Vertical transmission of coronavirus disease 2019, a response

We wish to respond to Mr Martinez-Portilla on his critique of our paper, "Vertical transmission of coronavirus disease 2019: a systematic review and meta-analysis."[1] Although several interesting points are raised, each of these points has been unfortunately handled with insufficient depth by the author.

To his first point, case series have been previously validated as sources, which can be used for pooled prevalence analyses. Murad et al[2] described how proportions in case series can be combined in a quantitative synthesis using fixed or random effects models to obtain estimates of prevalence, similar to what we accomplished in our study using both case series and cohort studies. This same group cited how case series can be used in a meta-analysis to determine a prevalence estimate, for example, for mortality, following aortic transection. Therefore, we disagree with his argument that case series should not be included in determining prevalence estimates. Excluding case series would discard potential vital information in the setting of such a novel emerging disease, such as coronavirus disease 2019 (COVID-19), particularly in the absence of high-quality evidence regarding vertical transmission.

As to our methodological quality assessment of study bias risk, Mr Martinez-Portilla's assessment misses a crucial point explicitly stated in our paper. We used the modified Newcastle-Ottawa Scale (NOS), which is designed to assess case series and has been validated in previous systematic reviews and meta-analyses cited in our methods section.[2] Although the Joanna Briggs Institute critical appraisal tool has been proposed as a method to assess bias in case series, we have not found any evidence that it is a superior tool than the modified NOS.[3]

As far as the third point regarding our pooled estimate result (3.2%) for COVID-19 positivity in neonatal nasopharyngeal (NP) swabs, our meta-analysis was conducted using the most recent version of the MedCalc software (MedCalc Software Ltd, Ostend, Belgium), which uses the commonly used Freeman-Tukey transformation (arcsine-based square root transformation) to calculate the weighted summary proportion under the fixed and random effects model. The method used by Mr Martinez-Portilla in an attempt to replicate our results was based on adding an arbitrary continuity correction factor (0.5) to the number of observed COVID-19 cases in each study that has zero cases of COVID-19. However, this fixed correction method has been shown by Sweeting et al[4] to have the undesirable effect of biasing study estimates toward no difference and artificially inflating the weight of each such zero study when the sample size is large. Here are 2 examples: using the arcsine square root transformation used in our study, the Ferazzi study (n=42; k=3) and the London study (n=48; k=0) have similar relative weights—4.41% and 5.03%, respectively (Figure 3).[1] In contrast, the 0.5 continuity correction factor method proposed results in 1.3% and 10.5%, respectively, which is counterintuitive and creates obvious bias. In another example using the arcsine square root transformation, the Yan study (n=86; k=0) has a weight of 8.93%, whereas the Knight study (n=244; k=12), which is the largest study in the meta-analysis, has a weight of 25.2% (Figure 3).[1] Moreover, the 0.5 continuity correction factor method results in a relative weight of 33.1% for the smaller Yan (zero) study and only 11.0% relative weight for the larger Knight study. Thus, using the 0.5 correction as proposed by Mr Martinez-Portilla is simply wrong and clearly inflates the relative weights of the zero studies, resulting in an underestimation of the pooled COVID-19 neonatal NP positivity proportion. In a recent Centers for Disease Control and Prevention report (November 2, 2020) representing the largest longitudinal data to date on pregnant women diagnosed as having COVID-19 from the Surveillance for Emerging Threats to Mothers and Babies Network (https://www.cdc.gov/mmwr/volumes/69/wr/mm6944e2.htm), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was found in 16 of 610 cases (2.6%) among neonates known to have been tested for SARS-CoV-2, which is very similar to the pooled estimates reported in our study (3.2%). ■

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