Invited Commentary

Invited Commentary: Induced Abortion and the Risk of Preeclampsia in a Subsequent Pregnancy

Olga Basso*

* Correspondence to Dr. Olga Basso, Purvis Hall, 1020 Pine Avenue West, Montreal, Quebec H3A 1A2 Canada (e-mail: olga.basso@mcgill.ca).

Initially submitted May 21, 2015; accepted for publication June 2, 2015.

Although it is well established that a pregnancy that ends in birth protects against subsequent preeclampsia, it is unclear whether a pregnancy ending in miscarriage or induced abortion confers any protection. In this issue of the Journal, Parker et al. (Am J Epidemiol. 2015;182(8):663–669) examine whether, in nulliparous women, a history of induced abortion is associated with a lower risk of preeclampsia in a later pregnancy, focusing on the hypothesis that endometrial injury facilitates later implantation. The authors take advantage of data obtained by linking several Finnish population-based registries that include detailed data on induced abortions, although information on miscarriages was of lower quality. Parker et al. found a modest reduction in risk among women with a history of induced abortion. However, there was little evidence that risk differed between women who had medical abortions and those who had surgical abortions (the latter of which is presumably associated with a higher degree of injury). History of miscarriage was not associated with preeclampsia risk. Although the study by Parker et al. adds to the evidence that suggests that women with a history of induced abortion have a lower risk of preeclampsia, it is difficult to evaluate whether the observed association is due to having had a previous pregnancy (however short) versus none, to confounding, or to an actual effect of induced abortion.

induced abortion; miscarriage; preeclampsia

It is well established that a pregnancy that ends in birth is protective against preeclampsia in subsequent pregnancies. However, it is less clear whether a prior pregnancy that did not end in a birth confers any protection. In 1958, MacGillivray (1) reported that, among nulliparas booked in the Aberdeen Maternity Hospital between 1948 and 1955, women with a previous abortion (presumably miscarriage) had a substantially lower risk of “severe” preeclampsia, defined as the presence of hypertension and proteinuria, than did nulligravid women. Since then, the risk of preeclampsia after abortion has been investigated in a number of studies, many of which distinguished between miscarriages and induced abortions. Although a reduced risk of preeclampsia after induced abortion and no association with miscarriage were reported in the majority of studies, findings have been inconsistent (2–8). In particular, in a later study, Campbell et al. (8) did not observe a reduction in risk after abortion (induced or not) if the pregnancy ended within 12 weeks.

In this issue of the Journal, Parker et al. (9) revisited the question of whether induced abortion is associated with a lower risk of preeclampsia in a later pregnancy as a function of number, method, and timing of previous induced abortions. The authors used data from Finland between 1996 and 2010, focusing on the risk of preeclampsia among nulliparous women. They hypothesized that endometrial injury might improve the odds of implantation based on evidence that, among women undergoing infertility treatment, endometrial biopsy is associated with a higher probability of clinical pregnancy in the following in vitro fertilization cycle (10). Although the mechanisms by which injury would improve endometrial receptivity are unknown, it has been speculated that it may increase endometrial decidualization (11) and that wound healing results in an inflammatory response that facilitates implantation (12).

Parker et al. (9) have good-quality data on induced abortions that were obtained through the Finnish Registry of Induced Abortion, which has nearly complete coverage of the procedures performed in Finland during the study period. Information on preeclampsia was obtained from the Hospital Discharge Registry, and data on other pregnancy characteristics...
were derived from the Medical Birth Register of Finland. Using a nested case-control design, the authors found a modest reduction in risk of preeclampsia among nulliparas with a previous induced abortion (odds ratio = 0.9, 95% confidence interval: 0.9, 1.0), which became slightly more pronounced after 3 or more procedures (odds ratio = 0.7, 95% confidence interval: 0.5, 1.0). However, their findings do not provide much evidence that type of abortion (surgical vs. medical) was associated with subsequent risk of preeclampsia, although surgical abortion would be expected to result in a lower risk (9).

A problem in interpreting these results is that, in the study, gravid women (with 1 or more induced abortions) were largely compared with nulligravid ones. The weak protection may thus result from having had a short pregnancy versus not having had any. The authors attempted to address this in a subanalysis in which they included history of miscarriage and of induced abortion. They found no association with previous miscarriage, with or without induced abortion. However, the available information on miscarriage was of lower quality than that on induced abortion, given that it resulted from a combination of International Classification of Diseases, Tenth Revision, codes ascertained from the Hospital Discharge Registry (and thus was restricted to instances in which the miscarriage led to a contact with the hospital and the women’s self-reported information at the time of delivery. Consequently, neither timing of loss nor whether a surgical procedure was performed was known. Had Parker et al. had more detailed data on miscarriages, it would have been possible to better characterize the association of abortions with subsequent preeclampsia risk as a function of method within strata of gravidity, taking into consideration timing and number of previous miscarriages and induced abortions.

Another obstacle to causal interpretation of the association reported in their study has to do with confounding as a possible alternative explanation (9). Parker et al. recognized that they lacked data on some potentially important covariates. For example, information on gravidity was incomplete, and they had no measure of fecundity, which is associated with preeclampsia (13) and might be higher in women with a prior induced abortion. Nevertheless, the authors did consider several other potential confounders (9), none of which changed the estimates by more than 10%, leading to the presentation of unadjusted estimates. The absence of confounding by the examined variables is somewhat surprising, in particular with respect to smoking. According to Table 2 of their article (9), women with a history of induced abortion were twice as likely to have smoked during pregnancy as were those with no such history. That smoking is associated with a lower risk of preeclampsia is well known; however, in this population, the association with smoking appears weaker than what is generally reported (14). It is possible that smoking failed to qualify as a confounder because it was not accurately captured by the registry or because of other sources of misclassification. (For example, it is not clear how the question was asked or how women who had quit smoking during pregnancy would be classified). However, in a study based on the Norwegian Mother and Child Cohort, which also reported a reduced risk of preeclampsia among women with a history of induced abortion (6), the adjusted estimates differed only slightly from the crude ones, suggesting a similar absence of confounding by smoking (as well as by other factors). Such lack of confounding might be the result of effect measure modification, whereby the estimated association between induced abortion and risk of preeclampsia differs between women who smoked during pregnancy and those who did not, an aspect that should be examined in future studies addressing this question.

Despite a number of limitations, the careful analysis by Parker et al. (9) adds to the existing evidence that suggests that women with a history of induced abortions have a lower risk of preeclampsia in a later pregnancy. It remains unclear, however, whether the reported (modest) reduction in risk is causal. It could be argued that establishing the nature of this association has limited public health importance because, clearly, induced abortion—like smoking—cannot be recommended as a measure to reduce preeclampsia risk, even if the protection were substantial. On the other hand, given that a sizable proportion of induced abortions are performed in young women who have not yet started a family, it would be important to establish whether the protection they appear to confer against preeclampsia is indeed causal, and the mechanism. Such knowledge could contribute another tantalizing piece to the puzzle that is the etiology of preeclampsia.

ACKNOWLEDGMENTS
Author affiliations: Department of Obstetrics and Gynecology, McGill University Faculty of Medicine, Montreal, Canada (Olga Basso); and Department of Epidemiology, Biostatistics, and Occupational Health, McGill University Faculty of Medicine, Montreal, Canada (Olga Basso).
Conflict of interest: none declared.

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