

Are Raised Blood Sugar Levels Contributory Towards Rapid Deterioration Of ARDS In Covid 19 Positive Pregnant Women?

Aarya V Barve^{1,3}, Prachi S Koranne^{1,3}, Aparna R Wahane^{1,3},
Meenakshi I Gajbhiye^{2,3}

1 Department of Obstetrics and Gynecology, Akola 444001, India

2 Department of Radiology, Akola 444001, India

3 Government Medical College and Hospital, Akola 444001, India

Correspondence: Aarya V Barve; aarya_barve@yahoo.co.in

ABSTRACT

The Coronavirus Disease 19 (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus and results in a range of severity of symptoms varying from fever, cough, cold, breathlessness to fatal pneumonia, sepsis, organ failure, disseminated intravascular coagulation etc. Owing to altered physiology and immunological mechanisms in the body, pregnant women are at a higher risk of acquiring the infection. A substantial number of patients have developed serious life-threatening complications of the disease which prompts us to search for factors that may have contributed towards clinical deterioration of the pregnant women as well as the fetus. Out of the total 300 and counting COVID-19 positive ANC and PNC patients being treated at our tertiary care hospital, around twelve have required ventilatory support in the COVID ICU and eight have succumbed to the deadly infection. We found similar findings of raised blood sugar levels in five of these cases, hence the analysis of this case series report.

Keywords: COVID-19, Coronavirus, pregnancy, hyperglycemia, obstetrics, mortality

Date of Submission: 12-01-2022

Date of Acceptance: 27-01-2022

I. Introduction

The World Health Organization first learned of COVID-19 on 31 December 2019 and its outbreak was declared a global pandemic on 12 March 2020.¹ The virus transmission is by respiratory droplets, direct contact with fomites and possibly aerosols by close contact with infected person. After entering via nasal cavity, it infects pulmonary cells via the 'SARS-CoV Angiotensin converting enzyme 2' receptor and uses 'transmembrane serine protease 2' for protein priming.¹ Release of the viral particles causes pyroptosis of host cell which releases damage-associated molecular patterns (DAMPs) which includes nucleic acids and ATPs thereby triggering an inflammatory response in nearby cells. In majority of cases, symptoms are mild because the immune system tackles the virus effectively. Ongoing research suggests inflammation due to the virus attracts CD4 helper T cells which help in clearing infected cells.² Further inflammation is controlled by macrophages and neutralizing antibodies. The inflammation may sometimes be exaggerated and is known as a 'cytokine storm' leading to multiple organ damage which is the reason for morbidity and mortality.

Pregnancy is a diabetogenic state. There is increased production of human placental lactogen, cortisol, estrogens and progesterone which, being insulin antagonists raise blood sugar levels physiologically.

The maternal immune system becomes ready to accommodate an allogenic fetus to grow, the flip side being it becomes susceptible to other infections.¹ The altered maternal immune system may lead to an altered way of tackling infections during pregnancy, especially viruses. Some considerations for the same in view of COVID-19 pathogenesis may be as follows:

- Progesterone reduces number of virus-specific antibodies and virus-specific CD8 cells in Influenza A infection leading to more severe disease. [This is based on a study in mice.]¹ Further studies are required to come to a conclusion.
- There is shift of CD4+ T cell population towards Th2 phenotype over Th1 phenotype in pregnancy, leading to altered immune response to viral infections in pregnancy.¹
- There is a decrease in circulating NK cells in pregnancy, resulting in altered immune response towards viral infections, leading to severe disease.¹

- Although tidal volume increases by 30-40%, reduction in chest volume is responsible for reduced residual volumes, end expiratory volumes and functional residual capacity in pregnancy beginning from first trimester itself. This leads to inability to clear secretions effectively and leads to accumulation of virus in lungs.¹ Physiological elevation of diaphragm due to gravid uterus and changes in chest shape can be contributory.
- Pregnancy is a hypercoagulable state. There are higher levels of circulating coagulation factors. Hence pregnant women are at increased risk of thrombosis and DIC due to COVID-19.³

II. Materials And Methods

Our tertiary care center has witnessed eight COVID positive maternal mortalities till date. Out of eight, we found similar findings in five cases as shown in Table no. 1. All of these cases reported raised blood sugar levels on admission. Due to their deteriorating condition and NIV requirement, oral glucose tolerance test could not be performed, hence we could not label the cases as gestational diabetes mellitus. Treatment was initiated for hyperglycemia in pregnancy based on standard guidelines.

All five cases were admitted to the COVID ICU and were on NIV support. Blood and serum markers were monitored on a regular basis. An X-ray Chest with abdominal shield was done after obtaining valid informed consent of the patients' relatives. Standard treatment was started for each case comprising of antibiotics, antacids, blood thinners in the form of Low Molecular Weight Heparin (LMWH) 0.6 mg subcutaneous 12 hourly.^{4,5}

Despite being diagnosed with hyperglycemia all cases were started on steroid treatment in order to curb cytokine storm related to COVID-19. Methylprednisolone 40mg intravenous 12 hourly was administered to all 5 cases because benefits outweighed the risks.⁴

Daily glucose monitoring was done every six hours for all cases, which incorporated fasting blood sugar levels as well. Total Insulin requirements per day for each patient have been put forth in Table no. 2. Their cumulative doses which were given as 75% rapid acting insulin and 25% basal insulin, exceeded the baseline requirements of 0.4 IU/kg/day based on guidelines issued by the MoHFW India.⁵

III. Results And Observation

Table no. 1

PARAMETERS	CASE 1	CASE 2	CASE 3	CASE 4	CASE 5
AGE	24	27	22	20	26
RTPCR FOR COVID-19	Positive	Positive	Positive	Positive	Positive
OBSTETRIC FORMULA	G3P1L1A1	G2P1L1	PRIMI	PRIMI	PRIMI
GESTATIONAL AGE (weeks)	21+1	29+2	24+3	28+6	24+0
PULSE, BP ON ADMISSION	108, 100/60	120, 110/80	140, 100/70	100, 110/70	104, 100/60
RESPIRATORY RATE	48/min	38/min	60/min	52/min	66/min
SPO2 (on RA*, HFO2**)	70%, 90%	78%, 98%	76%, 97%	70%, 84%	65%, 95%
NIV REQUIREMENT	Yes	Yes	Yes	Yes	Yes
X-RAY CHEST ON ADMISSION (LOBE INVOLVEMENT)	5 lobes	4 lobes	4 lobes	4 lobes	5 lobes
RANDOM BSL ON ADMISSION (mg/dl)	180	178	160	191	162
D-DIMER (ng/dl)	3990	1280	2080	4827	2553
LDH (IU/L)	260	666	1440	840	927
FERRITIN (ng/ml)	498	184	160	280	328
RFT/LFT***	WNL	WNL	WNL	WNL	WNL
BREATHLESSNESS SINCE	3 days	4 days	5 days	3 days	4 days
DAYS FROM ONSET OF SYMPTOMS TO PRESENTATION	3 days	4 days	5 days	3 days	4 days
DAYS ON NIV****	12 days	10 days	8 days	10 days	5 days
DAYS FROM ADMISSION TO DEATH	13 days	11 days	9 days	11 days	6 days
DAYS FROM ONSET OF SYMPTOMS TO PRESENTATION	3 days	4 days	5 days	3 days	4 days
DAYS ON NIV****	12 days	10 days	8 days	10 days	5 days
DAYS FROM ADMISSION TO DEATH	13 days	11 days	9 days	11 days	6 days

*Room air, ** high flow O2, *** renal function tests/liver function tests, **** Non-invasive ventilation

Table No. 2

Insulin Requirement per day (Rapid acting)	Case 1	Case 2	Case 3	Case 4	Case 5
Day 1	26 IU	26 IU	24 IU	28 IU	23 IU
Day 2	28 IU	26 IU	24 IU	28 IU	25 IU
Day 3	29 IU	28 IU	23 IU	28 IU	25 IU
Day 4	28 IU	28 IU	23 IU	27 IU	27 IU
Day 5	27 IU	27 IU	24 IU	27 IU	26 IU
Day 6	28 IU	27 IU	24 IU	27 IU	26 IU
Day 7	28 IU	26 IU	25 IU	26 IU	Death
Day 8	26 IU	26 IU	24 IU	27 IU	Death
Day 9	25 IU	28 IU	24 IU	27 IU	Death
Day 10	25 IU	28 IU	Death	28 IU	Death
Day 11	27 IU	28 IU	Death	28 IU	Death
Day 12	28 IU	Death	Death	Death	Death
Day 13	Death	Death	Death	Death	Death

IV. Discussion

Early diagnosis and treatment initiation is the underlying rule for any disease. It is all the more important in this pandemic where deterioration has been so sudden and unexpected. Majority of patients presented to us with respiratory distress. This can be attributed to lack of awareness of COVID-19 in rural settings of India and also lack of adequate antenatal checkup in these places. Dyspnea in pregnancy can be physiological. However, in the setting of COVID-19, it should not be neglected especially if it is associated with fever, cough, cold etc. Pregnant women should follow strict social distancing and hygiene, avoid unnecessary travel and crowded places, check temperature and keep a watch on fetal movements.³ A doctor or health care provider should be contacted if any doubts arise.

People with diabetes appear to be at an increased risk of having severe COVID-19.⁶ Due to paucity of data, it is not possible to quantify the relationship between severity of diabetes and severity of COVID-19. The International Diabetes Federation proposes two mechanisms. Contracting diabetes weakens the immune system of the body impairing its ability to fight the virus. Secondly, the virus may thrive better in an environment of raised blood glucose. Impaired metabolic control in patients with diabetes leads to obesity, IHD, hypertension, inflammation, impaired blood glucose levels and impaired coagulation which results in severe COVID-19.⁶ Increased blood glucose levels are contributory to increasing the osmolarity of blood, thereby favoring coagulation.

Every pregnancy should be screened for diabetes at usually 24-28 weeks gestation. The Society of Obstetrics and Gynecology, Canada has suggested an alternative for treating diabetes in pregnancy complicated by COVID-19 which is measuring glycosylated hemoglobin (HbA1c) levels in pregnant women to reduce the risks of infection.⁷ However, this has its own drawbacks. In a resource-challenged setting like ours, all patients cannot afford these investigations. More importantly, HbA1c reference values are not defined during pregnancy.⁷

According to International Federation of Gynecologists and Obstetricians (FIGO), pregnant women with raised sugar levels and COVID-19 should be started on insulin as soon as possible if dietary and lifestyle modifications are inadequate.⁷ Telemedicine is an innovative way of monitoring patients in the pandemic era for consultation, treatment modifications, psychological support from the doctor.

In our tertiary care center facilities like HbA1c testing and telemedicine cannot be employed due to lack of funds. Most of our patients belong to low socio-economic strata who are deprived of basic education. Teaching such patients and their caregivers about home glucose monitoring and telemedicine technologies is quite challenging, although not impossible.

In this scenario, an entity known as stress induced hyperglycemia cannot be overlooked. It is attributable to reduced glucose uptake by peripheral cells, increased hepatic glucose production and insufficient pancreatic insulin production which is the effect of various hormones like cortisol, catecholamines, growth hormone and glucagon. This environment of hyperglycemia is all the more favorable for supplying much-needed glucose to affected tissues and increasing the severity of sepsis, thereby contributing to morbidity and mortality.⁸

Funding: None

Conflicts Of Interest: The authors declare no conflicts of interest.

Consent: Valid informed written consent was taken from the patient and her relatives on admission as well as during the course of the treatment. No patient-specific data has been disclosed in this study.

V. Conclusion

Uncontrolled blood sugar has deleterious effects on COVID-19 prognosis in pregnancy. Measures should be taken to detect possible complications early. As routine health care has been hampered owing to the pandemic, we suggest starting the screening for raised blood sugar levels early, maybe as early as the booking visit because any pregnant woman can contract COVID-19 and worsen anytime. Once ARDS sets in, it is challenging to carry out OGTT and make a diagnosis of gestational diabetes. Owing to the novelty of this pandemic, research data is limited to decide specific treatment protocols for pregnant COVID-19 patients. Here, we have tried to make a small contribution towards dealing with the COVID-19 in pregnant women.

The primary research question we would like to raise is ‘Does intensifying the screening processes for hyperglycemia in pregnancy before the 24-28-week gestation mark have any benefit in delaying the possible complications of ARDS in COVID-19 positive pregnant women?’ Further studies need to be done to provide guidelines for the same.

References

- [1]. Wastnedge E, Reynolds R, van Boeckel S, Stock S, Denison F, Maybin J et al. Pregnancy and COVID-19. *Physiological Reviews*. 2021;101(1):303-318
- [2]. Chen M, Zeng J, Liu X, Sun G, Gao Y, Liao J, Yu J, Luo X, Qi H. Changes in physiology and immune system during pregnancy and coronavirus infection: A review. *Eur J Obstet Gynecol Reprod Biol*. 2020 Dec;255: 124-128. doi: 10.1016/j.ejogrb.2020.10.035. Epub 2020 Oct 16. PMID: 33125977; PMCID: PMC7566677.
- [3]. Antonakou A. The latest update on the effects of COVID-19 infection in pregnancy. *European Journal of Midwifery*. 2020;4(April)
- [4]. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at <https://www.covid19treatmentguidelines.nih.gov/>. Accessed 15/07/2021
- [5]. Clinical Guidance on Diagnosis and Management of Diabetes at COVID-19 Patient Management facility. Version 2.0. Available from: <https://www.mohfw.gov.in/pdf/ClinicalGuidanceonDiagnosisandManagementofDiabetesatCOVID19PatientManagementfacility.pdf> Accessed 03/08/2021.
- [6]. Riddle MC, Buse JC, Franks PW, et al. COVID-19 in People with Diabetes: Urgently Needed Lessons from Early Reports. *Diabetes Care* 2020; 43:1378–1381
- [7]. Priya G, Bajaj S, Grewal E, Maisnam I, Chandrasekharan S, Selvan C. Challenges in Women with Diabetes During the COVID-19 Pandemic. *European Endocrinology*. 2020;16(2):100.
- [8]. Xiu F, Stanojcic M, Diao L, Jeschke M. Stress Hyperglycemia, Insulin Treatment, and Innate Immune Cells. *International Journal of Endocrinology*. 2014; 2014:1-9.

Aarya V Barve, et. al. "Are Raised Blood Sugar Levels Contributory Towards Rapid Deterioration Of ARDS In Covid 19 Positive Pregnant Women?." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 21(01), 2022, pp. 44-47.