Delirium in a pregnant woman with SARS-CoV-2 infection in India

Niraj N. Mahajan

PII: S1876-2018(20)30626-2
DOI: https://doi.org/10.1016/j.ajp.2020.102513
Reference: AJP 102513

To appear in: *Asian Journal of Psychiatry*

Rahul K. Gajbhiye

PII: S1876-2018(20)30626-2
DOI: https://doi.org/10.1016/j.ajp.2020.102513
Reference: AJP 102513

To appear in: *Asian Journal of Psychiatry*

Rahi R. Pednekar

PII: S1876-2018(20)30626-2
DOI: https://doi.org/10.1016/j.ajp.2020.102513
Reference: AJP 102513

To appear in: *Asian Journal of Psychiatry*

Madhura P. Pophalkar

PII: S1876-2018(20)30626-2
DOI: https://doi.org/10.1016/j.ajp.2020.102513
Reference: AJP 102513

To appear in: *Asian Journal of Psychiatry*

Shweta N. Kesarwani

PII: S1876-2018(20)30626-2
DOI: https://doi.org/10.1016/j.ajp.2020.102513
Reference: AJP 102513

To appear in: *Asian Journal of Psychiatry*

Aishwarya V. Bhurke

PII: S1876-2018(20)30626-2
DOI: https://doi.org/10.1016/j.ajp.2020.102513
Reference: AJP 102513

To appear in: *Asian Journal of Psychiatry*

Smita D. Mahale

PII: S1876-2018(20)30626-2
DOI: https://doi.org/10.1016/j.ajp.2020.102513
Reference: AJP 102513

To appear in: *Asian Journal of Psychiatry*

Received Date: 4 September 2020

Please cite this article as: Mahajan NN, Gajbhiye RK, Pednekar RR, Pophalkar MP, Kesarwani SN, Bhurke AV, Mahale SD, Delirium in a pregnant woman with SARS-CoV-2 infection in India, *Asian Journal of Psychiatry* (2020), doi: https://doi.org/10.1016/j.ajp.2020.102513

Title: Delirium in a pregnant woman with SARS-CoV-2 infection in India

Running Title: Delirium in pregnancy with COVID-19

Authors: Niraj N. Mahajan, MD[1]*, Rahul K Gajbhiye, MBBS, PhD[2]*, Rahi R Pednekar, MRCOG[1], Madhura P Pophalkar, MS[1], Shweta N. Kesarwani, MS[1], Aishwarya V Bhurke, MSc[2], Smita D Mahale, PhD [2]

Affiliations:

[1]Department of Obstetrics and Gynecology, Topiwala National Medical College & BYL Nair Charitable Hospital, Mumbai, India, 400 008

[2]ICMR-National Institute for Research in Reproductive Health, Mumbai, India, 400 012

* These authors contributed equally

Corresponding Author

Dr Niraj Mahajan, MD
Associate Professor
Department of Obstetrics and Gynecology
B. Y. L. Nair Charitable Hospital and T. N. Medical College, Mumbai. 400008
Telephone +919004696920
Email: nirajdr@hotmail.com
&

Dr Rahul Gajbhiye, MBBS, PhD
Scientist D & DBT Wellcome India Alliance
Clinical & Public Health Intermediate Fellow,
Department of Clinical Research,
ICMR-National Institute for Research in Reproductive Health,
J M Street, Parel, Mumbai, 400012, INDIA
Email: gajbhiyer@nirrh.res.in

Word Count: 946

Highlights

- Pregnant woman with delirium and COVID-19 is extremely challenging to manage especially in low income and middle income countries (LMICs).

Keywords: COVID-19, delirium, LMICs, low resource settings, post-partum period, psychotic disorders, SARS-CoV-2

To the Editor

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is rapidly spreading all over the world affecting all aspects of health, most importantly the mental health. In the current healthcare crisis due to COVID-19 pandemic, immediate dissemination of evidence is a priority for empowering the healthcare providers and policy makers (Tandon, 2020). Currently, there is limited data on impact of COVID-19 on mental health of individuals residing in low income and middle-income countries (LMICs), especially pregnant women. Pregnant women are at increased risk of contracting COVID-19 and thus require special attention, especially while dealing with mental health issues. It is extremely challenging to manage the mental health problems of pregnant women with COVID-19 in India and other LMICs due to an inadequate health system infrastructure, lack of trained manpower and mental health services (Jungari, 2020). Several challenges are being faced in the COVID-19 hospitals in LMICs, especially for the management of pregnant and post-partum women with COVID-19. In a dedicated COVID-19 facility, we managed 885 pregnant women with COVID-19 wherein more than 600 women delivered. In these women, increased anxiety and psychological distress related to COVID-19 was observed (unpublished data). Three cases of post-partum psychosis associated with COVID-19 were successfully managed at our dedicated COVID-19 hospital (Mahajan et al., 2020, Subramanyam et al., 2020).

We report an unusual case of altered mental status with delirium in a 30-weeks pregnant woman positive for SARS-CoV-2 infection. She had preeclampsia, normal oxygen saturation and no

other symptoms of COVID-19. Her agitation started 14-hours after admission and delivered vaginally 6-hours after first episode of agitation. In this case of delirium, restraining her extreme agitation was very challenging, especially while wearing personal protective equipments. Neurological and psychiatric evaluation confirmed a diagnosis of delirium, secondary to co-morbidities related to pregnancy [anaemia, severe preeclampsia, bad obstetric history (BOH) and preterm delivery] and SARS-CoV-2 infection. She had similar episode on Day-4 post-partum. There was no psychotic phenomenon like delusion or hallucinations ruling out post-partum psychosis. Her neurological examination including a CT scan was normal, ruling out posterior reversible encephalopathy syndrome (PRES) which is also known to be present as delirium in cases of severe preeclampsia (Schusse et al., 2013). Her symptoms improved gradually and got discharged from the hospital on Day-31 (Table 1).

In this case, pregnancy coupled with COVID-19 and co-morbidities such as severe preeclampsia, preterm labour induction, anaemia requiring blood transfusions could have caused various biochemical changes. This might have led to aberrant stress responses manifesting as delirium. It is worth to note that certain patients with COVID-19 may have non-specific neurological symptoms such as delirium, preceding symptoms of even fever and cough (Cipriani et al., 2020). Eclampsia and severe preeclampsia are considered as differential diagnosis in patients with presentation of agitation and delirium (Aftab and Shah, 2017). Delirium is an acute, complex, organic brain syndrome occurring secondary to multifactorial aetiology which can be either due to direct brain insult or aberrant stress responses to stressors like infections, surgical trauma, anxiety, etc. (Brockington, 2004). Pregnancy and puerperium also cause considerable physical and psychiatric modifications that impose significant amount of stress placing a woman in a situation of restructuring her role as a mother. This may lead to psychological symptoms or

provoke various mental illnesses. The somatic alterations of pregnancy can lead to psychiatric problems and vice versa in different ways (Di Renzo, 2002). Acute agitation should be treated as an obstetric emergency as it can compromise the safety of the mother, the child or others present in the vicinity (Niforatos et al., 2019). Delirium as such is a rare disorder in pregnancy but was common in early 19th century with an incidence of 1/5000 deliveries. However, now it has become rare due to good antenatal care and labour analgesia (Brockington, 2004). Viral infection like SARS-CoV-2 with fever and hypoxemia may trigger delirium (Cipriani et al., 2020). Apart from lungs, central nervous system (CNS) has also been observed to be affected by SARS-CoV-2 infection (Mao et al., 2020). Neuropsychiatric manifestations including delirium are now recognized as presenting features of COVID-19 and delirium may be the only presenting symptom (Hosseini et al., 2020). However, it is not clear whether these neurological manifestations are due to direct injury to CNS or an indirect response to systemic inflammatory storm (Cipriani et al., 2020; Mao et al., 2020). Based on the emerging evidence of neuropsychiatric manifestations of COVID-19, further studies on its pathogenesis are required.

There are several challenges for managing the psychiatric emergencies in pregnant women with COVID-19 in LMICs. There is lack of trained counselors for addressing the multiple psychological problems of pregnant women with COVID-19, as they worry about transmission of infection to their child, anxiety about the safe delivery, fear of separation from newborn, etc. Unavailability of trained healthcare workers in maternity units on diagnosis and management of psychiatric emergencies, limited availability of mental health providers and services are some of the other challenges in LMICs.

There is an opportunity for healthcare providers engaged in maternity units for acquiring the skills on diagnosis and effective management of psychiatric disorders associated with viral

infections including the current pandemic of COVID-19. Based on our experience, we recommend the training of healthcare workers on early recognition and appropriate treatment of psychiatric emergencies in pregnancy and post-partum period. There is a need for creating specialist mental health services and provision of a psychologist counselor for specifically dealing with pregnancy care in public healthcare system. Accurate information about COVID-19 as well as counseling should be provided to the pregnant and post-partum women for reducing stress. The guidelines covering maternal health should have a provision for training the obstetricians in management of the psychiatric emergencies and use of short term psychotropic.

Funding:

The study is supported by intramural grant of ICMR-NIRRH (ICMR-NIRRH/RA/966/09-2020).

Trial Registration:

PregCovid study is registered with Clinical Trial Registry of India (Registration no: CTRI/2020/05/025423)

Ethics Approval:

The study was approved by the Ethics Committees of TNMC (No. ECARP/2020/63 dated 27.05.2020) and ICMR-NIRRH (IEC no. D/ICEC/Sci-53/55/2020 dated 04.06.2020).

Contribution to Authorship:

NM and RG had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: RG, NM

Acquisition of data: MP SK, NM, AB

Analysis, or interpretation of data: All authors

Drafting of the manuscript: RP, NM, RG

Critical revision of the manuscript for important intellectual content: NM, RG

Statistical analysis: NM, RG

Administrative and technical or material support: NM, SM, RG

Declarations of interest:

The authors declare that they have no conflict of interest.

Acknowledgements

The authors acknowledge the Director General, ICMR and Network of National Registry of Pregnant women with COVID-19 in India (PregCovid Registry, CTRI/2020/05/025423). The Dean, TNMC, Faculties, Resident doctors in the Department of Psychiatry and Department of Obstetrics and Gynecology at TNMC, Mumbai are sincerely acknowledged. RG is an awardee of the DBT Wellcome India Alliance Clinical and Public Health Intermediate Fellowship (Grant no. IA/CPHI/18/1/503933).

References

Aftab, A., Shah, A.A., 2017. Behavioral Emergencies: Special Considerations in the Pregnant Patient. Psychiatric Clinics of North America 40, 435–448. https://doi.org/10.1016/j.psc.2017.05.017

Brockington, I., 2004. Diagnosis and management of post-partum disorders: a review. World Psychiatry 3, 89–95.

Cipriani, G., Danti, S., Nuti, A., Carlesi, C., Lucetti, C., Di Fiorino, M., 2020. A complication of coronavirus disease 2019: delirium. Acta Neurol Belg 120, 927–932. https://doi.org/10.1007/s13760-020-01401-7

Di Renzo, G.C., 2002. Pregnancy as delirium. J. Matern. Fetal. Neonatal. Med. 12, 145–148. https://doi.org/10.1080/jmf.12.3.145.148

Hosseini, A.A., Shetty, A.K., Sprigg, N., Auer, D.P., Constantinescu, C.S., 2020. Delirium as a presenting feature in COVID-19: Neuroinvasive infection or autoimmune encephalopathy? Brain Behav Immun 88, 68–70. https://doi.org/10.1016/j.bbi.2020.06.012

Jungari, S., 2020. Maternal mental health in India during COVID-19. Public Health 185, 97–98. https://doi.org/10.1016/j.puhe.2020.05.062

Mahajan, N.N., Pednekar, R., Patil, S.R., Subramanyam, A.A., Rathi, S., Malik, S., Mohite, S.C., Shinde, G., Joshi, M., Kumbhar, P., Tilve, A., Lokhande, P.D., Srivastava, S.A., 2020. Preparedness, administrative challenges for establishing obstetric services, and

experience of delivering over 400 women at a tertiary care COVID- 19 hospital in India [WWW Document]. International Journal of Gynecology & Obstetrics. URL https://obgyn.onlinelibrary.wiley.com/doi/abs/10.1002/ijgo.13338 (accessed 8.25.20).

Mao, L., Jin, H., Wang, M., Hu, Y., Chen, S., He, Q., Chang, J., Hong, C., Zhou, Y., Wang, D., Miao, X., Li, Y., Hu, B., 2020. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. JAMA Neurology 77, 683–690. https://doi.org/10.1001/jamaneurol.2020.1127

Schusse, C.M., Peterson, A.L., Caplan, J.P., 2013. Posterior Reversible Encephalopathy Syndrome. Psychosomatics 54, 205–211. https://doi.org/10.1016/j.psym.2013.01.014

Subramanyam, A.A., Nachane, H.B., Mahajan, N.N., Shinde, S., D Mahale, S., Gajbhiye, R.K., 2020. Postpartum psychosis in mothers with SARS-CoV-2 infection: A case series from India. Asian Journal of Psychiatry 102406. https://doi.org/10.1016/j.ajp.2020.102406

Tandon, R., 2020. COVID-19 and mental health: Preserving humanity, maintaining sanity, and promoting health. Asian Journal of Psychiatry 51, 102256. https://doi.org/10.1016/j.ajp.2020.102256

Table 1: Socio-demographic and clinical characteristics of a woman with delirium and COVID-19 in India

Parameters	**Delirium with COVID-19**
Age	34 years
Socio-economic Status	Low
Gravida (G) /Parity (P) /Living children (L)	G5 P1L0
Bad Obstetric History	Previous 3 spontaneous abortions and one still birth
H/O Contact with Positive	No

Person/foreign travel	
Indication for COVID-19 RT-PCR testing	Universal Screening as per existing local guidelines
Spontaneous Conception	Yes
Antenatal Comorbidities	Severe Preeclampsia, Anemia, BOH
Family and previous history of Psychiatric illness and substance abuse	No
Symptoms	Agitation, aggression, mental confusion, alteration of sleep, headache, loss of appetite, sleep disturbance, violent behavior, disorientation, Not cooperating. Did not allow per-vaginal examination, monitoring foetal heart sounds and blood pressure. During labour she became agitated, violent and pulled off intravenous catheter, abused and attempted biting the healthcare workers in maternity unit.
Significant clinical findings	Severe preeclampsia, Minimal pleural effusion
Hemoglobin% (g/dl)	8.6
Total Leucocyte Count	10,200/µL
Blood Group and Rh type	O Positive
Duration of Delirium Symptoms	5 days
Obstetric Management	Induction of Labour with dinoprostone gel, magnesium sulphate therapy for severe preeclampsia
Management	Inj. mannitol, anti-hypertensives and three PCV transfusion. Restrained by six attendants. Inj. Midazolam followed by Inj. haloperidol to control agitation. Tab. haloperidol in tapering doses over 11 days
Duration of Hospital stay	31 days, as baby was in NICU till then,
Neonatal outcome	Neonatal death (female) on Day 31, owing to extreme prematurity and low birth weight (1.270 kg).

BOH, Bad Obstetric History; NICU, Neonatal Intensive Care Unit, Inj, Injection; PCV, Packed Cell Volume