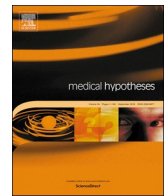




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Empiric antibiotics in management of inpatient pregnant women infected with coronavirus disease 2019 (COVID-19): Focusing on inflammation and preterm labor



Dear Editor

The outbreak of novel coronavirus (SRARS-CoV-2) caused Coronavirus disease 2019 (COVID-19) and led to emergency pandemic according to the World Health Organization (WHO) [1]. This disease with the main manifestation of pneumonia [2] may cause a wide range of morbidities which might lead to mortality [3]. Not only the maternal outcomes but also fetal/neonatal outcomes might be affected by COVID-19. Data have shown that prevalence of preterm birth among inpatient pregnant women with COVID-19 up to 47% [4–6]. Herein, we would evaluate one of possible cause of non-viral induced preterm labor in pregnant women diagnosed with COVID-19 which could be administration of empiric antibiotics with inflammatory properties in absence of bacterial infection in the inpatients.

In a recent paper [7], we have reviewed the role of inflammation as one of the most important key elements of preterm labor. Although, in most cases the inflammation cascade for preterm labor has been started with a bacterial infection. However, we have highlighted that the use of antibiotics in the absence of bacterial infection might result in the release of pro-inflammatory cytokine and therefore, an inflammatory storm. As we have shown, antibiotics (in absence of infection) seem to cause gut bacterial decontamination and lipopolysaccharide (LPS) release and therefore endotoxemia. During this endotoxemia, the activation of toll-like receptors (TLRs) cause the release/expression of pro-inflammatory cytokines (such as interleukin 1 β (IL-1 β), IL-6, and tumor necrosis factor α (TNF- α)), chemokines, prostaglandins, and proteases which are involved in preterm labor. We have called this pathway as the indirect pathway while some antibiotics have been shown to affect immune cells such as monocytes to release pro-inflammatory cytokines (direct pathway) [7]. Interestingly, a study has evaluated the outcome of empiric antibiotic therapy on gestational duration in two groups of microbe positive and negative pregnant individuals using rapid and high-sensitive polymerase chain reaction (PCR). Among 104 evaluated pregnant cases, it was shown that the antibiotic-treated microbe negative group had a significantly shorter gestation duration ($p < 0.0001$) [8]. Also, At the beginning of the pandemic, we have suggested avoiding any non-indicated antibiotic consumption to prevent pro-inflammatory cytokine storm which might be one of the causes of septic shock in critically ill COVID-19 patients who have been admitted in intensive care unit (ICU) [2].

Altogether, we have raised some concern regarding the increased risk of inflammation in patients received antibiotics without evidence of bacterial infection(s). After collecting data from critically ill pregnant patients with COVID-19, we have observed that the most of them had used antibiotics at admission or just a few days following admission and while most cases reported no evidence of bacterial infection [3,9]. Another study which has compared COVID-19 pregnant women with healthy controls showed the significant increase in the prevalence of

preterm labor while all the COVID-19 cases had received antibiotic from admission [10].

As we have shown, some antibiotics can induce inflammation [7]; on the other hand, some others (such as macrolides) could modulate inflammation. [11] It is reasonable to start empiric antibiotics for some hospitalized pregnant patients (especially those in ICU), however, we suggest to consider all aspects of the treatment first. If antibiotic(s) should be administrated, it is wiser to choose the one with anti-inflammatory activity such as macrolids which is able to reduce/modulate inflammation (especially in airways) as well as pro-inflammatory cytokines (such as IL-1, IL-6, TNF- α) [11] when there is no other significant difference between the choices. This issue may lead to a decrease in pro-inflammatory cytokines release and possibly preventing preterm labor in pregnant women with COVID-19.

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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.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2020.110269>.

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