Letter to the Editors

Vertical transmission of coronavirus disease 2019

TO THE EDITORS: With interest, I have read the article titled "Vertical transmission of coronavirus disease 2019: a systematic review and meta-analysis" published in the *American Journal of Obstetrics and Gynecology* by Kotlyar et al.¹

The article is a systematic review of case reports, case series, and cohort studies about the transmission of severe acute respiratory syndrome coronavirus 2 between the mother and fetus. The authors included 69 articles for qualitative synthesis and 38 articles for quantitative analysis. The results for the quantitative analysis were a pooled 3.2% possible vertical transmission from the mother to the newborn during the first 48 hours of delivery.

I noticed that the pooled estimate of 3.2% was obtained from case series in combination with cohort studies. Case

FIGURE

Forest plot the pooled proportion of possible vertical transmission divided by subgroups of studies assessing more or less than 15 included participants

Study	Events E	Eligible neonates	l.		Proportion	95%-Cl	Weight
More than 15 included	participan	its					
Baergen	0	21	e		0.000	[0.000; 0.161]	2.2%
Breslin 1	0	18	P:		0.000	[0.000; 0.185]	1.6%
Chenu	0	17	e :		0.000	[0.000; 0.195]	1.4%
Ferazzi	3	42			0.071	[0.015; 0.195]	1.3%
Khan	2	17	••		0.118	[0.015; 0.364]	0.3%
Knight	12	244	÷ 🔁 –		0.049	[0.026; 0.084]	11.0%
Liu 1	0	19	de:		0.000	[0.000; 0.176]	1.8%
Liu 2	0	51			0.000	[0.000; 0.070]	11.9%
London	0	48	.		0.000	[0.000; 0.074]	10.5%
Nie	1	28			0.036	[0.001; 0.183]	1.3%
Patane	2	22	•	9	0.091	[0.011; 0.292]	0.5%
Pereira	0	23	de		0.000	[0.000; 0.148]	2.6%
Pierce-Williams	1	33	: e		0.030	[0.001; 0.158]	1.8%
Qiancheng	0	23	a :		0.000	[0.000; 0.148]	2.6%
Shanes	0	16	•		0.000	[0.000; 0.206]	1.3%
Vintzileos	0	29			0.000	[0.000; 0.119]	4.0%
Yan	0	86			0.000	[0.000; 0.042]	33.1%
Yang 2	0	20	D <u>i</u>		0.000	[0.000; 0.168]	2.0%
Yang 3	0	17	a:		0.000	[0.000; 0.195]	1.4%
Yang 4	0	23	n :		0.000	[0.000; 0.148]	2.6%
Zeng 2	3	33			0.091	[0.019; 0.243]	0.8%
Random effects model		830	•		0.009	[0.000; 0.019]	95.8%
Heterogeneity: $I^2 = 0\%$, $\tau^2 =$	= 0, <i>p</i> = 0.46	6					
Less than 15 included	participan	ts					
Brenlin 2	0	2	:		0.000	[0.000; 0.842]	0.0%
Buonseno	0	2	:	\longrightarrow	0.000	[0.000; 0.842]	0.0%
Cao	0	5	:		0.000	[0.000; 0.522]	0.2%
Chen 1	0	6			0.000	[0.000; 0.459]	0.2%
Chen 2	0	5		\rightarrow	0.000	[0.000; 0.522]	0.2%
Govind	1	9	÷		0.111	[0.003; 0.482]	0.2%
Hu	1	7	÷ • •		0.143	[0.004; 0.579]	0.1%
Liao	0	7			0.000	[0.000; 0.410]	0.3%
Lokken	0	8	1		0.000	[0.000; 0.369]	0.4%
Penfield	0	10	+	-	0.000	[0.000; 0.308]	0.6%
Qadri	0	12			0.000	[0.000; 0.265]	0.8%
Wu 1	0	5	i	>	0.000	[0.000; 0.522]	0.2%
Wu 2	0	5	1		0.000	[0.000; 0.522]	0.2%
Yang 1	0	5	:	>	0.000	[0.000; 0.522]	0.2%
Yu	1	3	:	>	0.333	[0.008; 0.906]	0.0%
Zeng 1	0	6			0.000	[0.000; 0.459]	0.2%
Zhu	0	9			0.000	[0.000; 0.336]	0.5%
Random effects model		106	•		0.011	[0.000; 0.035]	4.2%
Heterogeneity: $I^2 = 0\%$, $\tau^2 =$	= 0, <i>p</i> = 1.00						
Random effects model		936	• • • • • • • • • • • • • • • • • • •	· · · · · · · ·	0.009	[0.002; 0.017]	100.0%
Heterogeneity: $l^{e} = 0\%$, $\tau^{e} = 0$, $p = 0.96$							
Residual heterogeneity: $l^{e} = 0\%$, $p = 0.94$ -0.1 0 0.1 0.2 0.3 0.4 0.5							
lest for subgroup difference	es: χ ^c = 0.03	dt = 1 (p = 0.86)	Proportion of possible vertic	cal transmissio	n		

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series are not the adequate design for pooling prevalence estimates, because they can be extremely misleading. Such is the example found in Figure 3 from Yu et al² with a 33.3% vertical transmission and from Hu et al³ with a 14.3% vertical transmission. Only cohort studies should be used to estimate the pooled proportion of vertical transmission. About the assessment of risk of bias, the preferred scale for case reports and case series is the Joanna Briggs Institute Critical Appraisal Checklist. The Newcastle-Ottawa Scale is for case-control and cohort studies. Another small point would be to add which articles were cohort studies and which were case series in Table 2 and Table 3. According to each study, it is very difficult to assess which ones were cohort studies and which ones were case series.

I tried to replicate the results obtained by the authors using a single proportion analysis by the inverse of the variance by random-effects model and raw and untransformed proportions. The statistical software used was R statistics for Mac (R studio v1.0.136 [The R Foundation for Statistical Computing, Boston MA; package "meta v4.2"]), "meta" package for meta-analysis.⁴ For cells with zero values, I used a continuity correction factor of 0.5. I performed a subgroup analysis on studies with more and fewer than 15 included participants. Although there was no difference between the subgroups, the pooled estimate was 0.9% (95% confidence interval, 0.2-1.7) instead of 3.2%, obtained using the random-effects model (Figure). I could not replicate the results from the authors with the given information in the article. I attached the forest plot with the mentioned results.

I am sure these extremely important methodological slips are completely unintended, but it is critical to fix them to give unbiased results that readers can rely on for future counseling of pregnant women.

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The author reports no conflict of interest.

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