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Wildfires in pregnancy: Potential threats to the newborn

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Climate change continues to result in increased exposure to wildfires in California and around the world with smoke reaching far more populations than in recent years. There is increased concern for the health effects of these fires, especially for pregnant people and their developing foetuses.

Ambient air pollution, particularly fine particles (particulate matter ≤2.5 microns [$PM_{2.5}$]), constitutes the main component of wildfire smoke that impacts human health. Such fine particles can impact circulatory and reproductive organs as well as the foetus through various mechanisms including oxidative stress and inflammation.[1] In addition, $PM_{2.5}$ levels decreased in the past decades in the United States except in wildfire-prone areas and the contribution of wildfire smoke to $PM_{2.5}$ is expected to drastically increase in the next decades.[2]

Gastroschisis is a rare birth defect of the intestinal wall that develops between Weeks 4 and 8 of gestation and its causes—as is the case with many birth defects—remain unknown. The prevalence of gastroschisis has increased between 1995 and 2012 and is more common in younger versus older women as well as among smokers.[3] Given the inflammatory mechanisms associated with exposure to fine particles during pregnancy, it is plausible that exposures to wildfire smoke could affect the risk of gastroschisis and other birth defect outcomes.

In this special issue on Climate Change and Reproductive, Perinatal, and Paediatric Health in *Paediatric and Perinatal Epidemiology*, Park and colleagues[4] provide the first investigation of wildfire exposure during pregnancy and risk of gastroschisis in a large cohort of births from 2007 to 2010 in California. They found that residential proximity (<15 miles) to wildfires in the first trimester was associated with a 28% higher risk (relative risk 1.28, 95% confidence interval: 1.07–1.54) of gastroschisis based on ICD-9 codes from state-wide data. Additionally, they found that the risk of gastroschisis was more than twofold higher among those exposed during the 30 days prior to pregnancy. It is unclear why this stronger association would be prior to conception as opposed to when the digestive tract is developing in utero, but the duration of toxicity of wildfire smoke following exposure is not

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well known. This study is also interesting in that it serves to highlight a few methodological considerations relevant to future studies investigating the role of wildfire (and smoke) exposure during pregnancy and birth defect as well as birth outcomes.

The strength of this study lies in its size with more than 2 million births including 1262 gastroschisis cases. Results from previous studies of air pollution (from other sources) and gastroschisis have been inconclusive. In a case-control study in California of 169 cases between 1997 and 2006, no associations were found between 6 criteria pollutants (including $PM_{2.5}$) estimated at participants' geo-coded residence during the first two months of pregnancy and risk of gastroschisis.[5] Another study in China found increased risk of gastroschisis (116 cases) associated with nitrogen dioxide (NO_2) during the third month of pregnancy, but did not find associations during the second month, nor with sulphur dioxide (SO_2) or PM_{10}.[6] Only one other study (to our knowledge) has been published recently examining birth defects (not including gastroschisis specifically) in Brazil among 16 million birth records[7] that found small but precise associations between the number of wildfires in the municipality of the mother's home and risk cleft lip or palate as well as two broad categories of birth defects of the respiratory and nervous system. These studies highlight the trade-off between studying birth defects in larger studies with less precise case ascertainment compared to smaller studies with more detailed covariate data with relatively accurate case ascertainment.

The exposure assessment regarding wildfires is a key concern in this context as many mechanisms may co-exist. First, fires contribute to enhanced concentrations of $PM_{2.5}$ through smoke that can then be transported over large areas via wind and impact pregnant women several miles away from the fires. Second, pregnant women living near fire perimeters may be impacted by other pollutants such as carbon monoxide or toxicants generated from burning build environments. However, living near wildfires may also imply some psychological mechanisms generating stress and other mental health issues via possible evacuation, disruption of social or healthcare activities or power outages. The psychological stress associated with wildfires is intense and amplified in pregnancy with the threat of losing one's home, evacuation, symptoms of inhaling smoke and fear that the smoke may be affecting one's developing foetus. Future studies of smaller scale are needed to address this combined environmental and psychosocial stress that occurs during wildfire events.

Therefore, clarifying the hypothesised mechanisms of interest before modelling the exposure is important to then justify the identification of windows of susceptibility. Short-term changes in air pollution from wildfires may coincide with narrow critical periods of gestation that are important to the development of the foetus. Previous research focussing on $PM_{2.5}$ from any source has identified specific windows of susceptibility for outcomes such as preterm birth and highlighted the importance of modelling short-term exposure windows (eg weeks) as well as adopting analytical approaches[8] that consider complex temporal patterns regarding this type of exposure. Therefore, trimester exposures may not be optimal to capture critical aetiological windows of interest especially for outcomes like gastroschisis that typically develops within the first weeks of gestation.

The Park et al. study used proximity to fire perimeters within a 15-mile radius. In an area that is highly exposed, such as California, this resulted in 40% of the population being exposed. However, besides the multiple possible pathways (as described above) related to such exposure metric, it is uncertain as to the degree to which these populations were exposed to wildfire smoke and how that varied among the exposed pregnant women. Different approaches exist to specifically isolate $PM_{2.5}$ attributable to wildfire smoke from other sources of emissions (*eg* traffic) and could rely on dynamical approaches (chemical transport models) or satellite products (*eg* atmospheric aerosol loading) combined with land use and meteorological data with statistical methods such as ensemble techniques.[9] Such approaches are recommended to capture more precisely spatial variations in smoke $PM_{2.5}$ instead of vague exposure estimates such as proximity to fires or smoke plumes.

Other challenges exist when studying the potential effects of wildfire exposures on birth defects. First, in California, there is a strong seasonality in the incidence of wildfires where the fire season typically takes place during the Fall in relation to at least two components: the change in precipitation regime under climate change and the seasonality of specific downslope winds such as Diablo or Santa Ana Winds.[10] Therefore, it becomes difficult to disentangle the specific role of wildfire in the aetiology of birth defects from other seasonal patterns which may explain the counterintuitive result that wildfire exposure 30 days before delivery was associated with a higher risk of gastroschisis. Using exposure metrics that capitalise on the fine-scale spatio-temporal variation in wildfire metrics would thus be a reasonable approach. Second, selection bias is an important threat to validity in perinatal epidemiology including in relation to environmental exposures. For example, live birth bias, where selective survival between conception and birth can be influenced by the exposure of interest (or factors correlated spatially or temporally), may lead to substantial biases. Existing techniques based on inverse probability of selection weights have been proposed to mitigate such biases and could be helpful for future studies.

With the increasing number and intensity of wildfires in the Western United States, it is crucial to better understand the role environmental exposures have on birth defects and other adverse birth outcomes. Doing so would enable the design and evaluation of targeted clinical and public health interventions designed to reduce exposures and their health effects among pregnant women. A recent systematic review by Amjad et al.[1] identified only 8 epidemiologic studies that mostly focussed on birthweight and preterm birth. The study by Park et al. adds to this growing literature on wildfire exposure during pregnancy and adverse reproductive and perinatal health by focussing on birth defects. The findings of this study are concerning, and more well-designed studies are needed to corroborate these findings. Additionally, other mechanisms besides smoke, such as the psychological stress associated with proximity to wildfires or being evacuated, should be examined similarly as it may also be contributing to the development of the foetus. Finally, this study adds to the mounting evidence of the health effects of climate change and the imminent danger that lies with the current slow pace of policy change to address such crises.

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