labeled as having been exposed to an infectious environment. The percent of infants at ≥35 weeks gestation admitted to the neonatal intensive care unit with a maternal diagnosis of chorioamnionitis ranges from 6.0 to 91.7%, with significant variation among hospitals. The management of neonates suspected to have been exposed to infection is not universally standardized; we encourage the awareness of institutional policies in the interpretation and application of our findings.

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TO THE EDITORS: The article published by Bergman et al.1 in a recent issue of the American Journal of Obstetrics and Gynecology reported altered dynamic cerebral autoregulation and cerebral perfusion pressure (CPP) in eclampsia. The estimation of CPP based on the formula proposed by Belfort et al.2 raises a few concerns related to the findings and interpretations of this study. The CPP is a difference in the mean arterial pressure (MAP) and intracranial pressure (ICP) or cerebral venous pressure. In the eclampsia group, the CPP exceeded MAP (mean CPP=109.5 mm Hg; MAP=103.6 mm Hg), which is physiologically implausible. According to the data provided in this study, the ICP (MAP−CPP) would be −5.9 mm Hg (negative), 6.9 mm Hg, 24.7 mm Hg, and 8.9 mm Hg in eclampsia, preeclampsia with severe features, preeclampsia without severe features, and normal pregnancy, respectively. Although the authors convincingly demonstrated a lower autoregulatory index in eclampsia, suggesting impaired autoregulation, the derived ICP value does not support impaired autoregulation in eclampsia. The abolition of cerebral autoregulation increases cerebral blood volume and ICP. In addition, a rise in ICP may also impair cerebral autoregulation. The derived ICP data indicate a maximum ICP level (24.7 mm Hg) in women with preeclampsia without severe features. Moreover, ICP levels appear normal in eclampsia, preeclampsia with severe features, and normal pregnancy. Accordingly, the impairment in cerebral autoregulation should have been at a maximum in preeclampsia without severe features. In patients with intact cerebral autoregulation, the ICP remains constant until a CPP of 150 mm Hg, and the CPP reflects a change in the MAP only. In this study, women with eclampsia had a mean CPP of 109.5 mm Hg, and the authors also noted impaired autoregulation. Therefore, a negative ICP level in eclampsia is indeed surprising. This apparent contradiction in the values of the autoregulatory index and ICP is difficult to explain if we believe that the CPP estimation based on the formula by Belfort et al.2 is correct. A constant cerebral blood volume is maintained by cerebrovascular resistance (CVR). A rise or fall in CPP is accompanied by an increase or decrease in CVR.4 The majority of women in the eclampsia group were receiving magnesium (75%) and antihypertensive medications (50%). The potent vasodilatory effects of magnesium and antihypertensive therapy could have reduced the CVR despite a higher CPP or MAP.5 Arguably, the cerebral blood flow velocity in all 3 phenotypes of preeclampsia and normal healthy controls could have been different because of cerebral vasodilatation. In addition, blood flow velocity may differ because of the extent of cerebral vasodilatation at constant CPP or MAP. Therefore, the estimation of autoregulatory index and CPP is based on the change in MAP, CPP, and blood flow velocity in the middle cerebral artery and their estimation based on the complex formula in different patient groups may not be ideal for comparison. To conclude, we suggest a revision in the formula for calculation of CPP or replicating the findings of this study by invasive estimation of ICP in these phenotypes of preeclampsia.

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Impaired cerebral autoregulation, cerebral perfusion pressure, and intracranial pressure in eclampsia
Impaired cerebral autoregulation, cerebral perfusion pressure, and intracranial pressure in eclampsia

Thank you for giving us the opportunity to reply to the letter from Drs Nivetida and Ajay regarding our study, “Cerebral perfusion pressure and autoregulation in eclampsia—a case control study.” We thank them for their interest in our work and for taking the time to provide us with their comments.

Regarding the formula to calculate cerebral perfusion pressure (CPP), this was validated in pregnant women by Belfort et al. in 2000, in a comparison between the estimated CPP (derived from transcranial Doppler and noninvasive blood pressure measurements) and the measured CPP (using spinal epidural pressure as a surrogate for intracranial pressure [ICP]). This study showed acceptable correlation between the estimated and measured CPP in terms of both Bland-Altman analysis and an $R^2$ of 0.86 ($P<0.0001$). The estimated CPP calculated using this formula was found to differ from the measured CPP (calculated using mean arterial pressure [MAP] – ICP) by a pressure of 7.4 mm Hg lower to 11.8 mm Hg higher, rendering a variability of 7%. Thus, if we use that same 7% variability, a CPP value of 109.5 mm Hg in the eclampsia group in the current study could range from 101.8 to 117.2 mm Hg with a standard deviation of 17.7 mm Hg.

Although a validation study of the CPP formula has not been conducted in women with eclampsia or severe preeclampsia (a recognized weakness in the study design), the formula by Belfort et al., has been validated in other critically ill patient populations, for example in patients with traumatic brain injury. Transcranial Doppler (TCD)-based methods to determine ICP noninvasively (nICP) are based on the assumption that $nICP=\text{arterial blood pressure (ABP) – noninvasive CPP}$. ICP is determined by the volumes of the intracranial contents, namely blood (arterial and venous), brain, and cerebrospinal fluid. Because the TCD technique depends on cerebral blood flow velocity (CBFV), this method of ICP monitoring is limited to detecting vasogenic changes in the arterial bed.

In healthy patients with a constant ICP, the ABP can vary widely without altering the CPP or cerebral blood flow (CBF) because of cerebral autoregulation. If cerebral autoregulation is disturbed, as in the case of eclampsia and severe preeclampsia, autoregulatory breakthrough may occur and CBF may become directly dependent on MAP in a linear fashion. Small inaccuracies in the TCD measurement or method and differences in the time at which CBFV and MAP are measured at different sites may then lead to negative values.

Drs Nivetida and Ajay raise an important point regarding the negative mean value for ICP in patients with eclampsia. These nonphysiological negative values are also a persistent problem in studies on the critical closing pressure (CrCP), which is assumed to reflect ICP and arterial tone. It has been suggested that if $\text{CrCP}>\text{ICP}$, which is often the case, then it would be more correct to express $\text{CPP}=\text{MAP}–\text{CrCP}$. One study explored 7 different ways to estimate CrCP (and corresponding resistance-area product [RAP]) and all 7 approaches (or equations) lead to a number of estimated values of CrCP that are negative. As said, the reasons for these negative, nonphysiological estimates are not clear, but are likely related to measurement error, time delays, and the inherent numeric extrapolation of values below the measured values of diastolic ABP and CBFV. Of the 7 methods, the lowest rate of negative values was seen for the “first harmonic method” and the use of mean and diastolic values for CBFV and ABP to estimate RAP and CrCP. According to that formula, the $\text{RAP} = (\text{mean BP}–\text{diastolic BP})/(\text{mean velocity}–\text{diastolic velocity})$. Given that mean velocity=$(\text{mean BP}–\text{CrCP})/\text{RAP}$ and if one assumes that $\text{CPP}=\text{mean BP}–\text{CrCP}$, then using these expressions, it leads to the same equation as validated in the study by Belfort et al. When encountering negative values of CrCP, or alternatively CPP>MAP, many investigators will reject these cases or artificially set CrCP=0, leading to...