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SARS-CoV-2/COVID-19 infection in pregnancy and its outcome in a rural tertiary care centre of West Bengal

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SARS-CoV-2 infection in pregnancy and its adverse outcome on the mother as well on the fetus is emerging as an important concern, but knowledge about the prognosis is limited. In our prospective observational study total of 56 pregnant women admitted in the isolation ward of our institution were included. All women were presented with common symptoms like fever, tiredness, headache, sore throat, and cough. Three women diagnosed SARS-CoV-2/COVID-19 positive by Reverse Transcription Polymerase Chain Reaction (RTPCR) examination of the nasopharyngeal swab. All three neonates were tested negative for SARS-CoV-2 infection. The three mothers also recovered with routine care and returned home after 7 days with advice for a safe home for further 7 days. SARS-CoV-2 infection in pregnancy mostly appears inthe later part of pregnancy and management is almost like the general population. There is no increased risk of severe disease during pregnancy. Neonates are mostly protected from disease transmission due to immune modulation during pregnancy.

Keywords: Bronchiectasis, CoV-2 in pregnancy, Hemogram, Nucleocapsid, Replicase

Novel coronavirus (nCoV) infection, also known as coronavirus disease 2019 (COVID-19) in pregnancy is an important concern, but currently, limited data are available to predict the risk of virus infection in pregnancy and its adverse outcome[1].It has been assumed that like another previous infection influenza (H_1N_1)[2,3], severe acute respiratory syndrome (SARS)[4], Middle east respiratory syndrome (MERS), SARS-CoV-2 is also associated with increased risk of maternal and neonatal mortality and morbidity. Coronaviruses belong to the RNA virus family and therefore RNA dependent RNA polymerase (RdRPs) is essential for the life cycle of the virus[5]. Coronavirus is approximately 120 nm in length, with spikes of protein which are club- shaped and projected from the surface of the virion looking like solar ray (Fig. 1). It has four canonical structural proteins as described: large trans-membrane spike protein (S; 1160-1400 amino acid- AA), a small envelope protein (E; 74-109 AA), glycoprotein (M; 250 AA), and phosphorylated nucleocapsid (N; 500 AA)[6]. Common characteristics of CoVs include (1) replicase-transcriptase gene which is with highly conserved structural and accessory genes; (2) nonstructural genes by ribosomal frameshifting; (3) replicase–transcriptase polyprotein for enzymatic activities; and (4) downstream genes by the synthesis of 3′ nested sub-genomic mRNAs[7].

Receptors for the different human coronavirus (hCoV) infections are angiotensin-converting enzyme 2 (ACE2) for SARS and dipeptidyl peptidase-4 (DPP4) for MERS[8,9]. The recent pandemic of SARS-CoV-2 share the same receptor ACE2, but it has a strong affinity to the receptor- binding domain (RBD)[10]. The availability of specific receptor protein on the host cell surface is essential for the interaction between virion and host and it determines the susceptibility of the virion. After binding with the specific receptor viral RNA is being released into the cytoplasm of the host cell for the production of replicase polyprotein (pp) by translation and split into 12-15 non-speific proteins (nsps)[11]. 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 act as a template for synthesis of positive-sense genomic

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Abbreviations: ACE2, Angiotensin-converting enzyme-2; COVID-19, Coronavirus disease-2019; ERGIC, Endoplasmic reticulum-Golgi compartment; hCoV, Human coronavirus; MERS, Middle East respiratory syndrome; nCoV, Novel Coronavirus; NP, Nasopharyngeal; pp, Polyprotein; RdRP, RNA-dependent RNA polymerase; RT-PCR, Reverse transcription- polymerase chain reaction; SARS, Severe acute respiratory syndrome

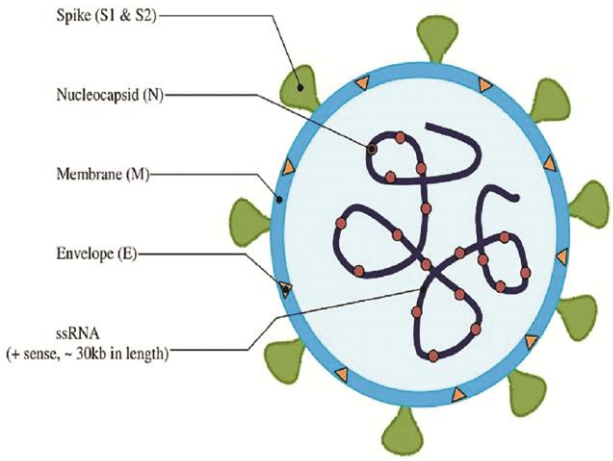


Fig. 1 — Structure of coronavirus (SARS-CoV-2/COVID-19)

and sub-genomic mRNAs. Viral N protein bind to the endoplasmic reticulum-golgi compartment (ERGIC)[12]. 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[13].

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[14]. There is limited information about pregnant women who tested positive for the virus in their first trimester and who may get infected with symptoms like a high fever that may increase the risk of birth defects[15]. Limited data available on SARS-CoV-2 in pregnancy do not show an increased risk of severe disease in pregnancy[16].The rate of caesarean section remains high, almost more than 60% in SARS-CoV-2 with pregnancy[17]. Association of co-morbidities like obesity, cardiac disease, and pulmonary disease increases the risk of disease progression to its severe form[18]. The objectives of this study were to evaluate the prevalence of clinical manifestations and maternal and perinatal outcomes of SARS-CoV-2 during pregnancy and presenting symptoms. We have also analysed the pregnancy outcomes along with the risk of transmission to neonates.

Materials and Methods

This prospective observational study included 56 pregnant women who attended at emergency and antenatal out-patient Department from the Obstetrics and Gynaecology (OBG) Department, College of Medicine & JNM Hospital, The West Bengal University of Health Sciences, Kalyani, Nadia, West Bengal with suspected of SARS-CoV-2 infection. They were admitted in the isolation ward fulfilling the criteria either presence of two most/less common symptoms or single severe symptoms as mentioned by the World Health Organization (WHO)[19]. The most common symptoms include fever, dry cough, tiredness; Less common symptoms: generalized body aches, sore throat, diarrhea, conjunctivitis, headache, loss of taste or smell, rash on the skin, or discoloration of fingers or toes. Serious symptoms include shortness of breath, chest pain, loss of speech or movement. After admission detailed clinical history was recorded. A nasopharyngeal swab from subjects was taken within 24 h of admission in the isolation ward, samples were transported to the COVID-19 laboratory maintaining a cold chain. Viral RNA was detected by Reverse Transcription Polymerase Chain Reaction (RT-PCR). RdRP gene and orf 1 gene both have to be detected simultaneously in the confirmatory protocol after the E gene is positive in screening protocol. The sequence RdRP_SARSr-R1 CARATGTTAAASACACTATT AGCATA uses 800 nM per reaction is specific for SARS-CoV-2, Wuhan strain COVID-19. The sample size was based on the number of admission in the hospital without any power calculation, proportion, and risk ratios with a 95% confidence interval (Table 1).

Management and treatment protocol SARS-CoV-2 in pregnancy

General Principles for patient management are mentioned in (Box 1). Specific precautionary measures for health care workers must be followed as per the guideline of the regulatory health authorities. (Table 2).

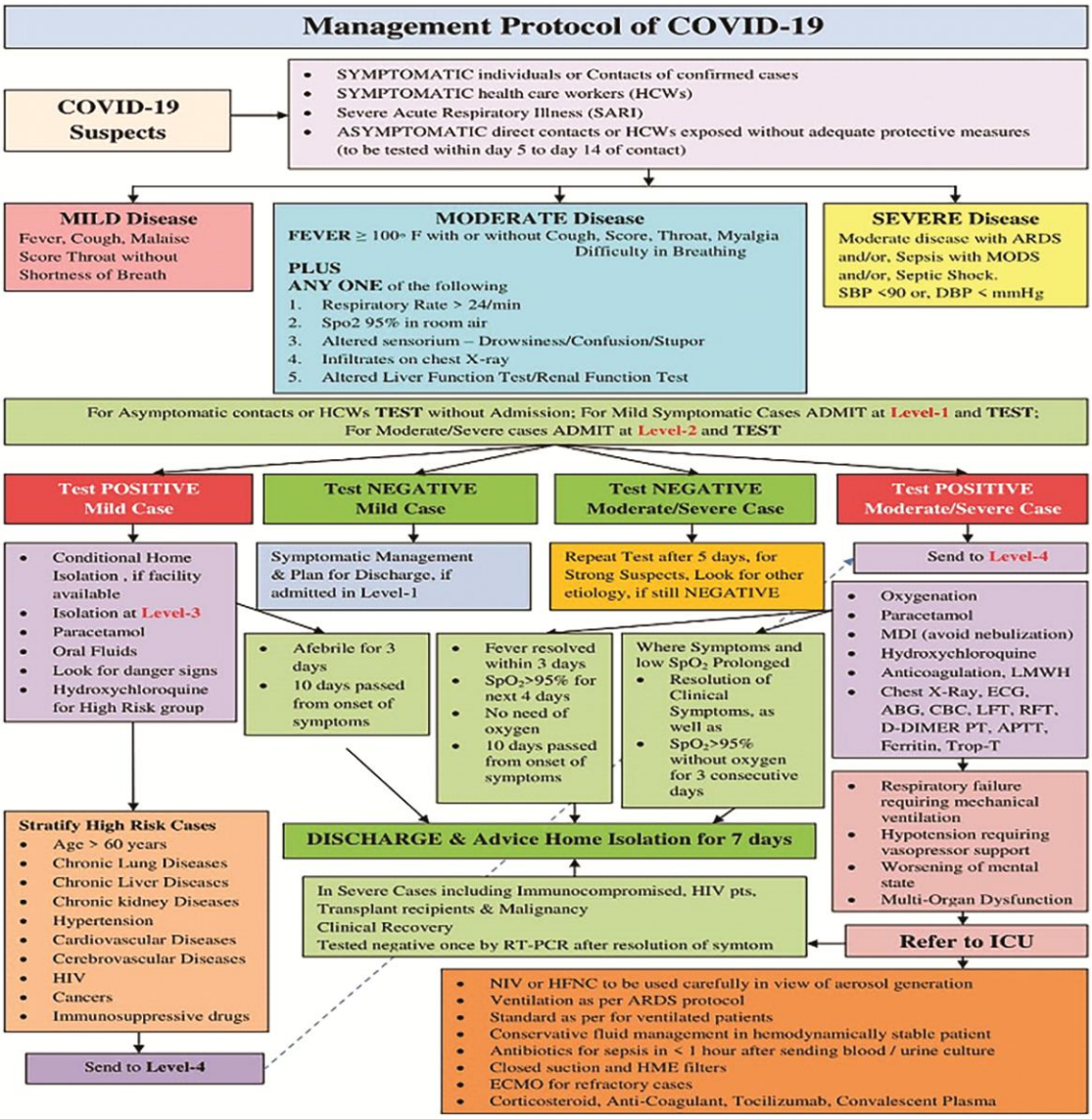
Results

Most of the patients were in- between the age group of 20-30 years with normal BMI (Table 3). No smokers were found in our study. Total of 11 women were suffering from pre-existing medical problems like asthma, diabetes, hypertension, and cardiac disease. Both primigravid and multi-gravid women were almost equally in our study. Only two patients were having a twin pregnancies. Almost two-third of patients were preterm and also six patients were admitted in the puerperal period. Women were presented with multiple symptoms and common

Box 1 — General principle of management for COVD-19 patients

1. All patients must always wear a 3-layer surgical mask after admission.
2. No family member will be allowed in patient areas to meet the patient.
3. Patient will not be allowed to carry any phone/mobile inside the ward along with him/her.
4. A designated helpline will communicate with patient relatives about the patient's condition.
5. Separate lifts should be used to transport the patients.
6. Patients should be placed in single rooms. If single rooms are not available, patients should be placed sufficiently apart. The distance between two beds should be more than one meter preferably 2 meters.
7. All the paper works, e.g. writing notes in BHT or Treatment Cards should be done in a separate area.
8. Avoid moving and transporting patients out of their room unless medically necessary.
9. Clean Environmental surfaces with detergents and 1% Sodium Hypochlorite solution.
10. Manage Laundry, Food Service, Utensils , and Medical Waste with safe routine procedures

Table 1 — Precautionary management protocol



Source: Department of Health, Government of West Bengal

Table 2 — Protective measures for a health care worker

Area	Health Caregiver/Category	Risk Level	Recommendation	Comments
Triage Area in OPD Doctors Chamber at OPD	Doctor Sister Sanitary Staff	Moderate	N-95 Mask and Gloves	Aerosol Generating Procedure Not Allowed
OPD	Patient Patient Party	Low	Triple Layer Medical Mask	Practice Hand Hygeine
Emergency Department Attending Non-SARI (Severe Acute Respiratory Illness)	Doctor Sister	Moderate	N-95 Mask and Gloves	Practice Hand Hygeine
Emergency Department Attending SARI (Severe Acute Respiratory Illness)	Doctor Sister	High	Full set of PPE	Aerosol Generating Procedure, allowed if indicated
Isolation Ward COVID Ward	Doctor Sister	High	Full set of PPE	Aerosol Generating Procedure, allowed if indicated
Critical Care Unit	Doctor Sister Technician	High	Full set of PPE	Aerosol Generating Procedure, allowed if indicated

Table 3 — Demographic characteristics of the study population (n=56)

Demographic Characteristics	Number of women (n=56)
Age	No of women (%)
<20	7 (12.5)
20-30	44 (78.6)
>30	5 (8.9)
Body mass index:	
Normal	36 (64.2)
Overweight	15 (26.8)
Obese	5 (9)
Smoking	
Yes	0
No	56 (100)
Pre-existing medical problems	
Asthma	6 (10.7)
Diabetes	2 (3.5)
Hypertension	2 (3.5)
Cardiac disease	1 (1.75)
Parity	
Primi	27 (48.2)
Multi	29 (51.8)
Multiple Pregnancy	2 (3.5)
Gestational age at admission	
<24	2 (3.5)
24-28	4 (7)
28-32	12 (21.4)
32-37	21 (37.5)
>37	11 (19.9)
Puerperium	6 (10.7)

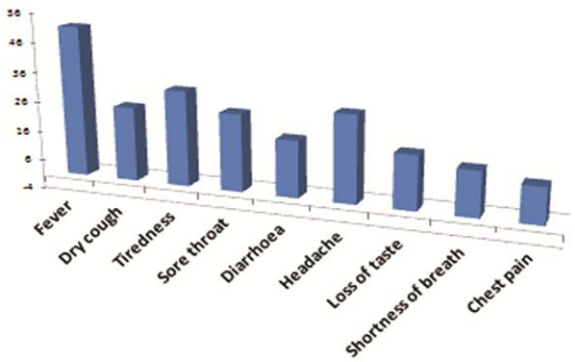


Fig. 2 — Symptoms of the patients (n=56) (single patient presents with multiple symptoms)

symptoms such as fever, tiredness, headache, sore throat, and cough (Fig. 2).

Three SARS-CoV-2/COVID-19 positive cases were identified

The neonates of the SARS-CoV-2/COVID-19 positive mothers were negative on subsequent RT PCR examination (Table 4).

Discussion

Depending on the symptoms and clinical findings, it was difficult to diagnose SARS-CoV-2 infection in pregnancy, as most of them are nonspecific which may concurrently be encountered in other viral infections also. It has to be done based on clinical and subsequent detection of the viral genes on RT-PCR through nasopharyngeal (NP) swab[20]. Among the clinical symptoms 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, and taste[21].

Table 4 — Clinical Details and outcomes of COVID mothers (n=3)

Parameters	Case 1	Case 2	Case 3
Identification	31 years old 3rd gravid female	26 years old female	20 years old female primigravid
Gestational Age	36 weeks	35 weeks 5 days	39 wks 2 days
Complaints/Issues	with antepartum hemorrhage	With severe anemia	Lower abdominal pain and difficulty to pass the stool.
Patient Vitals	Pulse 84/ min, BP 110/70 mmHg, SpO2 – 96%, mild pallor, no icterus and chest clear.	Pulse 104/ min, BP 110/70 mmHg, moderate to severe pallor, no icterus and chest fine crepitations.	Pulse 82/min, SpO2- 98%, BP 110/70 mmHg, mild pallor, no icterus and chest clear.
Physical Inspection	Per abdomen: uterus size - 32-34 weeks. Adequate fetal movements and fetal heart rate audible and regular. . Per vaginal examination: on inspection no active bleeding, cervical dilatation 3 cm, cervix thick in consistency, amniotic membrane present , show present, no dribbling, station of presenting part high up.	Per abdomen : uterus size - 34-36 wks, adequate fetal movements, fetal heart rate audible and regular, fetal head floating. Per vaginal examination: cervix closed, cervix thick tubular, no show, no dribbling.	Abdominal examination: uterus size – term, adequate fetal movements, fetal heart rate audible and regular. Vaginal examination: cervix 4 cm dilated, soft and 30% effaced, show present, no dribbling, vertex of the baby presenting part, and membrane present, station-1.
Pre Delivery	NA	Patient had been transfused 7 units of Purified RBC and 4 units Fresh Frozen Plasma during the total hospital stay to overcome severe anemia and four doses of injection dexamethasone had been completed for fetal lung maturity.	NA
Delivery Details	Delivered vaginally a healthy boy baby of 2.75 kg following spontaneous onset of labour pain and the neonate was healthy after delivery without any complications. After delivery mother and baby were kept in separate rooms	Six days after admission she underwent an elective caesarean section for post caesarean pregnancy at term after correction of anaemia. She delivered a healthy girl baby of 2.56 kg, cried after birth with a good Apgar score 7/10 without any complications.	Within 4 h after admission patient delivered vaginally, 3kg baby boy without any complications. During labour her vitals were pulse rate – 76/min regular, BP- 100/70 mmHg, SpO2 – 94% without oxygen , and Chest clear with bilateral broncho-vesicular sounds. SpO2 was monitored in every 30 m during intrapartum events
Symptoms	Fever (101.2°C) onset from the next day of admission.	The onset of fever on 3rd postoperative day. Moderate grade fever 102.5℃ and patient's vitals were as pulse 86/ min, BP 116/80 mmHg, SpO2 – 97%.	Dry cough for the past 4 days.
COVID-19 Test	A n asopharyngeal swab sample sent for RT-PCR on the same day and the report came as positive for SARS-CoV-2/COVID-19.	A nasopharyngeal swab was sent for RT-PCR immediately and within 24 h the result came as positive for SARS-CoV-2.	A nasopharyngeal swab was sent for RT-PCR and the report came as positive for SARS-CoV-2
COVID Treatment For Mother	After delivery mother and baby were kept in separate rooms. As per the COVID protocol empirical antibiotic azithromycin and hydroxychloroquine she received. But both of the drugs were only used on the based on expecting a good recovery rate. These molecules are not anti-viral agents	She received routine post-operative care along with paracetamol for fever management, azithromycin as antibiotics.	She received routine post natal care along with azithromycin.

(*Contd*.)

Table 4 — Clinical Details and outcomes of COVID mothers (n=3) (*Contd*.)

Parameters	Case 1	Case 2	Case 3
Lab Tests Done	Routine basic investigations such as Chest X Ray- brochovascular prominence ECG, Complete Hemogram and Blood Biochemistry for Sugar, LFT, Creatinine were performed and values were within normal limits.	Routine basic investigations Chest X-Ray – ground glass opacities and subsequently underwent HRCT Thorax Ground glass; Crazy paving; Vascular dilatation; Traction bronchiectasis, ECG, Complete Hemogram and Blood Biochemistry for Sugar, LFT, Creatinine were performed and values were within normal limit.	Complete Hemogram and Blood Biochemistry for Sugar, LFT, Creatinine were performed and values were within normal limit.
COVID Test For Neonatal	Neonate was tested 24 h after delivery and result was negative for SARS-CoV-2/COVID-19.	-do-	-do-
Discharge Protocol	She was discharged 7 days after delivery with negative NP swab test result with advice for another 7 days of strict safe home protocol.	She was discharged after 14 days with twice tested negative for SARS-CoV-2 24 h apart.	She was shifted to safe home four days after delivery for next 10 days and discharged total 14 days after delivery.

Due to the newly evolving SARS-CoV-2 infection, the exact extent of the fetal adverse effect remains unknown. There is no data suggestive of an increased risk of miscarriage[22]. Presently the adverse outcomes associated with SARS-CoV-2 infection in the first trimester are also very difficult to predict due to lack of evidence. A few studies and case series involving the second and third- trimester women revealed no increased risk of teratogenicity[14,23]. In a study involving nine pregnant women with SARS-CoV-2 infection showing none of their babies were involved, and another study also showed 38 newborns of positive mothers were tested negative for SARS-CoV-2 infection[24]. Another study involving 33 pregnant women with SARS-CoV-2 infection found that three of the neonates were having a clinical signs and tested positive for SARS-CoV-2 infection. The patho-physiology of the vertical disease transmission during the womb or after the birth is uncertain. In pregnancy, there is a dominance of Th2 (T-helper cell) which protects the fetus from viral infection[25].Neonates should be allowed for expressed breast milk feeding with proper hygiene and hand washing[26]. Royal College of Obstetrician and Gynecologists (RCOG) had reported that ~10% of affected pregnant mothers may require critical care and ~40% of the mother may deliver preterm with a higher chance of caesarean section[27]. An optimal prenatal visit is the key success for successful pregnancy outcomes.

Conclusion

Pregnancy itself with its inherent immunocompromised state poses an increased risk of acquiring corona virus infection. It appears that most of the women had uneventful course due to their young age and absent comorbidities, but still it poses huge burden to the existing health care system. SARS-CoV-2 virus is an RNA virus and infection during pregnancy is to be diagnosed preferably with RT-PCR of the nasopharyngeal swab to detect RdRP and orf-1antigen. SARS-CoV-2 infection during pregnancy is often present in the late gestational age and management almost the same as the general population. There is no increased risk of severe disease to the fetus during pregnancy, and newborn may show disease- free. Vertical transmission and neonatal COVID is still a possibility though no study has proven it. If neonates get infected the problem will multiply. Mother has to be isolated from the new-born until the mother becomes negative two times by RT-PCR at 24 h apart. A separate isolation room should be available for the new-born. Risk of transmission to the caregivers and subsequently lack of available caregivers is a genuine concern. The disease itself is in a nascent state and more studies may unravel many mystery. An effective vaccine seems to be very necessary to tide over the pandemic situation but we have to wait for that.

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Conflict of interest

All authors declare no conflict of interest.

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