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.

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Ivermectin for COVID-19: Concerns during pregnancy

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Besides the lack of demonstrated efficacy to Covid-19 disease, ingesting ivermectin is of concern for women who may be pregnant. Nicolas et al. [1] reviewed the safety of oral ivermectin during human pregnancy and concluded there was insufficient evidence of safety. The animal data discussed below raise concerns for pregnant women considering treatment with ivermectin.

According to product labeling, ivermectin produced an increase in malformations when given to pregnant mice at less than the human dose on a body surface area basis. The lowest teratogenic dose levels for animals in the 1996 NDA for ivermectin (NDA 50–742) are 0.4 mg/kg/day in mice, 3 mg/kg/day in rabbits, and 10 mg/kg/day in rats. The higher sensitivity of the original mouse strain was traced to a genetic variant in Pglycoprotein, a protein that inhibited transport of ivermectin across the placenta [2]. Fetal-placental units deficient in P-glycoprotein were 100 % susceptible to cleft palate, while fetuses with full P-glycoprotein expression had 0% cleft palate. A different outbred mouse strain with full P-glycoprotein expression showed no defects at the highest tested dose level (3 mg/kg/day of a related photoisomer). Similarly, as the aforementioned studies of the NDA reported, rats and rabbits required somewhat higher ivermectin doses to induce birth defects due to their full P-glycoprotein expression. The role of P-glycoprotein in ivermectin exposed human pregnancies may be pertinent since P-glycoprotein expression decreases with gestation [3], whereas expression in rats is higher as pregnancy approaches term [4]. A recent update on this protein in the placenta and fetus states that the distribution and activity of P-glycoprotein in rodents is similar to P-glycoprotein in humans [5].

Thus, besides the lack of adequate clinical safety of ivermectin in human pregnancies, healthcare providers should be aware of the animal data as an under-appreciated potential risk factor to pregnant women who take ivermectin for Covid-19. An additional risk factor to these women would be the coadministration of a P-glycoprotein inhibitor (e.g., clarithromycin, cyclosporin, diltiazem, erythromycin, felodipine, omeprazole, tamoxifen, and some statins to name a few). A number of coadministration studies in various species have shown increased systemic exposure, organ concentrations, or toxicity of ivermectin. The combination will likely cause an increased level of ivermectin in the developing embryo or fetus, potentially inducing birth defects.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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