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Abstract

Introduction: This article aims to discuss all the challenges faced in the diagnosis of coronavirus disease 2019 (COVID-19) in pregnancy, isolation of suspected and positive patients, their management, and the strategies to prevent the transmission of infection among the healthy population and medical fraternity. The diagnosis of COVID in pregnancy is influenced by many factors, including normal physiological changes in pregnancy, comorbid conditions associated with pregnancy, and the presence of asymptomatic infection in patients. Suspicion of COVID-19 in pregnant females is of utmost importance at a primary health center for risk mitigation of exposure to medical personnel. Material and Methods: A retrospective study was carried out in the labour room in a tertiary care center in India. Two groups were made, suspected COVID and confirmed COVID in pregnant patients. The case records were analysed. Results: Out of a total of 5164 admissions, 95 patients were admitted as suspected (1.8%), but only two patients were COVID-positive amongst them. 84% of COVID-positive patients were asymptomatic. Fever was the most common symptom in both groups (P-value: 0.15). Preeclampsia and anaemia were the most common comorbidities in both groups, not statistically significant. There were 32% of intensive acre unit (ICU) admissions in suspected COVID patients, and 77% of them were having respiratory distress. Conclusion: COVID-19 presents as an asymptomatic infection in most pregnant patients. Physiological changes to the cardiorespiratory and immune systems along with associated comorbidities in pregnancy, increase a woman's susceptibility and delay diagnosis. Consideration of patients as suspected COVID at triage stations on the basis of only contact or travel history poses a great burden on the health care system. Although triage is an essential tool to identify symptomatic COVID patients, universal testing strategies should continue simultaneously. Streamlining medical care professionals into self-sufficient teams ensures adequate clinical coverage amongst the suspected COVID, confirmed COVID, and routine labour room admissions.

Keywords: Confirmed COVID-positive, COVID-19, suspected COVID patients, triage checklist

Introduction

The world has been brought to a standstill by the newly bloomed viral infection of the coronavirus disease 2019 (COVID-19). This deadly and rapidly spreading viral infection has involved all ages, including the reproductive age group. The challenge faced is to make a diagnosis during pregnancy along with

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the development of strategies for isolation and infection prevention and to manage the clinical aspects as well. The World Health Organisation (WHO) had asserted COVID-19 as a pandemic when the confirmed cases approached 2,00,000 patients with around 8,000 deaths across over 160 countries.^[1] The causative organism of COVID-19 viral infection is a novel beta coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This newly-emerged virus shares the genetics with severe acute respiratory syndrome coronavirus-1 (SARS-CoV-1) and Middle East respiratory syndrome coronavirus (MERS-CoV).^[2]

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The biggest threat to the medical fraternity by the pandemic is to scrutinise patients amongst the population attending hospitals. There are a plethora of possibilities of presentation of COVID-19 viral infection in patients and their companions as they may be uninfected, silent carriers, primarily presenting with flu-like illness, or admitted for other illnesses and having a coexisting viral infection. Hence, there is a need to develop strategies for separation and segregation of suspected/confirmed COVID-19 cases during pregnancy. Another challenge for the physicians was to minimise the risk of infection among the healthcare forces. This was crucial to safeguard the physical and mental health of healthcare professionals and to prevent the healthcare system from becoming devastating.

Reverse transcription-polymerase chain reaction (RT-PCR) of oropharyngeal and nasopharyngeal swabs is the mainstay for making a diagnosis of the COVID-19 infection. Suspicion of COVID-19 in pregnant females is of utmost importance at triage stations for risk mitigation of exposure to medical personnel and other uninfected patients, especially in the early period of the pandemic. A checklist for symptoms and exposure, thermal screening, and measurement of oxygen saturation using a pulse oximeter can be used in the triage area.

Diagnosis of COVID in pregnancy is influenced by many factors, including normal physiological changes in pregnancy, comorbid conditions associated with pregnancy, and the presence of asymptomatic infection in patients. It is also essential for information and education of the whole healthcare workforce to be vigilant about the risks in order to improve the overall experience of self-care as well as of the affected patients and their companions.

The approach of universal testing for COVID-19 for its diagnosis in pregnancy remains a mainstay, but its need is determined mainly by institutional guidelines, the frequency and prevalence in the local population, and the health resource of the country. The present study was designed to identify the challenges faced in the detection of COVID-19 infection among antenatal women in low resource countries, measures taken to overcome those challenges, and to discuss the strategies developed in the management of this previously unknown infection of COVID-19 in humans, especially in pregnancy. Suspicion of COVID-19 in pregnant females is of utmost importance at a primary health care centre for risk mitigation of exposure to medical personnel and other uninfected patients, especially in the early period of the pandemic.

Material and Methods

We conducted a retrospective observational cohort study in the department of Obstetrics and Gynaecology, PGIMS, Rohtak, in the initial phase of COVID infection in India. The study was given ethical approval from the ethical board of the institute.

The labour room of our department was designated for the management of non-COVID patients. A separate hospital was

entitled for the treatment of COVID-positive patients in our institute. During the early period of COVID-19 spread in India, the screening of all patients presenting to the labour room for symptoms or history of contact and risk factors for COVID-19 was done, and testing of pregnant women was limited based on a checklist for COVID-19. A triage station outside the labour room was established where systematic and thorough screening for COVID-19 infection was done on the basis of the checklist [Figure 1].^[3] After screening, the women who required admission were separated into two different categories-suspected COVID and the others who were asymptomatic and not suspected of COVID-19 infection.

The labour room was divided into two parts with separate entry gates and separate teams of management; one for the suspected COVID patients till the report is awaited and the other for non-suspected routine admissions after screening. The oral and nasopharyngeal swab RT-PCR of the suspected COVID women was done at the triage station, maintaining a cold chain as per recommendations. Women who had stable vital signs and had no obstetric indication for admission were sent to physicians for follow-up. Subsequently, with the increase in the number of cases

Figure 1: Checklist used at triage station for symptoms
and TOCC risk factors

Influenza-like	e illness symptoms
Fever	
Cough	
Sore throat	
Shortness of	of breath
Diarrhea ar	nd/or vomiting
None of al	Dove
Informatio	n cannot be obtained
TOCC: 14 da	ays before the onset of symptoms
History of	recent Travel
Date of tra	vel: from
Area:	
0	Occupation (e.g., laboratory worker, healthcare worker, l-related work)
History of COVID-19	unprotected Contact with a person with confirmed
Clustering of al	of influenza-like illness/pneumonia (≥2 affected persons)
Informatio	n cannot be obtained
Types of isol	ation precautions* required:
	ecautions/Contact precautions/Airborne precautions/Nil
Date:	
Name & Si	gnature:
Designation	0
Airborne p	recautions for the patient with respiratory symptoms
-	ecautions If influenza-like illness symptoms are positive plus
*1. Droplet precau	tions: put a surgical mask on the patient: single room: healthcare worker uses persona

^{*1.} Droplet precautions: put a surgical mask on the patient; single room; healthcare worker uses personal protective equipment (PPE) appropriately, including mask, upon entry to the room. 2. Contact precautions: single room; healthcare worker uses PPE appropriately, including wearing gloves and gown, upon entry to room; use disposable equipment. 3. Airborne precautions: put a surgical mask on the patient; isolation room; healthcare worker uses PPE appropriately, including wearing fit-tested N95, FFP2 or equivalent-standard respirator, eye protection (goggles and/or face shield), disposable fluid-resistant and impermeable protective gown and double gloves, upon entry to room; restrict susceptible healthcare workers from entering room; use disposable equipment.^[5]

and exposure of health care workers with silent COVID carriers or asymptomatic patients wearing partial personal protective equipment (PPE), universal COVID-19 screening for all patients admitted to the labor room in addition to suspected patients at triage was started as per the guidelines.^[4]

Two groups were made as follows: 1. Suspected COVID pregnant women 2. COVID-positive pregnant women.

Suspected cases were defined as per the WHO's interim guidance, which includes patients with acute respiratory illness and/or with a history of travel to a community spread area or contact with positive patients or those requiring admission in the absence of an etiology that explains the condition.^[5]

Confirmed COVID cases had been defined as a patient with positive RT-PCR for COVID-19, regardless of symptoms or signs of COVID infection.

The clinical symptoms and associated comorbidities were analysed from the records of patients. Patients were managed as per standard protocols. The suspected cases were managed in separate isolation rooms, and operative procedures were done at the operation theatre designated for suspected patients wearing personal protective equipment, N-95 mask, and faceguard. The patients who required intensive care were transferred to the ICU (Intensive Care Unit) designated for COVID suspect patients. Doning and doffing had been done in the pre-defined area, and appropriate disposal of used equipment was done as per standard recommendations. COVID-positive patients with positive RT-PCR were shifted for management to the COVID-designated hospital of the institute. Repeat COVID testing of positive patients was done as per protocols. Patients were discharged after being negative for COVID or clinically stable and opted for home isolation as per recommendations.

Statistical analysis was conducted with the Statistical Package for Social Sciences (SPSS) version 21.0. The data will be compiled and statistically analysed by using the Student t-test for quantitative variables and Chi-square test for qualitative variables. A *P* value of < 0.05 was considered significant.

Results

Out of a total of 5164 admissions in the labour room, 3753 patients delivered. The total number of COVID-positive patients detected during the study period was 38. Out of 5164 admissions during the study period, 95 patients (1.8%) were defined as suspected COVID after screening on admission. Out of 95 suspected COVID women, 71 patients (74.7%) had flu-like symptoms, and the rest 24 patients (25.7%) were considered COVID suspects on the basis of risk factors (travel history, occupation, contact, and cluster (TOCC)). Intensive care was required in 30 out of 95 suspected patients. There were four maternal deaths among suspected patients. Two patients (2.1%) came COVID-positive among suspected patients. Out of the rest asymptomatic admissions in the labour room, 36 patients came out to be COVID-positive [Figure 2]. Hence, total COVID-positive patients in our institute were 38. A rising trend was observed with advancing year in the number of positive cases [Figure 3]. Four COVID-positive patients developed symptoms after two to three days of admission. 84% of COVID-positive patients were asymptomatic [Figure 4]. There were two mortalities in COVID-positive patients. Intensive care was required in one COVID-positive patient.

Comorbidities associated with suspected patients causing COVID-like symptoms were preeclampsia (34.7%), anaemia (30.5%), premature rupture of membranes (PROM) (16.8%), heart disease (7.3%), eclampsia (6.3%) and pulmonary oedema (5.2%), hypothyroidism (2%), asthma and meningitis (1.05%). Comorbidities associated among COVID-positive patients were anaemia (18.42%), preeclampsia (10.5%), hypothyroidism, and asthma (2.6%).

Intensive care was required in thirty suspected patients. The most common indication for intensive care was respiratory distress (76.7%). Other associated symptoms were fever (36.7%), cough (7.3%), orthopnoea, and diarrhoea. Among ICU admissions in suspected patients, the most common pregnancy-associated comorbidity was preeclampsia, eclampsia, and pulmonary oedema (60%). Other indications were heart disease and shock (10% each), sepsis (6%), and hepatic encephalopathy (3%). Only one patient was found to be COVID-positive among ICU admissions. Four patients expired out of these, and the rest recovered and were discharged subsequently.

Leucocytosis was observed in 42 patients out of 95 suspected COVID patients (44.2%). Twenty-three patients among these were admitted to the ICU.

There was no significant statistical difference in the clinical presentation, associated complications of pregnancy, and mode of delivery between the two groups of study. [Table 1].

The mean duration of COVID-19 infection in pregnancy in our institute was 8.93 days (2 to 20 days).

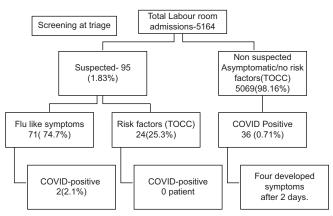


Figure 2: Flow chart of the study

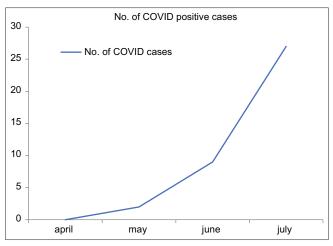


Figure 3: Rising trend of COVID in pregnancy in our institute

Discussion

The coronavirus infection was first notified in Wuhan province in China on December 31, 2019. It has gained much interest throughout the world since then.

The clinical scenario associated with COVID in pregnancy is graded into mild, moderate, and severe infection with a wide range of symptoms reported, ranging from mild symptoms to severe illness.^[6] Fever (80–100%), cough (59–82%), fatigue (44–70%), and breathlessness (31–54%) are the most frequently reported symptoms. 50% of symptomatic patients may develop pneumonia with infiltration or consolidation.^[7] In the present study, COVID-positive patients were mostly asymptomatic (84%). Fever was the most common symptom in symptomatic COVID-positive patients, followed by respiratory distress and shock.

The asymptomatic COVID-19 flu among antenatal females is rarely noticed as problems of late gestation and even labour concedes the possibility of accompanying signs of SARS-CoV-2 infection. In pregnant patients, nonspecific symptoms are more likely to be due to pregnancy than due to COVID-19, and these may lead to observer bias and considering patients as suspected COVID at triage stations even in the absence of infection. These findings endorse a universal testing approach for pregnant women even in the presence of nonspecific presentation. Hence, universal testing strategies are critically required for curtailing community transmission of COVID 19 disease.

A research from New York, USA, found that a substantial proportion (13.5%) of asymptomatic patients admitted for delivery tested positive for COVID-19. Fever was observed amongst 10% of these patients. This highlights a possible issue with triaging patients based solely on symptoms in places where the infection is prevalent.^[8,9] In our study, we have observed that two patients out of 95 suspected COVID after triage came COVID-positive (2.1%). Rest all came COVID-19-positive after universal testing of asymptomatic patients admitted to the labour room.

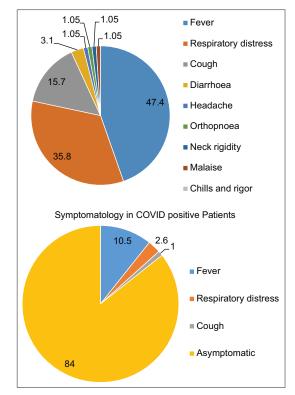


Figure 4: Symptomatology in suspected COVID positive patients

Fever (47.4%), followed by respiratory distress (35.8%) and cough (15.7%), was the most common symptom that categorised the antenatal women as suspected COVID-19 at the triage station. The main dilemma in managing these patients was to confirm the diagnosis in symptomatic patients and to keep them isolated to prevent the spread of COVID if they come positive. Breathlessness can be associated with the following differentials in pregnancy^[10]:

- 1) Physiological
- 2) Respiratory causes:
 - a. Obstructive airway disease: COPD (chronic obstructive pulmonary disease), asthma, bronchiectasis.
 - b. Parenchymal/interstitial lung disease: pneumonia (bacterial and viral), aspiration pneumonitis, acute respiratory distress syndrome/acute lung injury, tuberculosis, pulmonary metastasis, sarcoidosis, drug-induced lymphangioleiomyomatosis, lymphangitis carcinomatosa, fibrosing alveolitis.
 - c. Vascular: pulmonary embolism, amniotic fluid embolism, pulmonary hypertension.
 - d. Pleural: pneumothorax, effusion.
- Chest wall causes: kyphoscoliosis, obesity, ankylosing spondylitis, neuromuscular diseases like multiple sclerosis, polio.
- 4. Metabolic causes: anaemia, thyrotoxicosis, acute or chronic renal failure, metabolic acidosis, systemic sepsis.
- 5. Cardiac causes: congenital cardiac disease, rheumatic heart disease, cardiomyopathy, acute coronary syndrome, congestive heart failure.
- 6. Acute hypertensive crisis and pulmonary oedema.

Parameter	Suspected COVID n=95 (%)	COVID positive <i>n</i> =38 (%)	Р
Symptomatology			
Fever	45 (47.4)	4 (10.5)	0.15
Respiratory distress	34 (35.8)	1 (2.6)	0.49
Cough	15 (15.7)	1 (2.6)	0.71
Diarrhoea	3 (3.1)	0 (0.0)	-
Headache	1 (1.05)	0 (0.0)	-
Orthopnoea	1 (1.05)	0 (0.0)	-
Neck rigidity	1 (1.05)	0 (0.0)	-
Malaise	1 (1.05)	0 (0.0)	-
Chills and rigor	2 (2.1)	0 (0.0)	-
Mean age on admission (years) (IQR)	24.73 (18-40)	24.29 (18-32)	0.78
Mean gestational age on admission (years) (IQR)	32.8 (5-41.5)	35.5 (12-41.5)	0.12
Parity	0210 (0 (110)	5010 (12 (110))	0.112
Nulliparity	27 (28.4)	17 (44.7)	0.27
Multiparity	68 (71.6)	21 (55.3)	0.16
Associated comorbidities	00 (71.0)	21 (33.3)	0.10
Preeclampsia	29 (30.5)	4 (10.5)	0.41
Anaemia	33 (34.7)	10 (18.42)	0.33
PROM	16 (16.8)	0 (0.0)	0.55
Heart disease	7 (7.3)	0 (0.0)	_
Eclampsia	6 (6.3)	0 (0.0)	-
Pulmonary oedema	5 (5.2)	0 (0.0)	-
Previous caesarean	5 (5.2)	6 (15.7)	0.575
Malpresentation	4 (4.2)	3 (7.8)	0.39
H ypothyroidism	2 (2.1)	1 (2.6)	0.39
APH	3 (3.1)	1 (2.6)	0.88
Meningitis	1 (1.05)	0 (0.0)	-
Asthma	1 (1.05)	1 (2.6)	0.50
	1 (1.03)	1 (2.0)	0.50
Mode of delivery	29 /71 (52 5)	16/33 (48.5)	0.73
Vaginal Caesarean	38/71 (53.5) 33/71 (46.5)		0.73
	53/71 (40.5)	17/33 (51.5)	0.75
Other management	2 (2 1)	0.(0.0)	
Laparotomy	3 (3.1)	0 (0.0)	-
Suction evacuation	3 (3.1)	1 (2.6)	0.88
Hysterectomy	1 (1.05)	0 (0.0)	-
Not delivered	11 (11.6)	3 (7.8)	0.52
Admitted post delivery	5 (5.3)	1 (2.6)	0.49
CU admissions	30 (31.6)	1 (2.6)	0.53
ndications for ICU admissions			
Preeclampsia/eclampsia/pulmonary oedema	18 (18.9)	0 (0.0)	-
Heart disease	3 (3.1)	0 (0.0)	-
Shock	3 (3.1)	1 (2.6)	
Hepatic encephalopathy	1 (1.05)	0 (0.0)	-
Sepsis	2 (2.1)	0 (0.0)	-
Associated anaemia	11 (11.6)	0 (0.0)	-
Mortality	4 (4.2)	2 (5.2)	

Breathlessness is the most common symptom noticed in ICU admissions among suspected COVID patients. Diagnosis of COVID-19 in pregnancy can be made after a confirmatory test of RT-PCR; before that patients need isolation and a plethora of investigations to confirm the diagnosis. Furthermore, pregnancy and the physiological adaptations associated with it served as a diagnostic challenge for COVID-19 infection. Physiological changes to the cardiorespiratory and immune systems in pregnancy increase a woman's susceptibility to severe infection and hypoxic compromise but may also delay diagnosis. 35% of suspected patients were considered suspected COVID on the basis of shortness of breath in the present study. Physiologic dyspnea due to increased maternal oxygen demands from heightened metabolism, gestational anaemia, and fetal oxygen consumption is common in pregnancy.^[11] Additionally, lung volumes are adapted. Functional residual capacity, end-expiratory volumes, and residual volumes decrease steadily from early pregnancy due to diaphragmatic pressure by the gravid uterus, resulting in reduced total lung capacity at term and an inability to clear pulmonary secretions effectively.^[12]

Fever is diagnosed in pregnancy easily by a temperature above 38°C. The complexity lies in detecting an infectious disease earlier along. The challenge with fever in pregnancy during COVID-19 pandemic is to segregate and manage patients in isolation units before the confirmatory diagnosis. Fever in pregnancy may have the following differentials:

- 1) Obstetrical causes
- a. From genital tract: Chorioamnionitis Endomyometritis Septic abortion Scar site infections (SSE), necrotizing fasciitis b. Extra-genital: Pyelonephritis Mastitis Puerperal ovarian vein thrombophlebitis 2) Non-obstetrical causes HIV/AIDS (and associated opportunistic infections)

Bacterial, fungal pneumonia Tuberculosis Malaria

Viral infections (including influenza, varicella, and COVID-19)[13]

In our study, COVID positivity was two percent among suspected patients, and the rest 98% had either history of exposure/contact to COVID or symptomatology mimicking COVID. The majority of patients had comorbidities associated with pregnancy like preeclampsia (30%), anaemia (34.7%), PROM (16.8%), heart disease (7.3%), eclampsia (6.3%), and pulmonary oedema (5.2%) causing symptoms suspicious of COVID-19.

The diagnostic dilemma in the obstetric patient is compounded by the fact that testing in the initial phase of the pandemic was not only limited but also limited to suspected cases of COVID-19 only. Also, at triage stations, there were cases of patients hiding their travel history from their attending physicians. The implication of this was that such patients who could fulfil the COVID-19 suspected case definition criteria and tested in line with the country's testing protocol, would most probably be admitted and managed for other benign conditions without suspicion of COVID-19. This portended grave danger for not only the doctors but also for all other healthcare workers and patients who would come into contact with such patients. The recommendation of universal testing by the Government of India exposed the asymptomatic unsuspected COVID-19 infection amongst the parturients.

COVID-19 is not only a respiratory syndrome. Systemic infection with a significant impact on the haematopoietic and haemostasis systems has also been described. This systemic infection induces an excessive inflammatory response that is associated with high levels of circulating cytokines, severe lymphopenia, and substantial mononuclear cell infiltration in the lungs, heart, spleen, lymph nodes, and kidneys.^[14,15] Since the beginning of the pandemic, pregnant patients have been identified as a vulnerable group for complications and risk of death from COVID-19 due to previous experiences, such as pandemic influenza. We had two maternal mortalities among the COVID-19 positive pregnant women. First case was a primigravida with 35 weeks of gestation with sepsis and hepatitis; other two patients expired postnatally. One expired on day 2 of normal delivery with severe anaemia with pneumonia with cardiogenic shock with HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome, and the other was a post lower segment cesarian section (LSCS) patient with sepsis and acute kidney injury (AKI).^[16] Thromboembolism may contribute to the respiratory failure accompanying COVID-19, but whether this risk is altered by pregnancy is unknown. The obstetrician's concern is the timing and mode of delivery in COVID-19 as the possibility of the inflammatory response associated with labour may increase the risk for multiorgan system failure in the parturient with COVID-19 than in other critically ill parturients.^[17]

The duration of COVID infection clearance observed in our institute was 8.93 days (2 to 20 days). Similar findings have also been reported in the literature.^[18]

The major limitations of the present study were the small sample size and the observational nature of the study. Despite these limitations, our study provides irrefutable strategies to tide over the pandemic situation.

Obstetric care can be served by streamlining medical care providers into self-sufficient groups, each minimally comprising a consultant, an attending resident, an intern, and nursing staff. The individual teams function independently and provide inpatient labour and delivery or emergency operative services, including treating women with suspected or confirmed COVID-19 infection with full personal protective equipment (PPE) compliance. If a team member is exposed to or infected with COVID-19, their team will be quarantined for at least two weeks; workforce segregation thus ensures adequate clinical coverage by nonaffected teams in this event. Routine universal testing strategies should continue hand in hand for identifying asymptomatic patients so as to minimise exposure to healthcare workers and the rest of the patients and to ensure a functioning healthcare system in preparedness for inevitable potential health emergencies. This study emphasised the significance of understanding the physiological changes and comorbidities of pregnancy that influence the milieu to diagnose COVID in the antenatal period so that a timely referral could be done from a primary health care centre and maternal morbidity is reduced.

Conclusion

The chances of missing asymptomatic COVID-19 infection among antenatal women are particularly high as signs and symptoms of late pregnancy and even uncomplicated labor (like shortness of breath and fatigue) may overlap with symptoms of

SARS-CoV-2 infection. The diagnostic dilemma of COVID-19 in pregnancy is further compounded by the associated physiological alterations with pregnancy and pregnancy-associated comorbid conditions. Universal screening of all admissions in labour units along with the use of partial PPE (N-95 masks, visors, goggles, gloves, and surgical gowns) and hygiene practices should be considered strongly to avoid exposure to health care workers and spread of infection amongst patients. Various initiatives, such as preliminary surveys, and socio-behavioral and psychosomatic analysis, involving both governmental and non-governmental collaboration, should also be used or introduced to address knowledge gaps surrounding the effect of COVID-19 in pregnancy. In addition, in light of quickly evolving evidence, guidelines must be amended and adjusted to the specific needs of patients in each locality. This research will aid primary care providers in putting their plans into action and show their vigilance for future health emergencies. Support from every healthcare staff is crucial for the effective management of global pandemics.

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Conflicts of interest

There are no conflicts of interest.

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