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COVID-19 infection: ACE2, pregnancy and preeclampsia

Recent studies suggest that COVID-19 infection has a mild to moderate course in pregnant women [1,2]. This could be related to their younger age. Data from the Italian Surveillance System show that in women of reproductive age (20–39 years) the lethality rate is low (median 0.1 %; range 0.05–0.16) and lower than in men (median 0.4 %; range 0.30−0.47). Afterward it increases steadily from 0.5 % at 40–49 years to over 20 % at 80–89 years, but the imbalance between women and men remains [2].

Pre-clinical models suggest that angiotensin-converting enzyme 2 (ACE2) upregulation confers protective effects in acute lung injury. ACE2, overexpressed in women, is the enzyme through which coronaviruses bind to their target cells. In women of reproductive age oestrogens could be protective by increasing the expression of ACE2. The overexpression of ACE2 could also be explained by the observation that in the inactivated X chromosome there are some active regions encoding for ACE2 thus protecting also postmenopausal women. COVID-19 enters target cells by ACE2 mediation: virus-ACE2 complex formation could lead to ACE2 inactivation. Extra copies of ACE2 in women would continue to carry on protection [2]. Could there be other reasons beside age and being women to explain the mild to moderate course of the disease in pregnancy? Animal studies have demonstrated that in normal pregnancy there is an overproduction of ACE2, being the placenta and the uterus important sources of the enzyme. ACE2 exhibits high catalytic efficiency to generate Angiotensin 1–7 (Ang-1–7) that has a vasodilatory action and at the same time inactivates the vasoconstrictor Angiotensin II. Ang-1–7 plasma levels are significantly increased in third trimester pregnant women compared to non pregnant [3]. This would contribute to the systemic vasodilation and decrease in blood pressure and to other physiological adaptations that occur in normal pregnancy.

Interestingly, Ang-1–7 plasma levels are lower in pregnancies complicated by pre-eclampsia than in physiological pregnancies [4]. Pre-eclampsia is a pregnancy related syndrome characterized by the appearance of hypertension and proteinuria after 20 weeks of gestational age. Its aetiology is not completely understood, but there is agreement as far as its pathogenesis is concerned: an exaggerated inflammatory response leading to endothelial damage [5]. Also the most severe forms of COVID-19 are explained by an excessive inflammatory response, with high levels of proinflammatory cytokines (IL-6, TNF-*alfa*, IFN-*gamma*, etc) that are also overexpressed in mesenchymal stromal cells of pre-eclamptic placentas [6,7]. Investigation in this direction could help to develop new strategies for the prevention and treatment of both pre-eclampsia and COVID-19.

Declaration of Competing Interest

The authors reported no declarations of interest.

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