

Evaluation of Feto-Maternal Health Outcomes in Post-COVID Pregnant Women in a Rural Tertiary Care Hospital

Sanjukta Mukherjee¹, Swaralipi Misra², Mriganka Mouli Saha³

¹Senior Resident, Department of Psychiatry, Burdwan Medical College, Purba Bardhaman, West Bengal 713104

²RMO, Department of Obstetrics and Gynaecology, College of Medicine & JNM Hospital, The West Bengal University of Health Sciences, Kalyani, Nadia- 741 235, West Bengal, India

³Assistant Professor, Department of Obstetrics and Gynaecology, College of Medicine & JNM Hospital, the West Bengal University of Health Sciences, Kalyani, Nadia- 741235, West Bengal, India

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Corresponding Author: Dr. Mriganka Mouli Saha

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Abstract:

Introduction: Novel Corona virus infection (SARS-CoV-2), also known as COVID-19 in pregnancy is an important concern but currently limited data available to predict the risk of virus infection in pregnancy and its adverse outcome.

Objective/Aim: Evaluate SARS-CoV-2 infection in pregnancy and its adverse outcome on mother as well on fetus.

Materials and Methods: In this prospective observational study, total number of 1120 pregnant women admitted in the isolation ward of our institution were included. All women presented with common symptoms like fever, tiredness, headache, sore throat, and cough.

Results: Sixty women were diagnosed SARS-CoV-2/COVID-19 positive by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) examination of nasopharyngeal swab (NP), which was almost 5.3% of the isolated women. All neonates were tested negative for SARS-CoV-2 infection. All the study subjects recovered with routine care and were sent home after 7 days with advice for “safe home” (nearby place where the COVID patients can safely stay isolated in a room with all oral medications and report immediately to the healthcare facility if any adverse condition) for further 7 days.

Conclusions: SARS-CoV-2 infection in pregnancy most of the time presents in the latter half of pregnancy and management is similar to that in the general population. There is no increased risk of severe disease during pregnancy. Support of intimate partner, social support will promote mental health hygiene amongst the COVID positive mother. Due to immunological modulation in pregnancy, newborns are mostly protected from disease transmission.

Keywords: Corona Virus, Pregnancy, SARS, COVID 19, RT-PCR.

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Introduction

Novel Corona virus infection (SARS-CoV-2), also known as COVID-19 in pregnancy is an important concern but currently limited data available to predict the risk of virus infection in pregnancy and its adverse outcome [1]. It has been assumed that like other previous infection influenza (H1N1) [2, 3], severe acute respiratory syndrome (SARS) [4], Middle east respiratory syndrome (MERS) [5], SARS-CoV-2 also associated with increased risk of maternal and neonatal mortality and morbidity [6]. Outcome of COVID-19 infections in pregnancy are very unpredictable and widely variable.[7] Due to fear and safety of COVID vaccination among the pregnant women still poses a greater risk of very severe outcome [8]. Many pregnant women may remain

asymptomatic and subsequently can experience only mild or moderate cold and flu-like symptoms like coughs, fever, shortness of breath, headache and loss or change to your sense of smell or taste and so more [9]. There is still not much well-designed available study data on pregnant women who tested positive for the virus in their first trimester and who may get infected with symptoms like high fever may increase the risk of birth defects [10]. In this context based on the available studies published on SARS-CoV-2 in pregnancy, didn't to show any increased risk of severe disease in pregnancy [11]. The rate of caesarean section remains high almost more than 60% in SARS-CoV-2 with pregnancy [12]. Association of co-morbidities like obesity, cardiac disease,

and pulmonary disease increases the risk of disease progression to its severe form [13]. In India, March 2021 Delta variant of the SARS-CoV-2 was only accountable for 4% of all detected samples of through sequencing. At that time widespread vaccination was going on throughout the country where most of the peoples were not vaccinated. Due to this lack of immune status Delta variant was responsible of new cases of 70% in the month of May 2021[14]. Subsequently in November 2021 World Health Organization (WHO) declared Omicron wave replacing the Delta wave which was more transmissible in the community but caused less severe disease confining the variant in the upper respiratory tract only. The reason behind was probably acquired antibodies against SARS-CoV-2 and its variants by the 90% of the populations 15. SARS-CoV-2 and its variants associated with increased risks of adverse pregnancy outcomes like preterm labor, still birth and also long term neurological as well as psychiatric complications [16, 17]. COVID variants are associated with reversible cognitive impairments and various abnormalities in mental status examination [18]. The objectives of this study are to summarize the clinical manifestations and maternal and perinatal outcomes of SARS-CoV-2 during pregnancy and to observe the pregnancy outcomes including mental health status examination along with risk of vertical transmission to neonates and mental status of the women.

Materials and Methods

The study was done from 1st May 2021 to 31st October 2022 as prospective observational study including 1120 pregnant women attended at emergency: antenatal OPD at Department of Obstetrics and Gynaecology (OBG), College of Medicine & JNM Hospital, WBUHS, Kalyani, Nadia, West Bengal with suspected for SARS-CoV-2 infection. They were admitted in the isolation ward fulfilling the criteria either presence of two most/lesser common symptoms or single severe symptoms as mentioned by World Health Organization (WHO) [14]. Most common symptoms: fever, dry cough, tiredness; less common symptoms: generalized body aches, sore throat, diarrhoea, conjunctivitis, headache, loss of taste or smell, a rash on skin, or discoloration of fingers or toes; Serious symptoms: shortness of

breath, chest pain, loss of speech or movement. After admission detailed clinical history were recorded in a preformed proforma provided by the health department of West Bengal and for every patient ADHAAR number was mandatory for creation of unique ID as pre-test booking Then, within 24 hours after admission, a nasopharyngeal swab was taken in the isolation ward while wearing PPE equipment and completing all necessary safety precautions. After taking the swab, the PPE kit was then donned in accordance with ICMR guidelines. It was sent with the preservation of the cold chain to the COVID-19 laboratory.

Viral RNA was detected by (full form) RT-PCR testing. RdRP gene and ORF 1 gene both have to be detected simultaneously in confirmatory protocol after E gene was positive in screening protocol. The sequence RdRP_SARSr-R1 CARATGTTAAASACTATTAGCATA use 800 nM per reaction was specific for SARS-CoV-2/COVID19. The detailed history was being taken from the person as well as the informant, who was in close contact with the patient.

There is a semi structured proforma for taking the history. In the clinic, patients were evaluated thoroughly based on demographic data, vascular risk factors, family history of dementia or psychiatric disease, detailed chronological history, neuropsychological test (cognitive screening part modified by adding some further items on visuo-spatial ability and language functions in vernacular way also known as Bengal Mental Status Examination-BMSE was used for mental status examination in the study (Table 1). It was followed by discussion among neurologist and psychiatrist to reach to a diagnosis as per the established criteria. Any subject with uncorrected visual or auditory impairment and/or impaired performance in hand movements (significant motor or sensory or ataxic disorders that might confound the effect) and with gross comprehensive problem was excluded from the study. The sample size was not formally calculated as it was an observational study. It was based on the number of admissions in the hospital without any power calculation, proportion, and risk ratios with 95% confidence interval.

Table 1: Bengal mental status examination scale (BMSE) 19 (Bengali language)

Section of Mental Status	Questionaries
Memory and concentration	1. "Is it morning / afternoon / evening?"
	2. "What day of the week is today?"
	3. "What is today's date?"
	4. "Which month is this? You can tell me in English / Bengali / Hindi?"
	5. "Which season is this?"
	6. "What is the name of this place / locality?"
	7. "This locality falls under which city?"
	8. "What is the name of this state?"
	9. "What is the name of this country?"
	10. "Where are you standing at this moment?"

Registration	11. “Registration of three objects: “I went to the market and brought 3 things which are mango, chair and paisa.” With a gap of 2 seconds between each word, then ask: “Can you tell me which the three things I brought from the market are? Please try to remember these 3 things because I will ask you again after some time.”
	12. (a) Days of the week forward: “Tell me the names of the days of the week starting from Sunday?”;
	(b) Days of the week backwards: “Now tell me the names of these days in a backward way from Sunday?”
Recall	13. Delayed recall of objects: “Tell me the names of those three things which I told you that I have brought from the market?”
Show	14. Show the wristwatch and pen and ask the patient: “Can you see these objects?” Show the wristwatch and ask, “What is this?” If the patient is unable to see the objects, give the wrist watches to his/her hand and ask what he/she feel is this.
	15. Show the pen and ask, “What is this?” If the patient is unable to see the objects, give the pen to his/her hand and ask what he/she feel is this.
Command	16. Follow command: “Now I will ask you a different type of question. Look at my face and do exactly what I do.” If the patient has poor vision then give the instructions: “Listen carefully and do exactly what I say, CLOSE YOUR EYES.”
	17. Three step command: (oral) “I will give you a piece of paper and do exactly what I ask you to do. First, take the paper in your right hand, then fold it into half with both of your hand and then give the paper back to me.”
Construction	18. Sentence construction: “Tell me something about your house.”
Copy	19. Copy figure: “Exactly copy the above drawing in the space given below.”

One point each to Questions 1-10, 3 points for Question 11,

- 5 points for Questions 12,
- 3 points for Question 13,
- 2 points for Question 14,
- 1 point each for Questions 15, 16,
- 3 points for Question 17,
- 1 point each for Questions 18, 19.

For question 12, only proceed if able to name days of week forward. Give one point for each correct response to days of week backward from Sunday. For Question 17, give one point for take paper right hand, folds and return paper. Maximum score: 30 Range: 0-30.

Result

Most of the patients were in between age group of 20-30 years and also with normal BMI (Table 2). No smokers were found in our study. Total 220 women were suffering from pre-existing medical problems like asthma, diabetes, hypertension and cardiac disease. We have found both primigravida and multi-gravida women almost equally in our study. Surprisingly 40 patients were having twin pregnancy. Almost two-third patients were preterm and also 120 patients admitted in puerperal period. Women were presented with multiple symptoms and the common symptoms such as fever, tiredness, headache, sore throat, and cough (Fig. 1).

Table 2: Demographic characteristics of study population (n=1120)

Demographic Characteristics	Number of women (n=1120)
Age	No of women (%)
<20	140(12.5)
20- 30	880 (78.6)
>30	100 (8.9)
Body mass index:	
Normal	720 (64.2)
Overweight	300 (26.8)
Obese	100 (9)
Smoking	
Yes	0
No	1120

Pre-existing medical problems	
Asthma	120 (10.7)
Diabetes	40(3.5)
Hypertension	40 (3.5)
Cardiac disease	20 (1.75)
Parity	
Primi	540 (48.2)
Multi	580 (51.8)
Multiple Pregnancy	40 (3.5)
Gestational age at admission	
<24	40 (3.5)
24-28	80 (7)
28-32	240 (21.4)
32-37	420 (37.5)
>37	220(19.9)
Puerperium	120 (10.7)

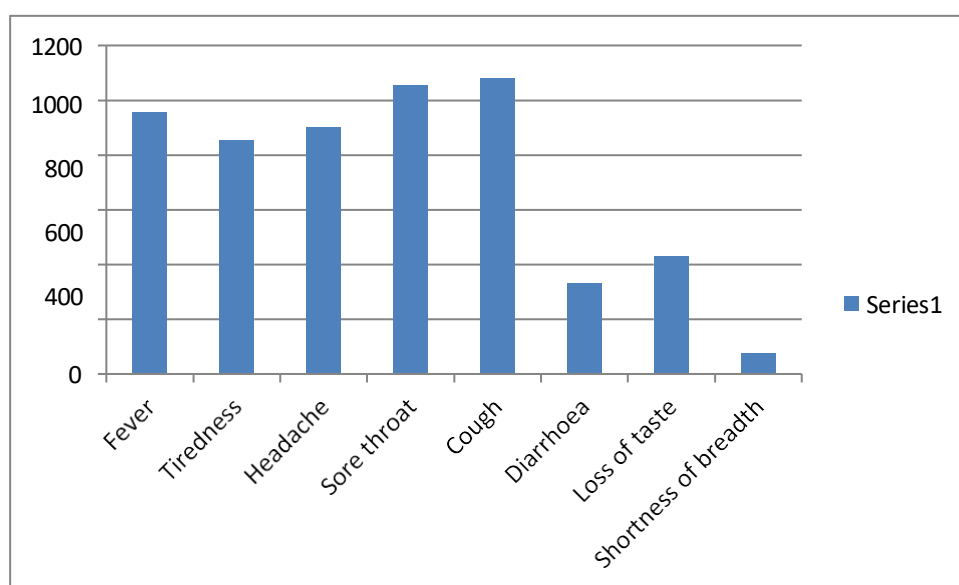


Figure 1: Symptoms of the patients (n=1120) (single patient presents with multiple symptoms)

Fever (n=956), Tiredness(n=852), Headache(n=902), Sore throat (n=1052), Cough (n=1079), Diarrhoea (n=331), Loss of taste (n=429), Shortness of Breath (n=76).

There were total 60SARS-CoV-2/COVID-19 positive cases which was almost 5.3% of the isolated women. All neonates of the positive mothers were tested negative.

According to Table 3; spontaneous miscarriage in 1 (1.6% vs. 1.3%), malpresentation in 1 (1.6% vs. 0.6%), intra uterine fetal demise (IUFD) in 1 (1.6% vs. 1.4%) and placental abruption in 1 (1.6% vs. 0.3%) were similar both in study group and control group.

But fetal growth restriction (FGR) in 6 (10% vs. 1.5%) was significantly higher in study group than control group (p <0.001). Among intra-natal events preterm labor in 9 (15% vs. 1.3%) (p <0.001) higher in study population and prolonged labor in 1 (1.6% vs. 1.2%), fetal bradycardia in 1 (1.6% vs. 1.8%) and

retained placenta in 1 (1.6% vs. 1.03%) which all were not significantly different in inter-group analysis. Preterm premature rupture of membranes (PPROM) or premature rupture of membranes (PROM) was found in 8 (13%) cases and it was significantly higher than control (p < 0.001).

In the study population 36 (60%) women were delivered by lower segment cesarean section and 18 (30%) women delivered vaginally compared to 20% and 75.5% in control group which were statistically significant. Rest 6 (10% vs. 4.5%) women delivered by assisted vaginal delivery and it was also significant finding (p <0.001). Postpartum hemorrhage (PPH) and Sub-involution of uterus were seen insignificantly associated in between both group i.e. 1 (1.6% vs. 0.9% and 1.3%). Total 9 (15% vs. 4.4%, p < 0.001) babies of study population had APGAR score less than seven and rest 49 (81.7% vs. 92.8% in control, p < 0.001) babies had APGAR score more than seven. Marked predominance of low-birth-weight babies i.e. 23 newborns (38.3%) were

determined to be under 2500 gram., of which 11 (18.3%) were between 2000 and 2500 gram. and 12 (20%) were under 2000 gram. Whereas only 12.9%

babies were low birth weight among control group ($p < 0.001$). The rest 35 (58.3% vs. 84.2%) in control group babies were of normal birth weight.

Table 3: Spectrum of adverse obstetric and fetal and mental health outcomes

Antenatal complications	Study group n= 60	Control group n= 1060	p value
Spontaneous miscarriages	1(1.6%)	14 (1.3%)	0.352
Malpresentations	1 (1.6%)	7 (0.6%)	0.254
Fetal growth restriction	6 (10%)	16 (1.5%)	<0.001
Intrauterine fetal death	1 (1.6%)	15 (1.4%)	0.631
Placental abruption	1 (1.6%)	4 (0.3%)	0.049
Intranatal complications			
Preterm labor Prolonged labor Fetal bradycardia Retained placenta PPRM or PROM*	9 (15%)	14 (1.3%)	<0.001
	1 (1.6%)	13 (1.2%)	0.546
	1 (1.6%)	20 (1.8%)	0.392
	1 (1.6%)	11 (1.03%)	0.464
	8 (13%)	36 (3.3%)	<0.001
Mode of delivery			
Cesarean delivery Vaginal delivery Assisted vaginal delivery	36(60%)	212 (20%)	<0.001
	18 (30%)	800 (75.5%)	<0.001
	6 (10%)	48 (4.5%)	<0.001
Postnatal complications			
Postpartum hemorrhage Sub involution of uterus	1 (1.6%)	10 (0.9%)	0.176
	1 (1.6 %)	6 (1.3%)	0.243
Fetal outcomes			
APGAR score at five minute	9 (15%)	47 (4.4%)	<0.001
<7	49 (81.7%)	984 (92.8%)	<0.001
>7			
Birth weight			
<2000 gm.	12 (20%)	56 (5.2%)	<0.001
2000-2500 gm.	11 (18.3%)	82 (7.7%)	<0.001
>2500 gm.	35 (58.3%)	893 (84.2%)	<0.001

Based on BMSE Score Table-4, dementia could be subdivided in 3 subgroups as BMSE from 21 to 24 for mild mental impairment, BMSE from 13 to 20 for moderate mental impairment and BMSE less than 12 for severe mental impairment. In present

study it was observed that the cases are predominantly of mild mental impairment 46 patient (76.6%), moderate mental impairment cases were 8 (13.4%) and severe mental impairment total observed in 6 (10%) which were significantly higher in study population than control.

Table 4: BMSE Score Parameters among Study (n=60) and Control (n=1060) group

BMSE Score	Study group (n=60)	Control group(n=1060)	P value
25-30 (Normal mental status)	0	848 (80%)	< 0.001
20 to <25 (mild mental impairment)	46 (76.6%)	212 (20%)	< 0.001
10 to <20 (moderate mental impairment)	8 (13.4%)	0	< 0.001
0 to <10 (severe mental impairment)	6 (10%)	0	< 0.001

BMSE Score interpretation: A score of 25 or higher is classed as normal. If the score is below 24, the result is usually considered to be abnormal, indicating possible mental impairment.

Discussion

Receptors known to us for the different human corona virus infections (HCoV) till now as like angiotensin-converting enzyme 2 (ACE-2) for SARS and dipeptidyl peptidase-4 (DPP4) for MERS [20,21]. The recent pandemic of SARS-CoV-2 share

same receptor ACE 2 but it has more strong affinity to the receptor binding domain(RBD) [22]. Moreover, it has similarity with the bat coronavirus (BatCoV-RaTG13) which indicates animal to human transmission may occur in this pandemic [23]. Considering the structural similarities SARS-CoV-2 resembles like beta-coronavirus family almost resembling SARS-CoV taxonomically [24]. To interact with the host and establish the virion's susceptibility, a particular receptor protein must be present

on the host cell surface. After binding with the specific receptor viral RNA is being released in to the cytoplasm of host cell for production of replicase polyprotein (pp) by translation and split into 12-15 non-specific proteins (nsps) [25]. These nsps alter the immune response and modulate the cell cycle. Subsequently negative sense copies of both genomic and sub genomic RNAs are produced and it act as template for synthesis of positive sense genomic and sub genomic mRNAs. Viral N protein will bind to endoplasmic reticulum-Golgi compartment (ER-GIC) [26]. M protein guides the interaction with both N protein and S protein. The E protein is required for virus formation and it induces membrane curvature and prevents aggregation of M protein. Newly assembled virions are released usually within 3-4 h after initial infection [27]. Depending upon the symptoms and clinical findings only, it is very difficult to diagnose SARS-CoV-2 infection in pregnancy, as most of them are non-specific which may be concurrently encountered in other viral infections also. It has to be done based on clinical and subsequent detection of viral gene on RTPCR through NP (nasopharyngeal) swab [28]. Among the clinical symptoms in our observation in the isolation ward of our institution the common symptoms were fever, tiredness, headache, sore throat, and cough. Other studies also depicted that fever is the most common symptom, followed by fatigue, dry cough, loss of smell & taste [29]. A sensitive technique for predicting SARS-CoV-2 infection is bilateral multi-lobular ground glass opacity on HRCT thorax associated with pneumonic alterations, however its use in pregnancy should be restricted due to radiation risks and, if performed, use of an abdominal shield is required [30]. Though there is evidence that the low dose radiation associated with CT is believed not to be teratogenic. The amount of exposure to the fetus from a two-view CXR of the mother is only 0.00007 rad, and 10 chest CT slices result in an exposure of <0.1 rad. As a result, CXR and CT can be considered in pregnant patients with suspected COVID-19 and safely done if necessary. Pulmonary ultrasound has also been suggested for a quick diagnosis of pneumonia in pregnant women. [31]

Due to the newly evolving SARS-CoV-2 infection, the exact extent of fetal adverse effect is not known to us. There is no data suggestive of increased risk of miscarriage [32]. Currently, it is very difficult to comment on the negative effects of SARS-CoV-2 infection during the first trimester due to a lack of data. A few studies and case series involving the second and third trimester women revealed no increased risk of teratogenicity [33, 34]. In a study involving nine pregnant women with SARS-CoV-2 infection showing none of their babies were involved and similarly in another study also showed 38 newborns of positive mothers were tested negative for SARS-CoV-2 infection [35, 36]. Similarly a study involving 33 pregnant women with SARS-

CoV-2 infection found that three of the neonates were having clinical sign and tested positive for SARS-CoV-2 infection [37]. Pathophysiology of the vertical disease transmission during womb or after the birth is uncertain. In pregnancy there is a dominance of Th2 (T cell helper) which protect the fetus from viral infection [38]. Neonates should be allowed for expressed breast milk feeding with proper hygiene and hand washing [39]. As reported by Royal College of Obstetrician and Gynecologists (RCOG), about 10% of affected pregnant mother may require critical care and about 40% mother may deliver preterm with higher chance of about 60% caesarean section rate [40]. COVID-19 has negative impact on mental health of the perinatal population as well as in the post-partum period. There are very limited studies which has evaluated the extent of the effect of this pandemic on the mental health. But in few studies demonstrated that domestic violence, low socioeconomic level, adverse obstetrics outcomes, gender preferences and history of psychiatric illness is associated with adverse mental outcomes. [41] It is of immense importance that the Mental State Examination should be done appropriately in regard to its subjects and items studied in a specified segment of population in relation to their language and socio-cultural background. [42] Mental State Examination had been translated and or modified in different languages. Study data suggests that carefully modified Bangla version of Mental State Examination i.e. Bengal mental status examination scale (BMSE) is not only effective as other examination scales but also effectively assessed most of the mental domains. [43] Irrespective of level of literacy our subjects were also more comfortable with Bengal mental status examination scale (BMSE) in vernacular language. In this study, BMSE was adapted in order to meet two goals; i.e. consistent with Bangla cultural contexts and feasible for use in illiterate and less educated elderly. In our study a significant intergroup difference in BMSE score was found in between study and control group.

Optimal prenatal visit is the key success for successful pregnancy outcomes. During SARS-CoV-2 pandemic tele-health visit may be an alternative option. Premature birth and increased caesarean section with special care for newborn to prevent SARS-CoV-2 infection is an emerging concern. [44,45] Currently rapid testing for antibodies against SARS-CoV-2 infection is widely being tested in different laboratories with almost 90% sensitivity and 80% specificity [46]. There are two types of antibodies IgM, which appears one week post infection and IgG which requires two to four weeks after SARS-CoV-2 infection [47]. It is an effective screening test with reasonable specificity, and a negative result means the patient is either not infected or has been infected in the past but failed to create immunological antibodies, or the test has produced the incorrect result. Confirmatory RTPCR testing is necessary in cases

of negative antibody testing and symptoms that point to SARS-CoV-2 infection. Positive rapid antibody testing requires no further testing and protocol of management of SARS-CoV-2 infection should be initiated [48].

Conclusions

SARS-CoV-2 infection in pregnancy has variable outcomes from asymptomatic to very severe disease. Wide awareness regarding safety and feasibility of COVID vaccination among the pregnant women is an important issue. Mental health support is also important for healthy mother and baby as pregnancy outcome.

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