Why we should not stop giving aspirin to pregnant women during the COVID-19 pandemic

During the current coronavirus disease 2019 (COVID-19) pandemic, several questions have arisen relating to the management of pregnant women. The risk of COVID-19 to pregnant women may be much lower than in the previous SARS epidemic. The case fatality rates (CFR) in pregnant women during the SARS and MERS epidemics were 15% and 27%, respectively[1,2], while

COVID-19 seems to have a milder natural history[2]. The available data regarding COVID-19 are limited; therefore, maternal outcomes may be underreported at present.

Published observations in non-pregnant patients have shown that non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, can cause progression of pulmonary disease. This relationship has been observed in bacterial pulmonary infections. Experimental data suggest that NSAIDs alter the function of neutrophils and delay bacterial clearance and inflammation resolution[3,4]. Observational data suggest an association between exposure to NSAIDs and the occurrence of pleuropulmonary complications (pleural empyema, excavation and abscess). Similar observations have also been made in a small group of young people taking ibuprofen for COVID-19 symptoms[3,4]. As a result, French health officials have issued a precaution regarding the use of NSAIDs, including aspirin. This has started an international debate among healthcare professionals regarding the usage of NSAIDs, primarily ibuprofen, in patients with COVID-19[5]. The Spanish Ministry of Health has stated that there is no evidence that ibuprofen (or other NSAIDs) could worsen SARS-CoV-2 infection. However, it stated that ibuprofen might mask the symptoms of infection, therefore delaying diagnosis[6]. The Royal College of Obstetricians and Gynaecologists in the UK recommends paracetamol for COVID-19 symptoms[7].

There is therefore cause for concern regarding the well-being of pregnant women taking aspirin for prophylaxis of pre-eclampsia and fetal growth restriction. The debate could have resulted in a misunderstanding among both healthcare professionals and pregnant women, leading to withdrawal of prophylactic low-dose aspirin therapy. Currently, there are no available data regarding the association between the risk of COVID-19 progression and intake of low-dose aspirin.

Pre-eclampsia affects 2–8% of pregnancies worldwide and is one of the leading causes of maternal death and perinatal mortality and morbidity[8]. Currently, around the world, there are more than 350 536 active cases of COVID-19 and this number is increasing every day[9]. On the other hand, there are fewer than 100 published cases of COVID-19 in pregnant women. Based on these case series and reports, it appears that the natural history of SARS-CoV-2 infection among pregnant women is not different from that in non-pregnant adults. A World Health Organization (WHO) report from China states that only 1% of the described cases in pregnant women have been critical and 8% were severe[10]. At the time of writing, there were no reported maternal deaths related to SARS-CoV-2 infection. None of the cases of COVID-19 in pregnant women in the series of Schwartz was severe[11].

Low-dose aspirin has been proven to be an effective regimen for the prevention of placental complications during pregnancy, including pre-eclampsia and fetal growth restriction. Intake of low-dose aspirin during pregnancy is not associated with an increased risk of congenital defects, bleeding or premature closure of the ductus arteriosus[8]. The recommended dosage of 150 mg of aspirin daily for the prevention of pre-eclampsia is based on the results of the ASPRE trial. In the trial, preterm pre-eclampsia occurred in 1.6% of women in the low-dose aspirin group, as compared with 4.3% in the placebo group (odds ratio, 0.38; 95% CI, 0.20–0.74; $P = 0.004$)[8].

The WHO has published an official statement recommending not to avoid the use of ibuprofen based on the current available data[12]. To our knowledge, there are limited data to suggest that there is an association between prophylactic use of low-dose aspirin and increased risk of progression of SARS-CoV-2 infection.

In our opinion, during the COVID-19 pandemic, it is still essential to provide first-trimester screening for placental complications and to prescribe low-dose aspirin in women who are identified as high risk for pre-eclampsia and fetal growth restriction. Based on the current knowledge of the epidemiological situation, the benefits of placental complication prevention outweigh the potential risks of adverse outcome related to the usage of low-dose aspirin in patients with SARS-CoV-2 infection.

S. Kwiatkowski[1], D. Borowski[2], A. Kajdy[3]*, L. C. Poon[4], W. Rokita[5] and M. Wielgos[6]
[1]*Clinical Department of Obstetrics and Gynecology, Pomeranian Medical University, Szczecin, Poland;* [2]*Ludwik Rydygier Collegium Medicum, Bydgoszcz, Poland;* [3]*Department of Reproductive Health, Centre of Postgraduate Medical Education, Warsaw, Poland;* [4]*Department of Obstetrics and Gynecology, The Chinese University of Hong Kong, Hong Kong SAR;* [5]*Faculty of Medicine and Health Sciences, Jan Kochanowski University, Kielce, Poland;* [6]*1st Department of Obstetrics and Gynecology, Medical University of Warsaw, Warsaw, Poland*
**Correspondence.*
(e-mail: anna.kajdy@cmkp.edu.pl)
DOI: 10.1002/uog.22049

References

1. Schwartz DA, Graham AL. Potential Maternal and Infant Outcomes from (Wuhan) Coronavirus 2019-nCoV Infecting Pregnant Women: Lessons from SARS, MERS, and Other Human Coronavirus Infections. *Viruses* 2020; **12**: E194.
2. Mullins E, Evans D, Viner RM, O'Brien P, Morris E. Coronavirus in pregnancy and delivery: rapid review. *Ultrasound Obstet Gynecol* 2020; **55**: 586–592.
3. Day M. Covid-19: ibuprofen should not be used for managing symptoms, say doctors and scientists. *BMJ* 2020; **368**: m1086.
4. Voiriot G, Chalumeau M, Messika J, Basille D, Philippe B, Ricard JD, Andrejak C, Jounieaux V, Sanchez O, Fartoukh M. [Risks associated with the use of non-steroidal anti-inflammatory drugs during pneumonia]. *Rev Mal Respir* 2018; **35**: 430–440.
5. FitzGerald GA. Misguided drug advice for COVID-19. *Science* 2020; **367**: 1434.
6. Agencia Española de Medicamentos y Productos Sanitarios, 2020. La AEMPS informa que ningún dato indica que el ibuprofeno agrave las infecciones por COVID-19. https://www.aemps.gob.es/informa/notasinformativas/medicamentosusohumano-3/2020-medicamentosusohumano-3/la-aemps-informa-que-ningun-dato-indica-que-el-ibuprofeno-agrave-las-infecciones-por-covid-19/ [Accessed 26 March 2020]
7. Royal College of Obstetricians and Gynaecologists. Coronavirus (COVID-19) infection and pregnancy. https://www.rcog.org.uk/en/guidelines-research-services/guidelines/coronavirus-pregnancy/ [Accessed 26 March 2020]
8. Rolnik DL, Wright D, Poon LCY, Syngelaki A, O'Gorman N, de Paco Matallana C, Akolekar R, Cicero S, Janga D, Singh M, Molina FS, Persico N, Jani JC, Plasencia W, Papaioannou G, Tenenbaum-Gavish K, Nicolaides KH. ASPRE trial: performance of screening for preterm pre-eclampsia. *Ultrasound Obstet Gynecol* 2017; **50**: 492–495.
9. Johns Hopkins University. Coronavirus COVID-19 (2019-nCoV). https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6 [Accessed 23 March 2020]

10. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf [Accessed 26 March 2020]
11. Schwartz DA. An Analysis of 38 Pregnant Women with COVID-19, Their Newborn Infants, and Maternal-Fetal Transmission of SARS-CoV-2: Maternal Coronavirus Infections and Pregnancy Outcomes. *Arch Pathol Lab Med* 2020. DOI: 10.5858/arpa.2020-0901-SA.
12. Updated: WHO Now Doesn't Recommend Avoiding Ibuprofen For COVID-19 Symptoms. https://www.sciencealert.com/who-recommends-to-avoid-taking-ibuprofen-for-covid-19-symptoms [Accessed 23 March 2020]

