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Invited Commentary

Invited Commentary: Physical Exertion and Placental Abruption—Public Health Implications and Future Directions

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Chahal et al. (*Am J Epidemiol*. 2018;187(10):2073–2079) assessed the risk of placental abruption due to physical exertion using a case-crossover design. The authors found an increased risk of placental abruption following increased physical exertion in the hour prior to the abruption. The risk was greater among women who were primarily sedentary during pregnancy or prior to becoming pregnant compared with those who were more physically active. The authors used a case-crossover design to assess the association of an intermittent exposure on an acute event. Chahal et al. address the limitations of the study, including the inability to control for time-varying confounders as well as the potential for recall bias. The public health implications of the study must be carefully evaluated given that physical activity prior to and during pregnancy can lead to healthy outcomes and is likely recommended. While the current study is unable to determine the type of physical exertion associated with placental abruption, future studies are recommended to determine the type of activity that presents increased risk. Additionally, studies among larger samples and in other countries will help determine the generalizability of the results.

abruptio placentae; case-crossover; exercise; physical exertion; placental abruption

In this issue of the *Journal*, Chahal et al. (1) report an interesting association between physical exertion and placental abruption. The risk of placental abruption was higher among women engaging in moderate or heavy physical exertion in the hour before the placental abruption than among women who engaged in light or no physical exertion. Furthermore, this association was modified by habitual physical activity, with those women who habitually engaged in moderate/heavy physical activity having a lower risk (although not null) than those who did not habitually engage in physical activity in the year prior to the pregnancy. There was also potential effect modification by the presence of preeclampsia/eclampsia.

This is a novel report; to the best of our knowledge, there are no prior case-crossover studies on physical exertion and placental abruption. Case-crossover studies have been used widely to study mostly intermittent exposures that have an immediate and transient effect on acute events (2). The case-crossover study design was first applied to the study of triggers of myocardial infarction (3). Interestingly, Chahal et al. made an intriguing parallel with cardiovascular disease and argued that, although unknown, similar mechanisms for the triggering of the acute event could be shared between myocardial infarction and placental abruption (1). If so, other factors that have been reported to act as triggers of myocardial infarction could also have similar effects on placental abruption, such as sexual activity, anger, or cocaine use, to name a few (4). Another interesting parallel with myocardial infarction is the effect modification by habitual physical activity. The associations between heavy physical exertion and myocardial infarction tend to be highly attenuated, or even null, among physically active people. Nonetheless, although the risk of placental abruption was much lower among women who habitually engage in physical activity compared with that of sedentary women, it was still not negligible (rate ratio = 3.0, 95% confidence interval: 1.6, 5.9). Additionally, we can consider the number of preventable cases of placental abruption due to heavy physical exertion given the elevated overall relative risk detected (rate ratio = 7.8, 95% confidence interval: 5.5, 11.0).

Although the study is not exempt from limitations, the authors are to be commended for how well they address the potential limitations in their analysis and discussion. Most of the limitations are inherent to the nature of the study design. Time-varying confounders, in particular concurrent triggers, cannot be easily addressed in case-crossover studies. However, the authors conducted sensitivity analyses to rule out

this possibility. More importantly, recall bias can clearly bias the results if there is differential between reporting of the hazard and control periods. In order to minimize the recall bias, women were not informed of the duration of the hypothesized hazard period and were asked sequentially about their activity during different periods of time prior to the placental abruption and prior to their pregnancy. However, it is still possible that women who report being exposed to heavy physical exertion before the outcome during the hazard period may tend to report no exposure in the control period more often, particularly among sedentary women. Pregnancy is an impactful point in a women's life given that there are known health risks and complications for both the mother and the child. It is possible that women with placental abruption were more likely to report exercise that was out of the ordinary for them as heavy physical exertion rather than low exertion, as they search for possible reasons that the high-risk event occurred. This type of differential reporting could lead to an overestimate of the risk among usually sedentary women compared with those who engaged in physical activity prior to the pregnancy.

Placental abruption is a dramatic, acute event during pregnancy and is associated with significant maternal morbidity and perinatal morbidity and mortality (5). These severe consequences may be even more drastic in developing countries where access to health care during pregnancy is usually more limited than in developed countries. The public health implications of these findings, however, must be evaluated very carefully, particularly in light of the known benefits of habitual physical activity during and prior to pregnancy. There is a high risk for these findings to be wrongly translated to the public. As Chahal et al. point out, and analogous to the case of myocardial infarction, habitual physical activity may provide a protective effect that offsets the transient hazardous association of moderate and heavy physical exertion on placental abruption risk. However, Chahal et al. recognize that this could not be assessed in the current study given the lack of a traditional control group (1). Until further studies can be done to evaluate this question, some caution is warranted to avoid sending the wrong message to all pregnant women. In the meantime, it may be important to emphasize that engaging in regular physical activity before pregnancy and maintaining a reasonable level of activity during pregnancy—while avoiding strenuous activities—may be best, particularly among women at high risk of placental abruption. However, in doing so, we should also consider the type of strenuous physical activity that places a woman at risk for placental abruption, again so as not to mislead the public of the risks of physical activity during pregnancy.

Furthermore, the results from case-crossover studies should always be evaluated in the context of the absolute risk of having the outcome at any given moment and the frequency and duration of the trigger, because the reported point estimates are relative risks for a transient exposure. In the case of placental abruption and physical activity, given the relatively short window of occurrence of the outcome during pregnancy and the relatively high frequency and duration of the exposure, this may not be that critical. Finally, for some acute outcomes, avoidance of the trigger may avoid the outcome completely. For example, in the case of cellular phone use and road traffic accidents, if people do not use a cell phone while driving, they will not have the potential accident triggered by using the phone. However, for other outcomes, avoidance of the trigger may only delay the outcome. For example, if people avoid heavy physical exertion, they may delay the acute event of myocardial infarction, but at some point the vulnerable atherosclerotic plaque may be broken by any other factor that increases sympathetic activity (2). It is interesting to speculate what the case would be for placental abruption, given the relatively short window of susceptibility for this outcome. Can cases of placental abruption be avoided by avoiding the exposure, or will they just be deferred by a few days?

In terms of future directions, some of the limitations addressed by the authors could be evaluated in future studies. Sample size can definitely be increased, and that could also help to explore other hypotheses that the authors were not able to explore in this particular study, such as whether risk varies according to vaginal bleeding during pregnancy, hypertensive disorders of pregnancy, and prior placental abruption, as Chahal et al. comment in the discussion (1). Also, type of physical activity remains an important question mark and one that could be explored in future studies. While a randomized controlled trial in which women are assigned to high-exertion physical activity, or various levels of physical activity, versus a sedentary pregnancy is not feasible, or ethical, observational studies of the general and at-risk populations starting at the first prenatal visit would likely be useful. The fact that the study population in Chahal et al. is from a developing country may affect some of the generalizability regarding the type of physical activity. Future studies could be conducted in countries in which rates of physical activity are higher in order to determine whether the association still exists and to determine the type, duration, frequency, and intensity of physical activity that is protective during pregnancy. It could be possible that some vigorous activities induce more risk than others, and that those vigorous activities could be more prevalent in this study population, such as heavy lifting. This remains speculative, because we are not certain whether there are differences according to type of physical activity, but investigation of these findings in other populations in future studies is definitively warranted. Finally, although other triggers, such as heat and air pollution (6, 7), have been explored with a similar epidemiologic design, many more could be addressed in future studies of placental abruption, either those triggers that have been explored for myocardial infarction, assuming that similar biological mechanisms may be in place, or others that involve other potential biological mechanisms linked specifically to this pregnancy outcome. Similarly, the literature on triggers of other pregnancy outcomes is still relatively scarce, and the case-crossover design is definitely a useful tool to explore these associations in more detail.

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