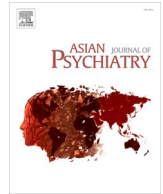




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Letter to the Editor

**Postpartum psychosis in mothers with SARS-CoV-2 infection: A case series from India**

To The Editor,

The current COVID-19 pandemic is causing severe damage to the mankind through direct impact on health and also collaterally affecting all aspects of life including the mental health. The impending mental health crisis has attracted the attention of global experts and organisations necessitating the documentation of impact of COVID-19 on mental health especially among the vulnerable populations (Tandon, 2020). Pregnancy and the postpartum period are known to have increased vulnerability to psychiatric disorders (Eberhard-Gran et al., 2002). Earlier studies reported the association of other coronaviruses with a range of psychiatric disorders (Cheng et al., 2004; Severance et al., 2011). However, there is no information on new-onset psychosis in asymptomatic patients or post-partum women with COVID-19. We report three cases of post-partum psychosis (PP) associated with asymptomatic COVID-19 managed at Topiwala National Medical College (TNMC) & B. Y. L. Nair Charitable Hospital (NH). NH is an academic tertiary care public hospital and a dedicated COVID-19 hospital in Mumbai, India, receiving referrals from all over the Mumbai Metropolitan Region (MMR) (Mahajan et al., 2020). In the initial phase of three months of COVID-19 pandemic (from 4th April 2020 to 31st July 2020), NH treated three asymptomatic, RT-PCR confirmed COVID-19 women with PP. The demographic, clinical characteristics, delivery details and management of COVID-19 mothers with PP are described in Table 1. This study was approved by Institutional Ethics Committees of TNMC, Mumbai and ICMR-National Institute for Research in Reproductive Health, Mumbai.

All three women had uneventful deliveries (two caesarean deliveries and one normal vaginal delivery) and gave birth to healthy new-borns (Table S1). They developed PP within seven days of giving birth (mean 5 days). Their other laboratory investigations, neurological work-up and general examination was normal. Diagnosis of PP was based on the presence of psychotic symptoms in the absence of other organic or mood disorders. All women recovered within seven days of treatment and were discharged. Duration of symptoms lasted till seven days in two patients and three days in one patient. Two patients received haloperidol, trihexyphenidyl and third patient was given olanzapine (Table 1).

Post-partum mothers are vulnerable to a number of psychiatric disorders, owing to physiological and psychological changes happening in the mother's body (Brockington, 2004). Our patients had only psychogenic type of PP, as affective symptoms were characteristically absent in all three cases. However, prospective studies are required to generate robust data on association of PP with COVID-19. Affective symptoms have been shown to occur in majority of the cases and many cases present with rapid mood fluctuations (Brockington, 2004). Onset of illness in all the three cases were in the first week following delivery. The most common symptoms in our cases were delusion of persecution and reference, which have been shown to be the most common in other

studies as well (Regmi et al., 2002; Sit et al., 2006). Two women in our series, had delusion surrounding the SARS-CoV-2 infection, which goes in favor of psychogenic rather than a structural cause. This could be due to added stress surrounding COVID-19, as stress is known to be one of the main factors in development of PP. Aggression has also been noted in PP and was present in all of the cases. Around 35% of the women with PP pose a risk to their infant (Sit et al., 2006). Two women required separation of infant from mother and one required supervision. A sense of well-being and hypomanic symptoms have frequently been shown to occur in prodrome of PP (Sit et al., 2006), however none were seen in our series. Established risk factors that were evident in our sample were parity (two primipara), CS (two) and gestational hypertension (one). First pregnancies and preeclampsia are greater psychosocial stressors. It has also been hypothesized that biological factors could be in play (Blackmore et al., 2006). Neuropsychiatric manifestations like depression, anxiety and psychosis of COVID-19 infection are accounted to a hypercoagulable state (Troyer et al., 2020). Infection or treatment with steroids was not present in our patients, ruling them out, as the cause (Valdés-Florido et al., 2020). Delirium was ruled out in all of our cases.

An important stressor is social isolation. Usually, new mothers are supported by their families during the stressful puerperium in India. Social isolation in SARS-CoV-2 causing psychosis has been documented (Brown et al., 2020). Women with first episode of PP have demonstrated elevations in IL-6, thereby supporting the immune mediated mechanism in PP (Sathyanarayanan et al., 2019). A profound inflammatory response to SARS-CoV-2 infection, known as 'cytokine storm' has been described and has been hypothesized to play a role in neuropsychiatric complications (Troyer et al., 2020). Raised antibody titers against HCoV was observed in recent psychotic episode (Severance et al., 2011). Although, we cannot directly explain the role of SARS-CoV-2 in PP, we can propose possible mechanisms based on the available information in the literature. It might be possible that altered immune mechanisms in patients with SARS-CoV-2 infection may be a risk factor for developing psychiatric illness. Neuropsychiatric sequelae can also be due to a direct neurotoxic effect of the virus or the host's immune response towards it. Having comorbid COVID-19 infection or the fact that these women had to deliver during the COVID-19 pandemic can itself put undue stress on them, leading to precipitation of psychiatric illnesses, such as PP.

Author Contribution

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

Concept and design: RG, NM

Acquisition of data: SS, NM, HN

Analysis, or interpretation of data: All authors

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Table 1
Characteristics, Symptoms and Treatment of Postpartum Psychosis Patients with SARS-CoV-2 Infection.

Sr. No.	PPP1	PPP2	PPP3
Age in years	24	23	23
Socio-economic Status	Low	Low	Low
Religion	Hindu	Hindu	Muslim
Gravida (G)/Parity (P)	G2P1	G1	G1
Contact with Positive Person	No	No	No
Foreign Travel	No	No	No
Indication for COVID-19 RT-PCR testing	Universal testing	Universal testing	Universal testing
Weeks of Gestation (+ represents days)	38 + 1	39 + 1	39 + 2
Previous Caesarean Section	Yes	No	No
Spontaneous Conception/ IVF	Spontaneous	Spontaneous	Spontaneous
Antenatal comorbidities	Gestational HTN	No	No
Past personal history of Psychiatric Illness	No	No	No
Family history of Psychiatric illness	No	No	No
History of substance use	No	No	No
Depression, Anxiety, or PTSD	No	No	No
Psychosis Symptoms	DOP, DOR, agitated behaviour SHB (suspiciousness that people are trying to harm her), AH (various unknown voices), reduced sleep and loss of appetite, severe fearfulness (drank two sips of methylated spirit in an attempt commit suicide)	DOP (suspicious of doctors and nurses around her that they were trying to make her and her child COVID-19 positive), aggressive behaviour towards hospital staff, belief that she was COVID-19 negative. Belief of doctors informing all other patients to stay away from her, Believed that people are keeping an eye on her, believed her conversations are being traced, loss of appetite as she felt she was being poisoned	IOR, guilt (people are blaming her for COVID-19), IOP and harm to baby, abusive behaviour without any provocation, had put talcum powder in the mouth and eyes of her baby. Fearful that she being scanned and passing this information to doctors. She felt that other people are discussing about her and blaming her COVID-19 spreader.
Duration of Symptoms	7 days	3 days	7 days
Treatment	Restrained, interaction of mother and baby restricted, Inj. Haloperidol 10 mg + Inj. Promethazine 50 mg T. haloperidol 15mg T. Trihexyphenidyl 2 mg increased to 6mg	close supervision and supervised breastfeeding, T. Haloperidol 5 mg bd T. Trihexyphenidyl 2 mg T. Lorazepam 2 mg ½ hs	interaction of mother and baby restricted, T. Olanzapine 10 mg
Chest X-ray changes	No	No	No
Oxygen Requirement	No	No	No
ICU admission	No	No	No
Mortality	No	No	No

DOP, Delusion of persecution; DOR, Delusion of reference; SHB, self-harm behaviour; AH, Auditory hallucinations; IOR, Ideas of reference; IOP, Ideas of persecution; ICU, Intensive Care Unit; PTSD, Post-traumatic stress disorder; IVF, In-Vitro Fertilisation.

Drafting of the manuscript: AS, HN

Critical revision of the manuscript for important intellectual content:

RG, AS, NM

Statistical analysis: AS, HN, NM

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

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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).

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.ajp.2020.102406>.

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