COVID-19.

Methods: A retro-prospective cross-sectional study was conducted at KIST Medical College after ethical approval. All women (1227) who delivered from 15 April 2020 to 15 October 2021 and underwent the COVID-19 screening by Reverse Transcriptase Polymerase Chain Reaction were studied. COVID-19 positive women (44) were further analyzed and classified as asymptomatic, mild, moderate, severe, and critical diseases. Data was collected in proforma by reviewing patients' records. The data analysis were done in SPSS version 26. A descriptive statistical test and chi-square test were done.

Results: The prevalence of COVID-19 among delivering pregnant women was 3.6% (44/1227). Majority were asymptomatic 79.5% (35). About 16% (7) had mild illness and 4.5% (2) had moderate illness. The caesarean rate was 34.1% (15/44) among COVID-19 positive women. Stillbirth and preterm birth was observed in 2.3% (1) and 4.5% (2) respectively. The COVID-19 infection rate in a neonate was 4.5%.

Conclusions: The severity of COVID-19 among delivering pregnant women was less. The perinatal outcome was also favourable. The overall prognosis of COVID-19 among mothers and newborns was good. Further research is needed to understand the true magnitude of risks and management, more so with the emergence of new variants.

Keywords: Asymptomatic; COVID-19; perinatal outcome; pregnant women; severity of disease.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) possess a serious health threats to vulnerable populations like pregnant women.[1-3] During pregnancy, the body undergoes significant physiologic, mechanical, and immunologic alterations to support and protect the fetus.[1,4] These changes increase susceptibility to infections,[1] thereby increases the risk of infection with respiratory viruses such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in pregnant individuals and their fetuses.[4] Generally, most cases among pregnant people are asymptomatic or mildly symptomatic.[5] However, pregnant or post-partum women are often at an increased risk for severe illness from COVID-19 when compared to non-pregnant. [6] The evidences on clinical presentation, disease severity, vertical transmissions and perinatal outcomes and overall prognosis of COVID-19 among pregnant women, are still insufficient and need further study.[7] This study explored the clinical and obstetric profile, disease severity, and perinatal outcomes of COVID-19 among delivering pregnant women in a tertiary care centre in Nepal.

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METHODS

This study was a descriptive cross-sectional study done in immediate postpartum mothers who were diagnosed with COVID-19 from April 15 2020 to October 15 2021 at KIST Medical College and Teaching Hospital. Ethical approval was taken from the institutional review committee (077/078). All women who delivered during the study period and who had undergone the COVID-19 screening test were studied. As per hospital infection control and prevention protocol, all the pregnant women admitted for delivery were screened for SARS-CoV-2 by RT-PCR test. A total of 1227 women delivered at the study site during the study period and as it was a census study, all of them were enrolled in the study. Out of 1227, 670 cases (April 15, 2020, to 14 January 2021) were enrolled retrospectively and 557 cases (15 January 2021 to 15 Oct 2021) were enrolled prospectively. All the pregnant women diagnosed with COVID-19 by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) for SARS-CoV-2 (44 cases) were further analyzed. Neonates born to COVID-19 positive mother were screened for COVID-29 by RT-PCR after 24 hour of delivery but within 48 hour of life with parental consent. All COVID-19 positive cases were classified as asymptomatic, mild, moderate, severe, and critical disease as per severity scale developed by the Society for Maternal and Fetal Medicine for the assessment of the pregnant patient with COVID-19.[8]

The patient who delivered outside the study site and had incomplete documentation were excluded from the study. Data was retrieved by reviewing patients' records from the medical record department for data that were taken retrospectively and patient medical files and reports were reviewed for those patients who were enrolled prospectively. Informed written consent was taken for the patient who was enrolled prospectively. Neonatal records belonging to COVID-19 mothers were also reviewed for required information. All required information was extracted and organized into a pretested self-designed proforma. The data was entry and analysis was carried out using Statistical Package for the Social Sciences (SPSS) version 26. Descriptive statistical tests were used to generate the result was generated as mean, standard deviation, frequencies, and percentage. Chi-Square test was also carried out. A significance level p-value of 0.05 was taken as significant.

Assessment of clinical profile included demographic characteristics of participants like age and obstetric characteristics like gestational age at delivery, gravidity, onset and augmentation of labor, mode of deliveries and indication for caesarean sections. Assessment of disease severity of COVID-19 was done by assessing duration from onset of the symptoms of COVID-19 to delivery, presence of symptomatology (asymptomatic or symptomatic), spectrum of symptoms, and severity of disease as mild, moderate, severe and critical. Perinatal outcome was assessed by assessing preterm birth, still birth, Apgar score at 5 minute, low birth weight, NICU admission and COVID-19 status of newborn. Also comparison was done between presence of symptomatology (asymptomatic or symptomatic) in mother with variable assessing clinical profile, disease severity and perinatal outcome.

RESULTS

Among 1227 deliveries during the study period, 44 women were diagnosed with COVID-19 by RT-PCR. The prevalence of COVID-19 among women admitted for delivery at our institute was 3.6%. Among them, 9 were directly admitted to the COVID-19 dedicated ward while 35 were initially admitted in the isolation ward waiting for PCR report for SARS-CoV-2. Eighteen women who were admitted to the isolation ward were discharged before their PCR report of SARS-CoV-2.

The mean age of the women was 25.8+/- 4.5 years with a range of 17 to 38 years old. The mean gestational age was 274.7 +/- 9.1 (39+2 +/- 7+2 week of gestation (WOG)) days with a maximum of 288 days (41+1 WOG) and a minimum of 242 days (34+4 WOG). The mean duration from onset of the symptoms of COVID-19 to delivery was 4+/-2.3 days with a minimum duration of two days and a maximum of seven days.

Out of 44 women, 19 (43.2%) were primigravida and 25 (56.8%) were multigravida. Thirty-nine (88.6%) had spontaneous onset of labor while augmentation of labor was performed for only 18 (40.9%) women. About 65% of total deliveries were normal delivery (Table 1).

The total caesarean rate among all delivery was 39.4 %(483/1227). The caesarean rate among COVID-19 positive women was 34.1% (15/44). The caesarean rate among COVID-19 negative women was 39.6% (468/1183) (Table 2).

All the cases were classified as asymptomatic, mild, moderate, severe, and critical diseases. [8] Majority of women were asymptomatic 79.5% (35) and only 20.5% (9) were symptomatic. About 16% (7) had mild illness and 4.5% (2) had moderate illness (Table 3).

Table 1. Onset of labor and mode of deliveries COVID-19 positive mothers.	
Onset of labor (N=44)	
Spontaneous	39 (88.6%)
Induced	2 (4.5%)
Caesarean done before onset of labour	3 (6.8%)
Mode of delivery (N=44)	
Vaginal Delivery	29 (65.9%)
LSCS (lower section caesarean Section)	15 (34.1%)
Emergency LSCS (EmLSCS)	13 (29.6%)
Elective LSCS (ELLSCS)	2 (4.5%)
Indications for elective LSCS (2)	
Previous LSCS	2
Indications for emergency LSCS (13)	
Fetal distress	4
Previous LSCS in labor	2
Severe oligohydramnios	2
Cephalopelvic disproportion	1
Failed induction of labor	1
Previous LSCS in PROM (Pre-labour rupture of membrane)	1
Prolonged second stage of labor	1
LSCS on maternal request.	1

Table 2. Comparison of caesarean rate among COVID-19 positive and COVID-19 negative mothers.			
	COVID-19 positive patients	COVID-19 negative patients	Total
Caesarean rate	34.1% (15/44)	39.6% (468/1183)	39.4% (483/1227)
Elective LSCS rate	13.3% (2/15)	39.1% (183/468)	38.3% (185/483)
Emergency LSCS rate	86.6% (13/15)	60.9% (285/468)	61.7% (298/483)

Out of 44 deliveries, 97.7% (43) resulted in live births and 2.3% (1) was a stillbirth. The stillbirth was probably due to the prolonged second stage of labor associated with delayed hospital presentation. Preterm birth was observed in 4.5% (2) cases, both of which had spontaneous onset of labor and vaginal delivery. Other outcomes are listed in Table 4.

Table 3. Symptomatology of COVID-19 positive mothers.	
Symptomatology (N=44)	
Asymptomatic	35 (79.5%)
Symptomatic	9 (20.5%)
The spectrum of symptoms among symptomatic (N=9)	
Runny nose	7 (77.8%)
Cough	7 (77.8%)
Bodyache	6 (66.7%)
Sore Throat	3 (33.3%)
Fever	2 (22.2%)
Shortness of breath	0
The severity of illness (N=44)	
Asymptomatic	35 (79.5%)
Mild	7 (16%)
Moderate	2 (4.5%)
Severe	0
Critical	0

Among 43 live births, only 51.1% (22) newborn was tested for SARS-CoV-2 by RT-PCR. Rest of newborn were not tested as parents did not give consent. Among those who were tested, only 2.3% (1) newborn was tested positive. The mean birth weight was 2918 +/- 425 grams. The mean Apgar score at 5 minutes was 8.6.

No significant association was found between symptomatology of mother (asymptomatic or symptomatic) with age group, gravidity, gestational age at delivery, mode of delivery, NICU admission, COVID-19 positive in the neonate, low birth weight, gestational age at birth and Apgar score at 5 minutes (Table 5).

Table 4. Neonatal outcome of COVID-19 positive mothers.	
Gestational age at birth (N=44)	
Preterm (<37 WOG)	2 (4.5%)
Term	42 (95.5%)
Condition at birth (N=44)	
Live Births	43 (97.7%)
Still Birth	1 (2.3%)
Apgar score at 5 minute (N=44)	
Low Apgar Score <7	1 (2.3%) (still birth)
Apgar Score>=7	43 (97.7%)
Birth weight (N=44)	
Low birth weight <2500 grams	5 (11.4%)
>=2500 grams	39 (88.6%)
Admission after birth (N=43)	
Rooming in with mother	22 (51.2%)
Nursery	12 (27.9%)
NICU (Neonatal Intensive Care Unit)	9 (20.9%)
Breastfeeding status (N=43)	
Breastfeeding started immediately after delivery	24 (55.81%)
Breastfeeding delayed due to isolation of the newborn	19 (44.2%)
COVID-19 test of newborn (N=22)	
Positive	1 (4.5%)
Negative	21 (95.5%)
Symptomatology in newborn (N=43)	
Newborn with respiratory symptoms	10 (23.3%) (diagnosed as respiratory distress due to prematurity, Meconium aspiration syndrome (MAS) with congenital heart disease (CHD) , MAS-2 , suspected neonatal sepsis (NNS)-2, assumed NNS with CHD, perinatal asphyxia, transient tachypnea of newborn)
Newborn without respiratory symptoms	33 (76.7%)

Table 5. Comparison between asymptomatic and symptomatic COVID-19 positive mother.			
	Asymptomatic	**Symptomatic**	**P value**
Age (N=44)			
<25 years	15	3	0.793
25-30 years	15	5	
>30 years	5	1	
Gravida (N=44)			
Primigravida	16	3	0.710
Multigravida	19	6	
Gestational age at delivery(N=44)			

Table 5. Comparison between asymptomatic and symptomatic COVID-19 positive mother.

	Asymptomatic	Symptomatic	P value
<37 WOG	2	0	0.596
37 to 40 WOG	24	7	
>40 WOG	9	2	
Mode of delivery (N=44)			
Normal delivery	22	7	0.695
Caesarean Delivery	13	2	
Caesarean Rate (N=44)	37.1%	22.2%	
Emergency caesarean rate (N=44)	31.4%	22.2%	
Condition at birth (N=44)			
Live Birth	34	9	1.000
Still Birth	1	0	
Low birth weight (N=44)			
Low birth weight (<2500 grams)	4	1	1.000
>=2500 grams	31	8	
Gestational age at birth (N=44)			
Preterm	2	0	0.332
Term	33	9	
Apgar score at 5 minute (N=44)			
Low Apgar (<7)	1	0	1.000
Apgar (>=7)	34	9	
NICU admission (N=43)			
Yes	5	4	0.067
No	29	5	
COVID-19 test in newborn (N=22)			
Positive	1	0	1.000
Negative	14	7	

DISCUSSION

COVID-19 cases are increasing exponentially; based on this a significant number of asymptomatic pregnant women may be presenting to health care facilities.[9] Pregnancy being a high-risk state; pregnant individuals are susceptible to pathogens of infectious diseases and likely to develop adverse outcomes. [10] However, our findings suggest that COVID-19 is frequently asymptomatic in pregnant women and the overall outcome among mother and their foetuses is favourable.

Considering the asymptomatic nature of COVID-19, the universal testing of all pregnant women admitted for delivery was done. As expected majority of cases were asymptomatic. Therefore, the universal testing strategy helped identify asymptomatic pregnant women who are currently under-represented in general population testing data. A similar finding was illustrated by other studies as well. [7, 9, 11, 12] Hence, universal testing for all pregnant women upon admission for delivery has potential value for several reasons. It facilitates early initiation of infection control precautions by identifying asymptomatic patients thus ensuring the safety of newborns, family members, and health care professionals. Our findings revealed a large proportion of asymptomatic patients which suggest implementing more restrictive visitor policies, strict hand, and respiratory hygiene precautions, and masking for all patients and health care professional.

The prevalence of COVID-19 in our study is 3.6%. The

prevalence in our study is greater when compared to 2.3%. [13] Approximately 80% of COVID-19 are mild or asymptomatic in the normal population whereas 15% are severe and 5% are critical requiring mechanical ventilation. [7] In pregnant women with COVID-19, 74% were asymptomatic or mild, 8% severe, and 4% critical in another study.[11] Another study revealed 95% of asymptomatic or mildly ill and only 3% critically ill in pregnant women.[12] Therefore, a similar pattern of clinical severity is observed between pregnant and non-pregnant individuals.

In our study, the majority 79.5% were asymptomatic which is likely due to universal testing. Among those who were symptomatic (20.5%) and 16% (7) had mild illness and 4.5% (2) had moderate illness. Other studies also has shown high asymptomatic rate 54.5% [5], 63% [15], 64.3% [16] and 70%.[12] Another study showed, 73.3% had mild symptoms, 22.2% had moderate and 4.4% had severe symptoms respectively. [14] Fortunately in our study there were no severe or critical cases. The numbers may change as new mutant viruses are being discovered and emerging rapidly, but only limited data about their effect on pregnancy are available.

The common symptoms were dry cough (65.6%), fever (48.3%), and myalgia (37.9%). Less commonly reported symptoms included headache, shortness of breath, and chest pain.[9] Similarly in other studies, cough and fever were common symptoms. [10,17] In our study, the most common symptom was cough and cold (77.8%), body ache (66.7%), sore throat (33.3%), and fever (22.2%). None of the patients had dyspnoea.

In our study the caesarean rate among COVID-19 positive pregnant women was 34.1% which is similar to 34.1[16], 34% [18], 36.9% [12] but lower when compared to 44.4% [9,] 59% [19] The risk of caesarean birth was higher in severe to critical COVID-19 in comparison with asymptomatic patients.[12] Indications for caesarean deliveries were fetal distress, previous caesarean, failure of progress of labor, and failed labor induction.[9] Similar to this the most common indication of caesarean deliveries in our study was previous caesarean section and fetal distress. Most of the indications for caesarean section were other than maternal compromise due to SARS-CoV-2 infection [9, 19] and similar was observed in our study. Caesareans section rate was found to be 39.5% among symptomatic and 34% among asymptomatic patients.[12] In our study rate of the caesareans section was less in symptomatic patients (22.2%) when compared with asymptomatic patients (37.1%).

In our study only 22 neonates were tested for COVID-19 by RT-PCR and only one was tested positive for COVID-19. The COVID-19 positive newborn was delivered by an emergency LSCS under standard infection control precautions. Skin-to-skin contact with the mother and delayed cord clamping was avoided. The baby was immediately isolated and breastfeeding was not done. Nasopharyngeal swab for SARS-CoV-2 RT-PCR sent at 42 hours of life was tested positive with CT value of 34 for ORF1 tab and 34 for N gene. Therefore it could be a case of vertical transmission. That makes the rate of vertical transmission in our study to be 4.5%. This rate is higher when compared to 3.2% [20] and 1.9%.[17] The similarity was noted in the proportion of neonates who tested positive in China (2.0%) and outside of China (2.7%).[20] Neonatal SARS-CoV-2 infection occurred in 3% of infants born to either asymptomatic or mildly symptomatic women.[12] The vertical transmission of COVID-19 although possible possesses very low risk. The evidence on maternal-fetal transmission of SARS-CoV-2 is largely unexplored. [19] SARS-CoV-2 RNA testing in neonatal cord blood was positive in 2.9%, 7.7% of placenta samples, and 0% of amniotic fluid. [20] As our institution had no provision for sampling and testing other samples like cord blood, placenta, and amniotic fluids, further testing was not done.

Studies had shown the preterm birth rate of 11.1% [16], 16.7% [12], 17.8% [21], 17.9% [15], 25%. [19] Unlike to above studies, the rate of preterm birth in our study is less (4.5%). A study revealed a 21.2% preterm birth rate among symptomatic and only 11.9% preterm birth rate in asymptomatic. [12] Contrary to this finding our study shows all preterm birth to be among asymptomatic women. A study showed the rate of iatrogenic preterm birth was very high at 80% [19] unlike which all preterm birth in our study was by vaginal delivery following spontaneous onset of labor. Overall it was found that COVID-19 during pregnancy subjects to increased risk of preterm birth. [6]

The rate of low birth in our study was 11.4%, which is very low when compared to 29.5% [15] and very high when compared to 3.7%. [17] Increased rate of low birth weight among newborns born to COVID-19 positive mothers was observed in various other studies. [15, 19] The mean Apgar score in our study at 5 minutes was 8.6 which is less when compared to 9.44. [21] A study also has shown that percentage of neonates with a 5-minute Apgar score of three or less was 2.9% in the severe-critical, 0.2% in the mild-moderate, and 0.7% in the asymptomatic group. [12] The rate of NICU admission among babies born to COVID-19 mothers was 9.4% [18], 13.6% [15], 11.6 [16] but in

our study NICU admission was 20.9%.

Studies showed maternal death rate 1.6% [18], 1.2% [19] 0.3% [11], 0.94% [12], fortunately there was no maternal mortality in our study. Sources also revealed that in comparison with the pre-pandemic period, maternal death remained stable. [16] A study showed the rate of stillbirth was 0.7% and early neonatal death was 0.2%. [16] In our study, the rate of stillbirth was 2.3% which is comparable with the first study while no neonatal death occurs in our study. Stillbirth among symptomatic patients was 0.78% and among asymptomatic was 0.86% which was significant. Neonatal death among symptomatic was 0.47% and that among asymptomatic was 0.34%. [12] In our study, one stillbirth occurred in an asymptomatic patient and none in the symptomatic patient. A study commented that people who have COVID-19 during pregnancy are at increased risk for stillbirth [6] but another study revealed stillbirth and neonatal death remained stable when compared with the pre-pandemic period.[16]

Studies showed that adverse maternal and neonatal outcomes were more frequent in patients with severe COVID-19 illness. [12] But overall adverse outcomes resulting from maternal infection with SARS-CoV-2 during pregnancy are infrequent. [5] The natural progression and effect of this disease on pregnancy in comparison to the general population are yet to be studied in detail.[10] Therefore, until further studies, COVID-19 should be considered in all pregnant women in areas where community spread has been established.

The main limitations of this study is that it is single centered study with small sample size. Result of this study may not be generalized in different clinical setting and different population.

CONCLUSIONS

In the context of the COVID-19 pandemic, infection during pregnancy remains an important and unexplored aspect. Our strategy of universal testing identified asymptomatic pregnant women with COVID-19. The universal testing for all pregnant women admitted to the labor unit has shown obvious benefits for the patient, newborn, family, and health care providers. Clinical feature of pregnant women was similar to general population. The severity of disease of COVID-19 was less among pregnant women. Perinatal outcome was also favourable. Our findings are consistent with the overall favourable prognosis published by the author from different countries and at different points of time during the pandemic. But almost all of the above-mentioned studies including ours have a small sample population; thus this result may not be universal. Therefore, the overall prognosis may vary and may be subject to change with emerging new mutants of the virus. Further research is needed to understand the true magnitude of risks and improve the management of disease progression in pregnant women and their foetuses.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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