OPEN

COVID-19 infection during pregnancy may result in foetal brain haemorrhage

Ruhul Amin, PhD^a, Ashok K. Shenoy, MD^b, Talha B. Emran, PhD^{c,d,*}

Dear Editor,

Individuals infected with Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2) during pregnancy may display no symptoms or a broad variety of symptoms. Individuals with symptoms of coronavirus disease 2019 (COVID-19) seem to be at a greater risk of having significant sequelae than asymptomatic reproductive-aged females^[1]. When children are exposed to viral infection and maternal immune activation during pregnancy, there is an increased risk of negative neurodevelopmental outcomes. Several viruses have been linked to abnormal neurodevelopment, most notably the Zika virus infection and the microcephaly crisis^[2]. The virus has been found in the embryonic brain tissue of pregnant women who pass the illness on to their unborn children. This has spurred doctors to study the disease's possible influence on the growing bodies of unborn children, in addition to their own.

Twenty-six of the 661 samples of human fetal tissue received between July 2020 and April 2022 were confirmed to have hemorrhages following evaluation. COVID-19 was present in all of the tissue samples that exhibited evidence of bleeding. Each and every one of the samples originated from pregnancies that were terminated on purpose^[3].

While brain hemorrhages in children are not uncommon, the occurrence of so many in such a short period of time is remarkable. It is thus critical that we do follow-up with children who were exposed to COVID-19 during pregnancy to evaluate if there are any long-term effects on neurodevelopment^[4].

Researchers linked tissue damage to markers of decreased blood vessel integrity and increased immune cell infiltration in the

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Department of Pharmacy, BGC Trust University Bangladesh, Chittagong 4381, Bangladesh. Tel: +880 303 356 193,

fax: +880 312 550 224, Cell: +880 181 994 2214. E-mail: talhabmb@bgctub.ac.bd (T. B. Emran).

Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Annals of Medicine & Surgery (2023) 85:2228-2229

Received 10 March 2023; Accepted 18 March 2023

Published online 6 April 2023

http://dx.doi.org/10.1097/MS9.000000000000564

brain^[5,6]. The mother's immune response or the COVID-19 infection itself might both be to blame.

Only fetal tissues were discovered to be infected with the coronavirus; however, this clearly implies that the infections began in the mothers. However, it is unclear whether the bleeding was caused by the mother's COVID or the fetus's illness, or whether the relationship contains some other undisclosed component. However, the correlation is large enough to arouse concern.

The majority of the samples with indications of bleeding were obtained late in the first trimester or early in the second, demonstrating that injury to the embryonic brain may begin as early as the first trimester of pregnancy. As is generally known, the developing brain builds defences throughout this time, making it critical.

This is the first large study to show that COVID-19 infection during pregnancy may affect fetal brain development^[5]. This study emphasizes the need of immunizing pregnant women against COVID-19 to avoid complications for both mother and child, whether as a direct effect of the virus or as a secondary outcome of maternal infection.

Tissue samples from the placenta, amnion, and umbilical cord also indicated low levels of SARS-CoV-2, suggesting that COVID-19 might create further problems. The Zika virus is only one of numerous recent high-profile cases highlighting the devastating repercussions that maternal viral infections may have on their offspring's neurological systems^[7]. Researchers have discovered a link between COVID-19 infection in pregnant women and fetal health issues, however, the available data is restricted^[8].

The findings of the research data show that the sensitivity of human embryonic brain tissue to COVID-19 infection is connected to its development throughout the first trimester of pregnancy.

Ethical approval

None.

Consent

All authors read the manuscript and agree for publications.

Sources of funding

None.

Author contributions

R.A.: conceptualization, data curation, writing-original draft preparation, writing- reviewing and editing; A.K.S.: data curation, writing-original draft preparation, writing- reviewing and

^aFaculty of Pharmaceutical Science, Assam Down Town University, Panikhaiti, Guwahati, Assam, ^bDepartment of Pharmacology, Kasturba Medical College Mangalore, Manipal Academy of Higher Education, Manipal, Karnataka, India, ^cDepartment of Pharmacy, BGC Trust University Bangladesh, Chittagong and ^dDepartment of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, Dhaka, Bangladesh

editing; T.B.E.: writing-reviewing and editing, visualization, supervision.

Conflicts of interest disclosure

None.

Research registration unique identifying number (UIN)

- 1. Name of the registry: Not applicable.
- 2. Unique Identifying number or registration ID: Not applicable
- 3. Hyperlink to your specific registration (must be publicly accessible and will be checked): Not applicable.

Guarantor

Talha Bin Emran, Ph.D., Associate Professor, Department of Pharmacy, BGC Trust University Bangladesh, Chittagong 4381, Bangladesh. Tel: +880 303 356 193, fax: +88 0 312 550 224, Cell: +880 181 994 2214. https://orcid.org/0000-0003-3188-2272. E-mail: talhabmb@bgctub.ac.bd

Provenance and peer review

Not commissioned, internally peer-reviewed.

References

- Lu-Culligan A, Iwasaki A. The role of immune factors in shaping fetal neurodevelopment. Annu Rev Cell Dev Biol 2020;36:441–68.
- [2] Einspieler C, Marschik PB. The developmental spectrum of prenatal Zika virus exposure. Lancet Child Adolesc Health 2020;4:345–6.
- [3] Massimo M, Barelli C, Moreno C, et al. Haemorrhage of human foetal cortex associated with SARS-CoV-2 infection. Brain 2023;146: 1175–85.
- [4] Long K. Evidence of haemorrhages in fetal brain tissue associated with the presence of SARS-CoV-2. King's College London; 2023 [cited 2023 Jan 18]. Available from: https://www.kcl.ac.uk/news/evidence-of-haemorrhages-infetal-brain-tissue-ass sociated-with-the-presence-of-sars-cov-2
- [5] Lee MH, Perl DP, Steiner J, et al. Neurovascular injury with complement activation and inflammation in COVID-19. Brain 2022;145:2555–68.
- [6] Amin R, Quispe C, Docea AO, et al. The role of tumour necrosis factor in neuroinflammation associated with parkinson's disease and targeted therapies. Neurochem Int 2022;158:105376.
- [7] Yuan L, Huang X-Y, Liu Z-Y, et al. A single mutation in the prM protein of Zika virus contributes to fetal microcephaly. Science 2017;358:933–6.
- [8] Zeng L, Xia S, Yuan W, et al. Neonatal early-onset infection with sars-cov-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China. JAMA Pediatrics 2020;174:722–5.