Original Research Article

Outfacing second wave of pandemic in COVID-19 positive mothers at Gandhi hospital

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ABSTRACT

Introduction: The novel coronavirus is a single stranded RNA virus with spike proteins triggering an immune response leading to cytokine storm and coagulopathy. Pregnancy is an immunocompromised and hypercoagulable state, with predisposition to severe illness. An insight into impact of COVID-19 in pregnancy is essential to combat its future.

Materials and Methods: This study was conducted at a tertiary care centre. Analytical study was conducted from the data collected regarding COVID-19 positive labour room admissions, deliveries and deaths during the second wave of pandemic.

Results: There was a discharge rate of 88.14% after safe delivery. Among COVID-19 maternal mortalities, most deaths were due to ARDS. Quick SOFA score was a good predictor for morbidity and mortality. Deranged coagulation profile and D-Dimer levels more than 500 ng/ml were good predictors of mortality. Silent hypoxia needs to be identified and corrected at admission. Delay in seeking medical advice was a major contributory risk factor.

Conclusion: Increasing awareness among public about seeking medical advice during early stages of disease. Early identification and treatment according to latest guidelines for a positive outcome.Making aware the policy makers regarding risk-benefits of vaccination in mothers can come a long way in changing the fate of COVID-19 in pregnancy.

1. Introduction

The novel coronavirus has affected 2.9 crore Indians till date, and about 3.8 lakh Indians have succumbed.[1] Coronaviruses are single stranded RNA viruses with spike glycoproteins on the envelope. The spike glycoprotein on the virus binds to the ACE-2 receptor on the epithelial cell in nasal cavity.[2] Viral replication results in virus mediated tissue damage and release of cytokines like IL-6 and TNF-α into the circulation causing cytokine storm. COVID-19 (coronavirus disease) coagulopathy caused by cytokine induced vascular endothelial damage leading to activation of platelets and clotting factors resulting in clot formation.[3] Pregnancy by virtue of its inherent physiological adaptations is expected to increase morbidity associated with COVID-19 due to 1) a relatively immunocompromised state 2) alteration in pulmonary function 3) a hyper coagulable state.[4] This study travels through the effect of COVID-19 in pregnancy and opines into possible strategies to combat the future of COVID-19 in pregnancy.

2. Materials and Methods

Data from Gandhi hospital, a designated COVID-19 hospital and tertiary care centre was collected from April 2021 to June 6, 2021. Analytical study was conducted

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after approval from internal ethics committee. Total number of COVID-19 positive patients admitted to labour room, deliveries and deaths was summarised. Lab parameters complete blood picture, coagulation profile, D-Dimer, Ferritin, Arterial blood gas analysis (ABG) and Q SOFA score of COVID-19 positive maternal deaths was analysed to obtain appropriate conclusions. All data was tabulated and the relationship between them was obtained. All data was represented in the form of percentage tables and graphs.

3. Results

Out of 447 admissions to labour room, 394 (88.14%) were discharged healthy, 20 patients left against medical advice and 33 patients succumbed. A total of 387 deliveries were conducted out of which (243) 62.79% were emergency Caesarean sections and (145)37.46% were normal vaginal deliveries. Among primigravida (67) 45.27% had normal vaginal deliveries and (83)56.08% underwent emergency Caesarean section. Six out of ten patients visiting the emergency room were high risk pregnancies.

Quick obstetric assessment of patients, availability of advanced lab and blood bank, prompt delivery and early discharge after quick work up for severe COVID-19 infection are major highlights to this success rate. Till date 35 patients required positive pressure ventilation of which 2 patients recovered and 33 could not survive.

A detailed analysis of 30 COVID-19 maternal mortalities was done which can be concluded as follows,

Majority of patients fell into 25 – 30 year age group of which 25% were 25 year old and 20.8% were 30-year-old. Total of (11)36.66% of cases had a typical presentation of fever, cough and shortness of breath grade four on admission. Around (13) 45% of cases had shortness of breath on admission.

Table 1:

Rural area	Percentage of patients
No	82.76%
Yes	17.24%

Saturation of oxygen (Spo2) reading in pulse oximeter was compared to partial pressure of oxygen (PaO2) in arterial blood gas analysis to diagnose silent hypoxemia. Metabolic acidosis was seen in (11)44% and (6)24% had silent hypoxemia. Most of COVID-19 maternal deaths 53.33% (16) in our study group were due to ARDS. Other important causes of death included obstetric causes like severe preeclampsia, post-partum haemorrhage, DIC, MODS.

ABG interpretation and distribution in study group.44% had metabolic acidosis and 24% had silent hypoxemia.

Comparison of pulse oximeter reading of Spo2 at room air with PaO2 in ABG. PaO2 in ABG (orange bars) was lower than Spo2 at room air (blue bars) in some patients suggestive of silent hypoxemia.

Table 2: Summary of causes of death other than ARDS in COVID-19 mothers

Other causes of death		Number of maternal deaths
SPE	PPCM	1
Traction Bronchiectasis	Congenital Heart Disease	1
Antepartum eclampsia	DKA, MODS	1
DIC, HELLP	Abruption	1
MODS	AKI	1
	Jaundice	1
PPH	Placenta percreta	1
SPE	AKI	1

Quick SOFA score of 2 predicted maternal morbidity and mortality in (13) 44.8% of patients. Q sofa score of 1 was associated with high WBC count(sepsis).

Table 3: Q Sofa score

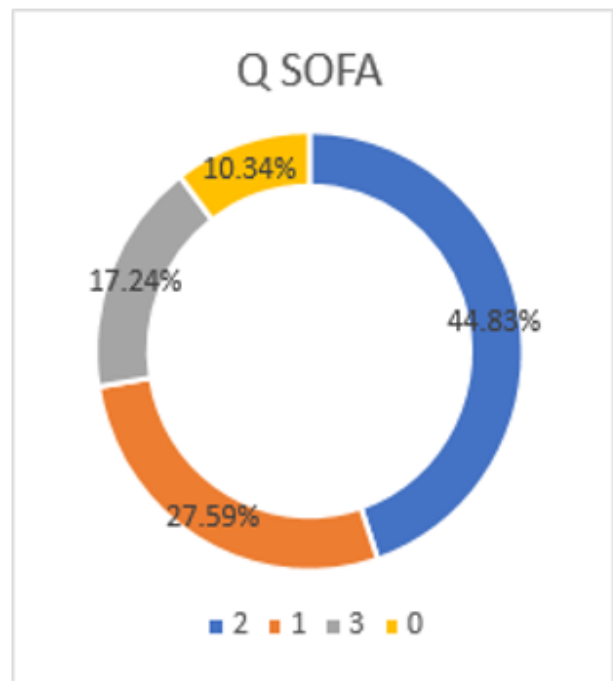| Low blood pressure SBP<100 mm Hg	1
Respiratory rate >22/min	1
Altered mental status (GCS <14)	1

Fig. 1: QSOFA score distribution among study group

3.1. SOFA score distribution among study group

Relationship of Q SOFA with WBC count. Q SOFA score of 1 was associated with sepsis (WBC count >18000/mm^3)

Only (2) 6.9% patients did not require positive pressure ventilation whereas (12) 41.38% of patients required non-invasive ventilation and (12) 41.38% patients required both non-invasive and invasive ventilation.
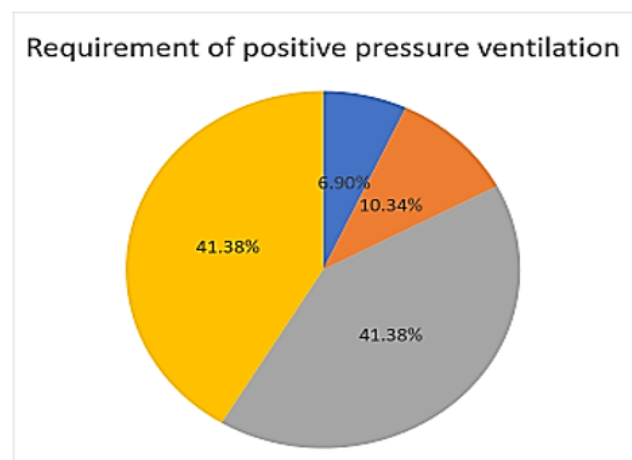

Fig. 2:

Non invasive ventilation was required in 41.38% and both invasive and non invasive ventilation was required in 41.38% of maternal mortalities.

Delay in seeking medical advice was the key factor contributing to maternal mortality in COVID-19 positive mothers.

Table 4:

Delay in seeking medical advice	Number of patients	Percentage of cases
No	5	16.67%
Yes	25	83.33%

Deranged coagulation profile was seen in 20% of cases. D-Dimer levels more than 2000 ng/ml was seen in (8) 34.78% patients.

Table 5:

D-DIMER (ng/ml)	Number of patients	Percentage of cases
<500	7	30.4%
500-1000	4	17.38%
1000-2000	4	17.38%
>2000	8	34.78%

Distribution of COVID-19 maternal mortalities according to various ranges of D-DIMER levels.

4. Discussion

Patients with SARS CoV2 can have mild, moderate or severe illness based on their clinical picture.[5] Severe Illness is caused by Variants of Concern, seen in patients who have respiratory distress or lung infiltrates >50%.

WHO classified the variants of SARS CoV2 as 1) Variants of Concern- demonstrate increased virulence, decreased effectiveness of public health measures. Alpha, Beta, Gamma and Delta – India Oct 2020. 2) Variants of Interest- causes community transmission in multiple countries. Epsilon, Zeta, Eta, Theta, Iota, Kappa-India Oct 2020, Lambda-Peru Aug 2020.[6] Of importance in India are,

Table 6:

Kappa	B.1.617.1	8%
Delta	B.1.617.2	76%

From the data analysis above we conclude that a presentation of fever, cough and shortness of breath was common to most patients of severe COVID-19 disease. Significant maternal mortality was as a result of ARDS and most of them required positive pressure ventilation. Q SOFA is a quick assessment tool which can predict morbidity and mortality among COVID-19 patients. Deranged coagulation profile and D-DIMER levels were significantly associated with mortality in COVID-19. Rate of Emergency Caesarean section is high due to various reasons, most commonly in an attempt to reduce respiratory distress in these critically ill patients. Delay in seeking medical advise is by far the most striking contributory factor associated with maternal mortality with COVID-19 in our study group. On an average there was delay of 3-4 days after the onset of shortness of breath and 7-8 days after onset of fever and cough. This can be due to various reasons like social stigma, fear of testing positive, fear of visiting the hospital, lack of transport and poor knowledge about the disease progression and severity.

Acute respiratory distress syndrome (ARDS) is characterised by tachypnoea, respiratory hypoxemia and diffuse pulmonary infiltrates. It is characterised by abrupt onset of inflammation with diffuse alveolar damage, increased vascular permeability, oedema and epithelial cell death. Type 2 alveolar cells are involved more than type 1 alveolar cells. Cells undergo apoptosis and die followed by scarring and fibrosis of lung tissue.[6]

According to ISTH (International Society in Thrombosis and Hemostasis) guidance normal values of PT is 9.9-13.1 sec, APTT is24-36 seconds, Fibrinogen is 2-4 g/l in COVID -19 coagulopathy and D-DIMER >500 ng/ml is a predictor of severe COVID-19 disease in pregnancy. RCOG recommends thromboprophylaxis with low molecular weight heparin in pregnant women unless contraindicated.[7] Steroids have been used to treat COVID-19 patients in order to avert cytokine storm. Methyl

prednisolone is used for the treatment of moderate-to-severe COVID-19 in pregnancy as it distributes well in the lung parenchyma but does not cross the placental barrier significantly.[8] Remdesivir, an RNA polymerase inhibitor, was used in severely affected COVID-19 positive mothers at Gandhi hospital. The interim results of WHO solidarity trial has reported little or no effect on mortality in COVID-19. Hence RCOG does not recommend the use of Remdisivir in pregnancy unless benefit outweighs risk.[9] Tocilizumab anti IL-6 agent improved survival in severe illness as per results of RECOVERY trial.[10] Human monoclonal antibodies against spike protein used in combined cocktail REGN-COV2 was effective in reducing viral load.[11] Colchicine has anti-inflammatory and immunosuppressive properties. It has been investigated in treatment of COVID-19 due to its widespread availability and favourable safety profile. Studies have demonstrated less need for oxygen supplementation and improvement of clinical status.[12]

4.1. Silent hypoxemia

Patients with COVID-19 described as exhibiting low oxygen levels that is incompatible with life without onset of breathlessness also known as happy hypoxia, but more precisely termed silent hypoxemia. It is possible that coronavirus has an idiosyncratic action on receptors involved in chemosensitivity to oxygen, thereby blunting the response of respiratory centre to hypoxia and hypercarbia.[13]
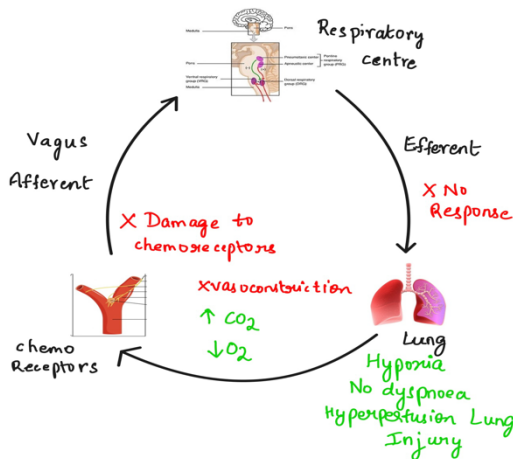

Fig. 3:

Mechanism of silent hypoxemia in COVID-19, SARS CoV2 is hypothesised to cause damage to chemoreceptors, inhibition of efferent response to hypoxia and blocks vasoconstriction. This results in hypoxia and hypercarbia without dyspnoea.

4.2. Vaccine

Bharat Biotech has reported COVAXIN showed a 100% efficacy against severe SARS-CoV-2 infection and has an impact on the drop in hospitalisations. Furthermore, a 70% efficacy against asymptomatic COVID-19 was observed indicating reduced transmission in individuals receiving COVAXIN.[14] CDC and the Federal Drug Administration (FDA) gather information about COVID-19 vaccination during pregnancy. Preliminary data did not identify any safety concerns for pregnant people who were vaccinated or for their babies.[15] As of now vaccination in pregnant population is not recommended by the government of India.

Table 7:

Vaccine	Efficacy
Bharat Biotech	80.6%
Pfizer	95%
Oxford-AstraZeneca	82.4%
Sputnik V	91.6%

Another important conclusion was the association between residents of urban areas and high mortality rate. This could probably be due to overcrowding, air pollution and less exposure to vitamin d. The lesser number of cases from rural area also uplifts this fact and forces us to ponder about the possibility of role of vitamin D supplementation in treatment of COVID-19.

5. Conclusion

The second wave of COVID-19 pandemic and the maternal outcome during this time has enlightened us for a better future. We can conclude that increasing public awareness about the disease progression, when to seek medical advise and early hospital admission and treatment can bring about tremendous positive outcome. Use of simple assessment methods like Q SOFA score and routine evaluation of coagulation profile and D-DIMER levels can help in prediction of morbidity and tune the treatment strategy accordingly. Early identification of silent hypoxemia followed by a vigorous approach can help reduce mortality. Vaccination of all individuals can avert severe morbidity in the population. Hence policy makers should be aware of the possible risk-benefit ratio of vaccination in pregnant population. Treatment with steroids in pregnancy can help in fetal lung maturation as well as reduce the chances of cytokine storm. Use of newer drugs like colchicine, tocilizumab can possibly alter the disease course and speed up recovery. Encouraging public for exposure of skin to sunlight and probable role of vitamin D in COVID-19 treatment are newer aspects for further research.

6. Conflict of Interest

None.

7. Source of Funding

None.

References

1. Dong E, Du H, Gardner L. An Interactive Web-based Dashboard to track COVID-19 in real time. *Lancet*. 1920;20(5):533–4.
2. Zhou B, Thao TTN, Hoffmann D, Taddeo A, Ebert N, Labroussaa F, et al. SARS-CoV-2 spike D614G change enhances replication and transmission. *Nature*. 2021;p. 122–7. doi:10.1101/2020.10.27.357558.
3. Bonaventura A, Vecchié A, Dagna L. Endothelial dysfunction and immunothrombosis as key pathogenic mechanisms in COVID-19. *Nat Rev Immunol*. 2021;21:319–29.
4. Wang CL, Liu YY, Wu CH, Wang CY, Wang CH, Long CY. Impact of COVID-19 on Pregnancy. *Int J Med Sci*. 2021;18(3):763–7.
5. Clinical spectrum in COVID-19. National Institutes of Health; 2021.
6. Batah SS, Fabro AT. Pulmonary pathology of ARDS in COVID-19: A pathological review for clinicians. *Respir Med*. 2021;176:106239. doi:10.1016/rmed.2020.106239.j.
7. Kadir RA, Kobayashi T, Iba T, Erez O, Thachil J, Kazi S, et al. COVID-19 coagulopathy in pregnancy: Critical review, preliminary recommendations, and ISTH registry-Communication from the ISTH SSC for Women's Health. *J Thromb Haemost*. 2020;18(11):3086–98.
8. Ssekandi AM, Sserwanja Q, Olal E, Kawuki J, Adam MB. Corticosteroids Use in Pregnant Women with COVID-19: Recommendations from available evidence. *J Multidiscip Healthc*.

2021;14:659–63.
9. Coronavirus Infection in Pregnancy, information for health care professionals. *RCOG*. 2021;13:43–51.
10. Wei Q, Lin H, Wei RG, Chen N, He F, Zou DH, et al. Tocilizumab treatment for COVID-19 patients: a systematic review and meta-analysis. *Infect Dis Poverty*. 2021;10(1):71. doi:10.1186/s40249-021-00857-w.
11. Weinreich DM, Sivapalasingam S, Norton T, Ali S, Gao H. REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19. *N Engl J Med*. 2021;384(3):238–51. doi:10.1056/NEJMoa2035002.
12. COVID-19 Treatment Guideline Panel.National Institutes of Health; 2021.
13. Tobin MJ, Laghi F, Jubran A. Why COVID-19 Silent Hypoxemia Is Baffling to Physicians. *Am J Respir Crit Care Med*. 2020;202(3):356–60.
14. Available from: www.icmr.gov.in.
15. Available from: www.cdc.gov.

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