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SARS-COV-2 INFECTION AND PREGNANCY OUTCOME: A CROSS-SECTIONAL STUDY FROM EASTERN U.P. POPULATION, INDIA

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ABSTRACT

Pregnant females with severe COVID-19 are more likely to develop additional health problems as a result of the infection. This study evaluates and compares the clinical features and pregnancy outcomes among women with and without SARS-CoV-2 infection. Pregnant women were divided into two groups: those with SARS-CoV-2 infection and those without (control group). Blood samples were collected for a COVID panel, including D-Dimer, Ferritin, IL-6, CRP, and Procalcitonin (PCT). Additionally, oral nasal swabs were taken to assess the SARS-CoV-2 viral load. Both SARS-CoV-2 positive and negative women were monitored every trimester for any pregnancy-related complications. The study found that pregnant women infected with SARS-CoV-2 had significantly shorter gestation periods compared to their SARS-CoV-2 negative counterparts. There was also a notable increase in the rates of caesarean and pre-term deliveries among the SARS-CoV-2 positive group, indicating a higher incidence of these outcomes due to the infection. The present study highlights a significant correlation between SARS-CoV-2 infection in pregnant women and adverse pregnancy outcomes, such as reduced gestation periods, increased caesarean sections, and higher pre-term delivery rates. These findings highlight the need for vigilant monitoring and management of pregnant women with SARS-CoV-2 to mitigate risks and improve maternal and fetal health. Continued research is essential to understand these associations and develop targeted interventions to protect this vulnerable population.

KEY WORDS: COVID-19, Coronaviruses, Pregnancy, Registry, Viruses

INTRODUCTION

Following the global onset of COVID-19 infection in 2020, the World Health Organization declared the outbreak a public health emergency in international concern (Sohrabi *et al*., 2020). At present, there is a scarcity of clinical research concerning the novel coronavirus, SARS-CoV-2. Furthermore, various strains of SARS-CoV-2 are circulating worldwide (Harvey *et al*., 2021). The clinical effects of these variants on pregnant women remain undetermined. While prior research has investigated pregnant women's experiences with diseases caused by the coronavirus family, such as Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) and Middle East Respiratory Syndrome coronavirus (MERS-CoV), it has highlighted significant associations with severe complications during pregnancy. These complications may include miscarriage, preeclampsia, Fetal growth restriction, preterm birth, pre-labor rupture of membranes, and maternal mortality (Fathi & Mobina *et al.,* 2020; Schwartz & Graham, 2020).

Pregnant women face an elevated risk of contracting SARS-CoV-2 infection and experiencing related illnesses if their condition is ignored or untreated. This increased susceptibility is due to physiological changes in the immune system, respiratory system, and cardiovascular

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function during pregnancy, which can exacerbate the effects of COVID-19 and lead to more severe outcomes. It is crucial to provide appropriate medical care and monitoring to pregnant women to mitigate these risks and ensure both maternal and fetal health (Knight *et al.*, 2020). Research indicates that pregnant women are primarily vulnerable to respiratory pathogens and severe pneumonia (Kayem *et al*., 2020; Ellington, 2021). The rapid physiological alterations in the immune and cardio-pulmonary systems of pregnant women following SARS-CoV-2 infection—such as an elevated diaphragm, increased oxygen consumption rate, and inflammation of the respiratory tract mucosa—heighten the risk of developing hypoxia. These changes can significantly impair respiratory efficiency, leading to reduced oxygen delivery to vital organs and the fetus. Consequently, pregnant women are at an increased risk for severe complications, underscoring the importance of vigilant monitoring and timely medical intervention to mitigate these risks and ensure maternal and fetal well-being (Chakraborty *et al.,* 2020). Therefore, it is crucial to gather population-specific data from pregnant women to examine the social-epidemiological and clinical etiology that influence COVID-19 outcomes in this group (Ellington, 2021).

The steady increase in COVID-19 cases in India reported as of September 7, 2021, the Ministry of Health and Family Welfare (MoHFW), Government of India, has documented approximately of 3,30,58,843 confirmed cases and 441,042 deaths nationwide. Notably, Uttar Pradesh

Table 1: Clinical parameters from pregnant females with and without SARS-CoV-2 infection

Condition	Maternal age (years)	Maternal body temperature (°F)	Maternal Systolic BP (mmHg)	Maternal Diastolic BP (mmHg)	Maternal haemoglobin content (gm/dL)	Gestation period (days)	Fetal heart rate (per minute)	Neonatal weight (Kg)
SARS-CoV-2 positive pregnant females	27.47±0.92[a]	97.87±0.31[a]	130.00±4.54[a]	76.95±2.76[a]	10.67±0.37[a]	246.05±4.36[a]	142.18±3.02[a]	2.24±0.14[a]
SARS-CoV-2 negative pregnant females	26.71±0.46[a]	97.86±0.16[a]	121.18±3.39[a]	76.47±2.23[a]	11.36±0.51[a]	259.44±3.83[b]	137.20±1.50[a]	2.64±0.15[a]
t-value	t=0.75	t=0.04	t=1.56	t=0.13	t=1.09	t=2.31	t=1.48	t=1.90
P-value	P=0.462	P=0.970	P=0.129	P=0.894	P=0.284	P=0.028	P=0.153	P=0.067
df-value	df=26	df=25	df=32	df=33	df=25	df=32	df=23	df=32

(Values are Mean±SE; t-values significant at P<0.05; small letters represent comparison of means between negative and SARS-CoV-2 positive females)

Table 2: Chi-square of the parameters related to childbirth in females with and without SARS-CoV-2 infection

Parameters	SARS-CoV-2-positive pregnant females	SARS-CoV-2 negative pregnant females	χ^2-value; P-value; df
Normal delivery (%)	5.26[a]	23.53[b]	χ^2=14.559; P<0.0001; df=1
Caesarean delivery (%)	94.74[a]	76.47[a]	
Full-term delivery (%)	61.11[a]	88.24[b]	χ^2=19.187; P<0.0001; df=1
Pre-term delivery (%)	38.89[b]	11.76[a]	
Immediate cord clamping (%)	13.33[a]	7.14[a]	χ^2=2.000; P=0.157; df=1
Delayed cord clamping (%)	86.67[a]	92.86[a]	
Oxytocin administered (%)	84.21[a]	92.86[b]	χ^2=3.979; P=0.046; df=1
No oxytocin administered (%)	15.79[b]	7.14[a]	

(Values are percent values; χ^2-value significant at P<0.05; small letters represent comparison of means between negative and SARS-CoV-2 positive females)

state alone has reported approximately 17,09,457 cases, resulting in about 22,861 deaths attributed to COVID-19 (*Johns Hopkins,* 2021). Therefore, it is imperative to prioritize special attention to Uttar Pradesh when devising strategies to combat SARS-CoV-2 infection among pregnant women. In the present study, we assessed divergent clinical features and pregnancy outcomes among both uninfected females and those with SARS-CoV-2 infection. The present findings enhance our understanding of the intricate relationship between SARS-CoV-2 infection and pregnancy. This knowledge is crucial for informing the development of future strategies to manage SARS-CoV-2 infection in pregnant individuals, ensuring better health outcomes for both mothers and their infants.

MATERIALS AND METHODS

A cross-sectional study was conducted with 36 pregnant females between February 2021 and June 2021 at Sir Sunderlal Hospital, Banaras Hindu University (BHU), Varanasi, India. Participants were identified and examined based on their health history and in adherence to standard SARS-CoV-2 infection precautions, following their proper consent. The study was approved by the Institutional Ethical Committee of Banaras Hindu University (No. Dean/2021/EC/2762).

Blood samples from these participants were analyzed at the Institute of Medical Sciences (IMS), BHU, Varanasi, for a COVID-19 panel, which included D-Dimer, Ferritin, IL-6 (Interleukin-6), CRP (C-Reactive Protein), and PCT (Procalcitonin). Additionally, oral and nasal swabs were taken to test for SARS-CoV-2 infection and sent to the Multidisciplinary Research Unit at IMS, BHU, Varanasi. Pregnant women who tested positive for SARS-CoV-2 were admitted to the COVID-19 ward for further investigation and observation. Those who tested negative were considered as the control group.

Both SARS-CoV-2 positive (n=19) and control (n=17) participants were monitored every trimester for any pregnancy-related complications, with data meticulously recorded for subsequent statistical analysis. This study aims to provide insights into the clinical features and pregnancy outcomes among SARS-CoV-2 infected and uninfected pregnant women, thereby contributing valuable information for the development of effective management strategies for SARS-CoV-2 infection in pregnant populations.

In this study, the normality of the data sets was assessed using the Kolmogorov-Smirnoff test. For data sets that were normally distributed and had homogeneous variances (confirmed by Bartlett's test for equal variances), means were compared using Tukey's test. The data collected, including maternal age, maternal systolic and diastolic blood pressures, maternal body temperature, hemoglobin content, gestation period, fetal heart rate, and neonatal weight, for both SARS-CoV-2 positive and negative individuals, were analyzed using unpaired t-tests. The Post hoc comparison of means conducted using Tukey's test.

Nonetheless, the percentage data comparing: (i) normal delivery versus caesarean delivery, (ii) full-term delivery versus pre-term delivery, (iii) immediate and delayed cord clamping, and (iv) oxytocin administered versus non-administered delivery, among both SARS-CoV-2 positive and negative individuals, were analysed using a two-variable chi-square test. All statistical analyses were conducted using MINITAB 16 software (Minitab Inc., State College, Pennsylvania, USA).

RESULTS

In the present study, all the subjects were young pregnant females of age group 26-27 years. They were either normal females without SARS-CoV-2 infection (n=17) or the females having SARS-CoV-2 infection (n=19). The physiological parameters revealed that irrespective of SARS-CoV-2 infection, the systolic and diastolic blood pressures of the females were 118-134 mmHg and 74-78 mmHg, respectively. The haemoglobin content, foetal heart rate and neonatal weights were 10-11 gm/dL, 136-145 per minute and 2-2.5kg, respectively. Unpaired t-test did not detect significant difference in the maternal systolic and diastolic blood pressures, maternal haemoglobin content, foetal heart rate and neonatal weight of SARS-CoV-2 positive and SARS-CoV-2 negative females. However, the values of gestation period differed significantly between SARS-CoV-2 positive and SARS-CoV-2 negative females. Tukey's *post-hoc* comparison of means revealed that females suffering from SARS-CoV-2 infection had reduced gestation periods than those without SARS-CoV-2 infection.

The χ^2-values further exposed significant differences in normal versus caesarean delivery, full-term versus pre-term delivery, and oxytocin administered versus no oxytocin administered delivery of SARS-CoV-2 positive and SARS-CoV-2 negative females. Comparison of means revealed that SARS-CoV-2 negative females had higher percentage of oxytocin administered (92.86%) normal (23.53%) and full term (61.11%) delivery than SARS-CoV-2 positive females (84.21%, 5.26% and 61.11%, respectively). In contrast, SARS-CoV-2 positive females had higher percentage of caesarean (94.74%) and pre-term (38.89%) delivery than SARS-CoV-2 negative females (76.47% and 11.76%, respectively).

DISCUSSION

The study suggests that women with SARS-CoV-2 infection exhibited shorter gestation periods and a higher

proportion of cesarean and preterm deliveries compared to those without SARS-CoV-2 infection. The observed reduction in gestation periods and the increased incidence of preterm delivery may be attributed to maternal respiratory compromise associated with SARS-CoV-2 infection. These findings align with reports from the United Kingdom, where pregnant women diagnosed with SARS-CoV-2 infection also experienced similar adverse pregnancy outcomes. This highlights the critical need for heightened clinical attention and tailored management strategies for pregnant women with SARS-CoV-2 to mitigate these risks and improve maternal and neonatal health outcomes (Knight *et al.*, 2020). Marian Knight found that 12% of women hospitalized with SARS-CoV-2 infection delivered prematurely, and nearly 60% underwent caesarean section. Additionally, one in twenty new-borns tested positive for SARS-CoV-2, with half diagnosed within 12 hours of birth based on oral swab analysis.

The higher rates of caesarean births by SARS-CoV-2 infected females in our study also indicate towards the maternal compromise due to SARS-CoV-2 infection. In a meta-analysis involving 1316 pregnant women, researchers discovered that three-quarters of those infected with coronaviruses underwent caesarean deliveries (Diriba *et al*., 2020). Regarding prenatal outcomes, fetal distress and neonatal asphyxia were frequently observed abnormalities in infants born to mothers with SARS-CoV-2 infection. These complications are likely linked to the maternal respiratory issues and systemic inflammation caused by the virus, which can impair fetal oxygenation and lead to adverse neonatal conditions. These findings underscore the importance of comprehensive prenatal monitoring and timely interventions for pregnant women with SARS-CoV-2 infection to mitigate the risks of fetal distress and neonatal asphyxia, ensuring better health outcomes for both mothers and their infants. Many previous studies have also reported that the SARS-CoV-2 infection during pregnancy may cause complications to both the mother and the fetus (Lei *et al.,* 2020; Villar *et al.,* 2021). These complications encompass heightened blood pressure, preeclampsia, premature rupture of placental membranes, fetal growth restriction, and/or miscarriage. Many pregnant women infected with corona virus, particularly those with severe cases, required admission to the intensive care unit, leading to fatalities among some mothers.

In contrast to our results, others did not find any link between SARS-CoV-2 infection during pregnancy and a increased risk of recurrent miscarriages and spontaneous preterm births (Wan *et al*., 2020; Yan *et al*., 2020).

In the present study, a clear association between SARS-CoV-2 infection in pregnant women and an increased likelihood of shorter gestation periods, spontaneous cesarean sections, and preterm deliveries was observed. These findings suggest that maternal SARS-CoV-2 infection significantly impacts pregnancy outcomes, leading to higher rates of obstetric complications.

However, additional research is warranted to validate and expand upon these findings. Future studies should encompass diverse population groups across various regions of India to ensure the generalizability of the results. Such research will provide a more comprehensive understanding of the relationship between SARS-CoV-2 infection and pregnancy outcomes, facilitating the development of targeted strategies to improve maternal and neonatal health in the context of the ongoing pandemic.

CONCLUSION

The study demonstrated that pregnant women infected with SARS-CoV-2 exhibit distinct clinical features and pregnancy outcomes compared to uninfected women. Although there were no significant differences in maternal systolic and diastolic blood pressures, hemoglobin content, fetal heart rate, or neonatal weight between the two groups, a notable difference was observed in gestation periods. SARS-CoV-2 positive women had significantly shorter gestation periods than their uninfected counterparts.

Additionally, the study found significant disparities in delivery methods and outcomes. SARS-CoV-2 positive women had a higher incidence of caesarean and pre-term deliveries compared to SARS-CoV-2 negative women, who had higher rates of normal and full-term deliveries. Furthermore, the administration of oxytocin was more common among SARS-CoV-2 negative women.

These findings highlight the need for targeted management strategies to address the specific risks faced by pregnant women with SARS-CoV-2 infection, emphasizing the importance of specialized prenatal care to improve maternal and fetal health outcomes in this vulnerable population.

Statements and Declarations Competing Interests

The authors declare no competing interests.

Conflict of Interest: None

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REFERENCES

Chakraborty, C *et al.* (2020). "SARS-CoV-2 causing pneumonia-

associated respiratory disorder (COVID-19): diagnostic and proposed therapeutic options." *European Rev. Med. Pharmacol. Sci.,* 24(7): 4016-4026. doi:10.26355/eurrev_202004_20871

Diriba, K., Awulachew, E., & Getu, E. (2020). The effect of coronavirus infection (SARS-CoV-2, MERS-CoV, and SARS-CoV) during pregnancy and the possibility of vertical maternal-fetal transmission: a systematic review and meta-analysis. In: *European Journal of Medical Research* (Vol. 25, Issue 1). https://doi.org/10.1186/s40001-020-00439-w.

Kayem, Gilles *et al*. (2020). "A snapshot of the Covid-19 pandemic among pregnant women in France." *J. Gynecol. Obstet. Human Reprod.* 49(7): 101826. doi:10.1016/j.jogoh.2020.101826

Ellington, S. (2021). Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status—United States, January 22–June 7, 2020. MMWR. *Morbidity and Mortality Weekly Report,* 69(25): 769-775. https://doi.org/10.15585/MMWR.MM6925A1

Harvey, W.T., Carabelli, A.M., Jackson, B., Gupta, R.K., Thomson, E.C., Harrison, E.M., Ludden, C., Reeve, R., Rambaut, A., Peacock, S.J., & Robertson, D.L. (2021). SARS-CoV-2 variants, spike mutations and immune escape. *Nat. Rev. Microbiol.,* 19(7): 409-424. https://doi.org/10.1038/s41579-021-00573-0

Kayem, G., Lecarpentier, E., Deruelle, P., Bretelle, F., Azria, E., Blanc, J., Bohec, C., Bornes, M., Ceccaldi, P.F., Chalet, Y., Chauleur, C., Cordier, A.G., Desbrière, R., Doret, M., Dreyfus, M., Driessen, M., Fermaut, M., Gallot, D., Garabédian, C., & Schmitz, T. (2020). A snapshot of the Covid-19 pandemic among pregnant women in France. *J. Gynecol. Obstet. Human Reprod.,* 49(7). https://doi.org/10.1016/j.jogoh.2020.101826

Knight, M., Bunch, K., Vousden, N., Morris, E., Simpson, N., Gale, C., Obrien, P., Quigley, M., Brocklehurst, P., & Kurinczuk, J.J. (2020). Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: National population based cohort study. *The BMJ,* 369. https://doi.org/10.1136/bmj.m2107

Lei, S., Jiang, F., Su, W., Chen, C., Chen, J., Mei, W., Zhan, L.Y., Jia, Y., Zhang, L., Liu, D., Xia, Z.Y., & Xia, Z. (2020). Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. *E Clinical Med.,* 21. https://doi.org/10.1016/j.eclinm.2020.100331

Fathi, Mobina *et al*. (2020). "Coronavirus diseases and pregnancy: COVID-19,SARS, and MERS." *Przeglad Epidemiologiczny,* 74(2): 276-289. doi:10.32394/pe.74.21

India-COVID-19 Overview-Johns Hopkins https://coronavirus.jhu.edu/region/india Retrieved September 7, 2021.

MoHFW | Home. (n.d.). Retrieved September 7, 2021, from https://www.mohfw.gov.in/

Schwartz, D.A., & Graham, A.L. (2020). Potential maternal and infant outcomes from coronavirus 2019-NCOV (SARS-CoV-2) infecting pregnant women: Lessons from SARS, MERS, and other human coronavirus infections. In Viruses (Vol. 12, Issue 2). https://doi.org/10.3390/v12020194

Sohrabi, C., Alsafi, Z., O'Neill, N., Khan, M., Kerwan, A., Al-Jabir, A., Iosifidis, C., & Agha, R. (2020). World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). In: *Intern. J.of Sur.* (Vol. 76, pp. 71-76). https://doi.org/10.1016/j.ijsu.2020.02.034

Villar, J., Ariff, S., Gunier, R.B., Thiruvengadam, R., Rauch, S., Kholin, A., Roggero, P., Prefumo, F., Vale, M.S. do, Cardona-Perez, J.A., Maiz, N., Cetin, I., Savasi, V., Deruelle, P., Easter, S. R., Sichitiu, J., Conti, C.P.S., Ernawati, E., Mhatre, M., & Papageorghiou, A.T. (2021). Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection: The Intercovid Multinational Cohort Study. *JAMA Pediatrics,*175(8): 817-826. ttps://doi.org/10.1001/Jamapediatrics.2021.1050

Wan, Y., Shang, J., Graham, R., Baric, R.S., & Li, F. (2020). Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. *J. Virol.,* 94(7). https://doi.org/10.1128/jvi.00127-20

Yan, R., Zhang, Y., Li,Y., Xia, L., Guo, Y., & Zhou, Q. (2020). Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2. *Sci.,* 367(6485): 1444–1448. https://doi.org/10.1126/science.abb2762