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Peer Reviewer of *World Journal of Experimental Medicine*, A. Vijaya Anand, PhD, Professor, Department of Human Genetics and Molecular Biology, Bharathiar University, Coimbatore 641046, Tamil Nadu, India.
avahgmb@buc.edu.in

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LETTER TO THE EDITOR

Update on hydroxychloroquine use in pregnancy

Wassan Nori, Nabeeha Najatee Akram, Raid M Al-Ani

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Wassan Nori, Department of Obstetrics and Gynecology, Mustansiriyah University, Baghdad 10052, Iraq

Nabeeha Najatee Akram, Department of Pediatrics, Mustansiriyah University, Baghdad 10052, Iraq

Raid M Al-Ani, Department of Surgery/Otolaryngology, University of Anbar, Anbar 31001, Iraq

Corresponding author: Wassan Nori, PhD, Academic Editor, Academic Research, Senior Researcher, Department of Obstetrics and Gynecology, Mustansiriyah University, No. 58 Al-amin Street, Baghdad 10052, Iraq. dr.wassan76@uomustansiriyah.edu.iq

Abstract

It is well-known that hydroxychloroquine (HCQ) treats malaria, systemic lupus erythematosus, and rheumatoid arthritis in women for its immunomodulatory and anti-inflammatory action. Additionally, HCQ was used in cases with refractory antiphospholipid syndrome. HCQ safety was reinforced in pregnant women owing to insignificant reports of adverse pregnancy outcomes and major congenital malformation. Recently, HCQ was tested in cases with chronic placental inflammation with a promising result of increased life birth; however, its benefit needs further validation. We aimed to highlight the recent updates for HCQ use in various conditions in pregnancy.

Key Words: Pregnancy; Hydroxychloroquine; Preeclampsia; Antiphospholipid syndrome; Chronic placental inflammation; COVID-19

Core Tip: The immunomodulatory, anti-inflammatory, and anti-thrombotic activity of hydroxychloroquine (HCQ), an anti-malarial drug, made it recommendable for rheumatoid arthritis and systemic lupus erythematosus. HCQ was also implemented in refractory antiphospholipid syndrome showing a successful outcome. Recent evidence supports the benefits of its use to outweigh the risk during pregnancy as it reduces the disease activity and the associated adverse pregnancy outcome. Chronic placental inflammation is another condition for which HCQ proved to be helpful. Further investigations are required to verify HCQ's efficacy in chronic placental inflammation as well as its action in reducing the severity of coronavirus disease 2019 in pregnant women.

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TO THE EDITOR

With interest, we read the Bajpai *et al*[1] study published in the *World Journal of Experimental Medicine* (issue 3, volume 12, 2022) that discussed the role of hydroxychloroquine (HCQ) in treating high-risk groups with coronavirus disease 2019 (COVID-19). Indeed, HCQ gained much interest during the current pandemic owing to its anti-inflammatory and immunomodulatory effects[1].

HCQ had an update regarding its use among pregnant, first in autoimmune diseases and its safety profile-second, its therapeutic role in cases with chronic placental inflammation. Finally, we discuss its potential use in pregnant with COVID-19, which is worth mentioning and was not discussed by Bajpai *et al*'s study[1].

HCQ was already used for treating women suffering from malaria, systemic lupus erythematosus (SLE), and rheumatoid arthritis (RA)[2]. In 2020, the American College for Managing SLE, RA for women of reproductive age, advised that those cases should receive HCQ before and throughout pregnancy[3]. In addition, pregnant women with refractory antiphospholipid syndrome may consider HCQ in addition to standard treatment (aspirin and low molecular weight heparin)[4].

HCQ was used as an adjunctive therapy for cases with refractory antiphospholipid syndrome[5]. It is a beneficial role proposed to be mediated *via* anti-thrombotic, antiplatelet, and immunomodulatory properties[6]. Others suggested that HCQ reduces endothelial dysfunction and improves vascular elasticity, thus improving blood flow[7].

Bérard *et al*'s study addressed pregnancy outcomes related to HCQ use in a cohort study that recruited 233748 pregnant women[8]. Interestingly the study showed that HCQ had a good safety profile. There was no increased risk of preterm labor among drug users; the adjusted odd ratio was 1.39, with respective 95% confidence interval (CI): 0.83 to 2.3. As for the low birth weight, the adjusted odd ratio was 1.12, 95%CI: 0.59 to 2.07. Finally, the adjusted odd ratio for major congenital malformation was 1.02, 95%CI: 0.68 to 1.53[8].

Another study confirmed no substantial rise in significant congenital malformations in newborns exposed to HCQ during the first trimester of pregnancy[9]. In line with earlier work[10,11]. These results reinforce that therapy advantage during pregnancy is likely to exceed the risks for the majority of patients with rheumatic disease.

Ye *et al*[12] discussed that HCQ application might alleviate the risk of high lupus activity during pregnancy and the incidence of preeclampsia. However, in their meta-analysis, Hu *et al*[13] found no value of HCQs in reducing preeclampsia in antiphospholipid syndrome. Moreover, HCQ had no value in reducing fetal growth defects in SLE and/or antiphospholipid cases.

The promising results observed with the use of HCQ to treat autoimmunity in pregnancy have laid the foundation for its use in chronic placental inflammation, a condition characterized by the disruption of healthy placental tissue. They can only be confirmed by a post-delivery histopathological examination[14]. Chronic placental inflammation has been linked to severe complications of pregnancy, such as fetal growth restriction, premature labor, and miscarriage[15].

Brady *et al*'s study examined the value of adding HCQ to pregnant women with a positive history of chronic placental inflammation, showing a decrease in disease severity and a trend for a higher live birth rate[16]. There are currently no prospective, informatively constructed, controlled trials on the efficacy of HCQs in these settings, which emphasizes the need for such work. Since some forms of chronic placental inflammation are recurrent, determining the cause is crucial for future pregnancies care.

The use of HCQ in COVID-19 cases will depend upon if the ongoing clinical trials demonstrate significant benefits of HCQ in reducing the incidence or severity of COVID-19[9,17,18]. Even though initial trials utilizing HCQ to treat COVID-19 failed to demonstrate efficacy, pre-exposure preventative trials are yet to be reported[9].

In conclusion, HCQ has demonstrated efficacy in mitigating the activity of autoimmune diseases and some of their adverse pregnancy outcomes while maintaining a favorable safety profile. HCQ has emerged as a potential therapeutic option for cases with chronic placental inflammation, as it enhances live birth rates while decreasing the severity of the associated disease. Nevertheless, the efficacy and safety of HCQ in pregnant individuals with COVID-19 have not been thoroughly assessed. Further research is needed to unveil more applications in practice.

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FOOTNOTES

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Country/Territory of origin: Iraq

ORCID number: Wassan Nori 0000-0002-8749-2444; Nabeeha Najatee Akram 0000-0001-8964-8943; Raid M Al-Ani 0000-0003-4263-9630.

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