

## Reply to Reza Hosseini

TO THE EDITOR—We thank Dr Reza Hosseini for his valuable comments [1] on our study. We agree that multiple measures must be undertaken to increase the robustness of results in observational studies and that the results need to be interpreted carefully.

The combination of diagnoses used to define acute liver injury in our study has been previously evaluated in different settings with reported positive predictive values ranging from 75% to 95% [2, 3]. Furthermore, we excluded patients who were hospitalized for any other diagnoses, which in this case would include patients admitted for sepsis. We do agree with the author's comment that the fluoroquinolones are more often used in gram-negative infections as compared to amoxicillin and that the lack of indication of treatment is a weakness, as described in the article. However, since we excluded any treatment episodes that were preceded by hospitalization in the past 2 months, we find it unlikely that the choice of antibiotic in an outpatient setting is based on a specific pathogen (ie, gram negative or gram positive) rather than a presumed site of infection for which there are overlapping areas between the compared antibiotics. Furthermore, biochemical markers of liver insults, such as increased values of aminotransferases, bilirubin, and international normalized ratio, are sometimes seen in septic patients (without regard of causative organism). However, in a large epidemiologic study from 2017 looking at patients with severe sepsis according to Sepsis-2, only 2151 of 197 724 (1.1%) patients had a hepatic Sequential Organ Failure Assessment score  $\geq 2$ , making it a rare occurrence [4].

## Notes

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## The Detection of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Virus in the Vaginal Fluid of Females With Severe Coronavirus Disease 2019 (COVID-19) Infection: Scientific Facts

TO THE EDITOR—We read with much interest the published article by Qiu et al [1]. At this juncture, we would like to express our scientific thoughts related to

the published article. The sample using patients with severe cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was a good approach, as it is postulated that there is systemic spread of the virus via blood, including at the vaginal area. The usage of nucleic acid amplification tests, such as reverse-transcription polymerase chain reaction (RT-PCR), is a gold standard. Therefore, in the present study, any undetectable virus in the vaginal fluid is considered to be reliable.

There are a few critical points to highlight. The first study conducted in Huazhong University of Science in China analyzed 35 female coronavirus disease 2019 (COVID-19) patients (average age of 61.5 years) and performed RT-PCR analyses of SARS-CoV-2 by obtaining anal swabs and vaginal environment samples. Interestingly, all the vaginal swab samples showed negative results, while 1 anal swab sample tested positive for SARS-CoV-2 [2]. To date, no single study has shown the presence of SARS-CoV-2 virus in vaginal swabs.

In an earlier study conducted in Wuhan, the mean incubation period for COVID-19 was 5.2 days among 425 cases, though it varied widely between individuals [3]. Therefore, to date, the virus shedding patterns are not well understood, and further investigations are needed to better understand the timing, compartmentalization, and quantity of viral shedding to inform optimal specimen collection. In the present study, the sample was taken 17 days postinfection and revealed negative results. If there is a small amount of virus, the amplification may not be detected, and the authors have rightly admitted such facts. It would be interesting to consider (1) the amount of virus, which may be too little in relation to the incubation period; or (2) the prevailing atrophic conditions of the vagina and cervix, which have less or even an absence of expression of Angiotensin-converting enzyme 2 (ACE2) receptors. It is interesting to note that the ACE2 receptor is a receptor for the viruses [2]. An earlier study elaborated numerous expressions of ACE2 receptors