



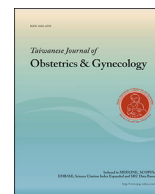
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Editorial

Pregnant women with COVID-19



Editorial

Severe acute respiratory syndrome coronavirus 2, SARS-CoV-2 (coronavirus disease 2019, COVID-19) is a pandemic disease with widely disseminating to the world, resulting a biggest change in health care systems [1–5], due to disease-related morbidity and mortality (241, 411, 380 confirmed cases of COVID-19, including 4,912,112 deaths) based on the World Health Organization (WHO) report on 21 October 2021, globally, as of 5:09pm CEST, 20 October 2021 [6]. As a new disease, evidence-based knowledge about COVID-19 in pregnancy is limited [7]; therefore, the decisions about prevention, diagnosis, and management can be made according to previous experience with influenza or other novel coronavirus infections, clinical judgements, basic knowledge, and of the most importance, medical records or literature reports addressing the topic about COVID-19 in pregnancy [7–10]. It is well known that pregnant women are vulnerable to infectious disease pandemics for centuries that predispose them to untoward outcomes compared with the general adult population [7]. However, based on the fact that pregnant women are always excluded in the clinical trials which target nearly all clinical situations, initiated from the prevention, management, and final therapeutic protocols for SARS-CoV-2 infection, the real-world experience in the management of pregnant women with SARS-CoV-2 infection is of urgent need and paramount importance. Therefore, we are happy to introduce one article entitled “perinatal outcomes of pregnant women having SARS-CoV-2 infection” published in the last issue in 2021 of the *Taiwanese Journal of Obstetrics and Gynecology*, which explored this topic [11].

Dr. Arzu Arinkan and colleagues conducted a prospective observation study to evaluate the outcome of pregnant women with SARS-CoV-2 infection and further compare the difference of perinatal outcome of pregnant women with ($n = 46$) and without ($n = 70$) SARS-CoV-2 infection [11]. Among the SARS-CoV-2 infected pregnant women, 5, 13 and 28 women occurred in the first, second, and third trimester, respectively. The symptoms included cough (42.3%), dyspnea (26.2%), myalgia (15.2%), fever (8.7%), and loss of taste, fatigue or diarrhea (2.2%), respectively. Two-thirds of pregnant women were hospitalized. It is interesting to find that no statistically significant difference of delivery week, newborn weight, Apgar scores (at one or five minute) was found between pregnant women with and without SARS-CoV-2 infection. The current study is interesting and worthy of further discussion.

First, as shown by authors, 40% (2/5) of the first trimester pregnancies complicated with SARS-CoV-2 infection were ended by abortion [11]. Although the case number is extremely small, the question about the relationship between SARS-CoV-2 infection

and risk of abortion is raised. Based on the Dr. Arzu Arinkan's study [11], the risk of abortion seemed to be increased in the first trimester. To respond to this question, a recent systematic review may give us some hints. According to the summary of 11 studies, the authors found that there is an increased risk of abortion with SARS-CoV-2 infection, which several case reports and case series, have identified during the pandemic [12]. Additionally, studies related to abortion in pregnant women with SARS-CoV-2 infection show that most of abortions due to SARS-CoV-2 infection in the first trimester were due to placental insufficiency [12]. This placental insufficiency can be supported by finding the deposition of perivillous fibrin and multiple villous infarcts in the placenta in pregnant women with SARS-CoV-2 infection [12]. Another etiology for abortion in the first trimester may be secondary to the inflammatory events, although these may not be always involved in placenta directly [12]. However, the association between SARS-CoV-2 infection and abortion is not always reproducible, and the results from the studies are conflicted. We suppose this uncertainty may be related to severity of the diseases, since in non-hospitalized pregnant women with SARS-CoV-2 infection did not significantly differ in nuchal translucency thickness and double test in the first trimester screening as well as there was no significantly increased risk of abortion in these subjects [12]. All hint us that the association between abortion and SARS-CoV-2 infection needs more studies to clarify their relationship.

Second, in the current study, management of pregnant women with SARS-CoV-2 infection regardless of hospitalization or not is worthy of discussion. The therapeutic agents were varied greatly, including 30.4% ($n = 14$) with hydroxychloroquine, 17% ($n = 8$) with kaleta (50 mg ritonavir plus 200 mg lopinavir), 10.9% ($n = 4$) with favipiravir, 2.3% ($n = 1$) with hydroxychloroquine plus favipiravir, and 39.1% ($n = 18$) without any aforementioned treatment [11]. Among these patients, 67.4% ($n = 31$) were hospitalized, and all of whom were treated with low molecular weight heparin therapy and 16.1% ($n = 5$) needed oxygen supplementation [11]. Although the authors did not mention how many hospitalized patients did not receive the therapeutic agents, we believed 3 patients who received low molecular weight heparin alone during the hospitalization. In fact, the pregnant women with COVID-19 have a four-fold increase of venous thromboembolism risk than age-matched controls do [1]. Additionally, consensus recommends that thromboprophylaxis is needed in pregnant women with laboratory-confirmed SARS-CoV-2 infection [13]. Moreover, as shown above, the deposition of perivillous fibrin and multiple villous infarcts in the placenta in pregnant women with SARS-CoV-2 infection has been found [12]. All suggest that adequate thromboprophylaxis is needed for pregnant women with SARS-

CoV-2 infection [1]. Therefore, the current study reminded us the importance of consideration of thromboprophylaxis in our routine obstetrics practice.

However, it is interesting to find that the role of steroid seemed to be neglected in their study. Additionally, the need of oxygen supplement was relatively rare in their study (less one fifth). Based on the recommendation of the National Institutes of Health (NIH) in United States (US) to provide supportive care with close monitoring for clinical worsening for patients who do not need oxygen supplement [14]. However, if the clinical course was downhill dramatically and progressed rapidly, oxygen supplement is needed. With continuous progression to level II of patients, the use of dexamethasone for 10 days and considering remdesivir was recommended for patient needing supplemental oxygen by NIH [14]. The application of glucocorticoid to patients with SARS-CoV-2 infection (pregnant women were included) is based on the Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial [15]. In the corticosteroid regimen of pregnant women in RECOVERY trial, prednisolone 40 mg by mouth daily, or hydrocortisone 80 mg, intravenous injection twice daily were used rather than dexamethasone [15,16]. In pregnant woman who have a risk of preterm birth, and meet criteria for the use of corticosteroid, 6 mg of dexamethasone given by intramuscular injection in every 12 h for two days is a better choice, not only being active for the therapy of symptomatic pregnant women but also offering the benefits of enhancing lung maturity based on the concept that dexamethasone will cross the placenta while prednisolone and hydrocortisone will not, when the choice of glucocorticoids are needed [1]. However, it is important that when the goal to make fetal lung maturity successful is achieved, prednisolone or hydrocortisone are still recommended to give these pregnant women with SARS-CoV-2 infection [1]. The side effect of the patients during and after glucocorticoid treatment should be monitored for hyperglycemia and the risk of infection, since the pregnant women are vulnerable to glucose intolerance and attacks by infection [1].

In summary, as shown above, evidence-based knowledge about pregnant women with SARS-CoV-2 infection is still limited. We are looking forward to learning more and more articles focusing on this population who are vulnerable to infection pandemic.

Declaration of competing interest

All authors declare no conflict of interest.

Acknowledgements

This article was supported by grants from the Ministry of Science and Technology, Executive Yuan, Taiwan (MOST 109-2314-B-075B-014-MY2 and MOST 110-2314-B-075 -016 -MY3), and Taipei Veterans General Hospital (V110C-082, and VGH109E-005-5). The authors appreciate the support from Female Cancer Foundation, Taipei, Taiwan.

References

- [1] Yang ST, Yeh CC, Lee WL, Lee FK, Chang CC, Wang PH. A symptomatic near-term pregnant woman recovered from SARS-CoV-2 infection. *Taiwan J Obstet Gynecol* 2021;60:945–8.
- [2] Wang LM, Lai SP, Liang SJ, Yang ST, Liu CH, Wang PH. Maternal and fetal outcomes of the pregnant woman with COVID-19: the first case report in Taiwan. *Taiwan J Obstet Gynecol* 2021;60:942–4.
- [3] Salma U. Relationship of COVID-19 with pregnancy. *Taiwan J Obstet Gynecol* 2021;60:405–11.

- [4] Wang PH, Lee WL, Yang ST, Tsui KH, Chang CC, Lee FK. The impact of COVID-19 in pregnancy: Part II. Vaccination to pregnant women. *J Chin Med Assoc* 2021;84:903–10.
- [5] Tsai PH, Lai WY, Lin YY, Luo YH, Lin YT, Chen HK, et al. Clinical manifestation and disease progression in COVID-19 infection. *J Chin Med Assoc* 2021;84:3–8.
- [6] World Health Organization (WHO). Coronavirus disease-19 dashboard. Available online: <https://covid19.who.int/>. [Accessed 21 October 2021].
- [7] Wang PH, Lee WL, Yang ST, Tsui KH, Chang CC, Lee FK. The impact of COVID-19 in pregnancy: Part I. Clinical presentations and untoward outcomes of pregnant women with COVID-19. *J Chin Med Assoc* 2021;84:813–20.
- [8] Hung JJ, Wang FD, Ma H, Tsou MY, Dai HD, Lin YH, et al. The precaution strategy toward the COVID-19 pandemic in the operating room of a tertiary hospital in Taiwan. *J Chin Med Assoc* 2021;84:171–6.
- [9] Abedzadeh-Kalahroudi M, Sehat M, Vahedpour Z, Talebian P, Haghghi A. Clinical and obstetric characteristics of pregnant women with Covid-19: a case series study on 26 patients. *Taiwan J Obstet Gynecol* 2021;60:458–62.
- [10] Yang TH, Chou CY, Yang YF, Chien CS, Yarmishyn AA, Yang TY, et al. Systematic review and meta-analysis of the effectiveness and safety of hydroxychloroquine in treating COVID-19 patients. *J Chin Med Assoc* 2021;84:233–41.
- [11] Arzu Arinkan S, Ceren Dalli Alper E, Topcu G, Muhcu M. Perinatal outcomes of pregnant women having SARS-CoV-2 infection. *Taiwan J Obstet Gynecol* 2021;60:1043–6.
- [12] Kazemi SN, Hajikhani B, Didar H, Hosseini SS, Haddadi S, Khalili F, et al. COVID-19 and cause of pregnancy loss during the pandemic: a systematic review. *PLoS One* 2021;16:e0255994.
- [13] The Royal College of Obstetricians and Gynaecologists. Information for health-care professionals. Coronavirus (COVID-19) infection in pregnancy. Version 13. <https://www.rcog.org.uk/globalassets/documents/guidelines/2021-02-19-coronavirus-covid-19-infection-in-pregnancy-v13.pdf>. [Accessed 21 October 2021].
- [14] Therapeutic management of hospitalized adults with COVID-19. COVID-19 treatment guidelines panel. Coronavirus disease 2019 (COVID-19) treatment guidelines. Natl Inst Health. Available at: <https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/hospitalized-adults-therapeutic-management/>. [Accessed 21 October 2021].
- [15] RECOVERY Collaborative Group, Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Linsell L, et al. Dexamethasone in hospitalized patients with covid-19. *N Engl J Med* 2021;384:693–704.
- [16] Li AFY, Wang CL, Tai HY, Fu YJ, Tsai FT, Tsai YC, et al. Pandemic aspect of dexamethasone: molecular mechanisms and clinical application. *J Chin Med Assoc* 2021;84:245–7.

Wen-Ling Lee

Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan

Department of Medicine, Cheng-Hsin General Hospital, Taipei, Taiwan

Department of Nursing, Oriental Institute of Technology, New Taipei City, Taiwan

Shu-Chen Kuo

Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taipei, Taiwan

Department of Nursing, Taipei Veterans General Hospital, Taipei, Taiwan

Peng-Hui Wang*

Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan

Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taipei, Taiwan

Female Cancer Foundation, Taipei, Taiwan

Department of Medical Research, China Medical University Hospital, Taichung, Taiwan

* Corresponding author. Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, 201 Section 2, Shih-Pai Road, Taipei 11217, Taiwan.

E-mail addresses: phwang@vghtpe.gov.tw, pongpongwang@gmail.com (P.-H. Wang).