



Comment to “Pregnancy and COVID-19, focus on vaccine and pharmacological treatment”

Dear Editor,

We read with interest the short communication on COVID-19 and pregnancy by Vitiello and colleagues (Vitiello et al., 2022), and thank the authors for referring to our earlier published manuscript on medication use among pregnant and breastfeeding women in Europe during the COVID-19 pandemic (Ceulemans et al., 2022). However, we would like to comment on a misleading statement in their publication, and their inadequate reference to our manuscript used to substantiate this statement. Vitiello et al. stated that “*some oral analgesic drugs used for self-medication can be used in pregnancy, such as ibuprofen, which has been shown to be safe for pregnant patients with covid-19*” and referred to our manuscript. However, our manuscript and follow-up publication (Gerbier et al., 2022) present the results of drug utilization studies and only provide prevalence estimates on the perinatal use of the non-steroidal inflammatory drug (NSAID) ibuprofen during the COVID period (<1% in pregnancy). Such studies neither aim to provide evidence of safety, nor obtain insight into specific risks associated with the use of ibuprofen or NSAIDs in pregnancy.

We are concerned about Vitiello et al.’s misleading statement as ibuprofen, and NSAIDs in general, are not necessarily safe to use during pregnancy. It has even been the topic of a warning from the American Food and Drug Administration (FDA) in Spring 2020, recommending to avoid the use of NSAIDs in pregnancy at 20 weeks or later due to the risk of serious kidney problems in unborn infants and low levels of amniotic fluid (Food Drug Administration, 2020). Other potential complications caused by NSAID use late in pregnancy are an increased risk of premature closure of the ductus arteriosus and pulmonary hypertension in the newborn, decrease in labor activity and delay of childbirth, and increased bleeding risk (Antonucci et al., 2012). We referred to this in our discussion, highlighting that the use of “*some medicines, such as ibuprofen after 20 weeks gestational age, may have detrimental effects on the developing fetus*” (Ceulemans et al., 2022), and should therefore be avoided in this population. In conclusion, NSAIDs should not be taken in pregnancy to treat minor symptoms of COVID-19 or any other indication without having a proper discussion with a healthcare professional.

References

- Antonucci, R., Zaffanello, M., Puxeddu, E., Porcella, A., Cuzzolin, L., Pilloni, M.D., Fanos, V., 2012. Use of non-steroidal anti-inflammatory drugs in pregnancy: impact on the fetus and newborn. *Curr. Drug Metab.* 13 (4), 474–490. <https://doi.org/10.2174/138920012800166607>.
- Ceulemans, M., Foulon, V., Panchaud, A., Winterfeld, U., Pomar, L., Lambelet, V., Cleary, B., O’Shaughnessy, F., Passier, A., Richardson, J.L., Nordeng, H., 2022. Self-Reported Medication Use among Pregnant and Breastfeeding Women during the

- COVID-19 Pandemic: A Cross-Sectional Study in Five European Countries. *Int J. Environ. Res Public Health* 19 (3), 1389. <https://doi.org/10.3390/ijerph19031389>.
- Food Drug Administration, 2020, FDA recommends avoiding use of NSAIDs in pregnancy at 20 weeks or later because they can result in low amniotic fluid. (<https://www.fda.gov/drugs/drug-safety-and-availability/fda-recommends-avoiding-use-nsaids-pregnancy-20-weeks-or-later-because-they-can-result-low-amniotic>).
- Gerbier, E., Favre, G., Tauqeer, F., Winterfeld, U., Stojanov, M., Oliver, A., Passier, A., Nordeng, H., Pomar, L., Baud, D., Panchaud, A., Meyer-Massetti, C., Ceulemans, M., 2022. Self-reported medication use among pregnant and postpartum women during the third wave of the COVID-19 pandemic: a European multinational cross-sectional study. *Int J. Environ. Res Public Health* 19 (9), 5335. <https://doi.org/10.3390/ijerph19095335>.
- Vitiello, A., Ferrara, F., Zovi, A., Trama, U., Boccellino, M., 2022. Pregnancy and COVID-19, focus on vaccine and pharmacological treatment. *J. Reprod. Immunol.*, 103630 <https://doi.org/10.1016/j.jri.2022.103630>.

- Michael Ceulemans^{a,b,c,*}, Laure Sillis^a, Veerle Foulon^a, Alice Panchaud^{d,e}, Ursula Winterfeld^f, Léo Pomar^{g,h}, Brian Cleary^{i,j}, Fergal O’Shaughnessy^{i,j}, Anneke Passier^b, Jonathan Luke Richardson^k, Hedvig Nordeng^{l,m}
- ^a Clinical Pharmacology & Pharmacotherapy, Department of Pharmaceutical and Pharmacological Sciences, KU Leuven, Belgium
- ^b Teratology Information Service, Pharmacovigilance Centre Lareb, The Netherlands
- ^c L-C&Y, KU Leuven Child & Youth Institute, Belgium
- ^d Service of Pharmacy, Lausanne University Hospital and University of Lausanne, Switzerland
- ^e Institute of Primary Health Care (BIHAM), University of Bern, Switzerland
- ^f Swiss Teratogen Information Service, Clinical Pharmacology Service, Lausanne University Hospital, Switzerland
- ^g Materno-Fetal and Obstetrics Research Unit, Lausanne University Hospital, Switzerland
- ^h School of Health Sciences (HESAV), University of Applied Sciences and Arts Western Switzerland, Switzerland
- ⁱ Rotunda Hospital, Ireland
- ^j School of Pharmacy, Royal College of Surgeons Ireland, Ireland
- ^k UK Teratology Information Service, Newcastle upon Tyne Hospitals NHS Foundation Trust, UK
- ^l Pharmacoepidemiology and Drug Safety Research Group, Department of Pharmacy, and PharmaTox Strategic Initiative, Faculty of Mathematics and Natural Sciences, University of Oslo, Norway
- ^m Department of Child Health and Development, Norwegian Institute of Public Health, Norway

* Corresponding author at: Clinical Pharmacology & Pharmacotherapy, Department of Pharmaceutical and Pharmacological Sciences, KU Leuven, Belgium.

<https://doi.org/10.1016/j.jri.2022.103639>

Received 6 May 2022; Accepted 9 May 2022

Available online 10 May 2022

0165-0378/© 2022 Elsevier B.V. All rights reserved.