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Ambient temperature and risk of cardiovascular events at labor and delivery: A case-crossover study

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ABSTRACT

Background: Extreme ambient temperatures are linked to cardiac events in the general population, but this relationship is unclear among pregnant women. We estimated the associations and attributable risk between ambient temperature and the risk of cardiovascular event at labor/delivery, and investigated whether these associations vary by maternal race/ethnicity.

Methods: We identified 680 women with singleton deliveries affected by cardiovascular events across 12 US sites (2002–2008). Average daily temperature during the week before, delivery day, and each of the seven days before delivery was estimated for each woman. In a case-crossover analysis, exposures during these hazard periods were compared to two control periods before and after delivery using conditional logistic regression adjusted for other environmental factors.

Results: During the cold season (October-April), 1 °C lower during the week prior to delivery was associated with a 4% (95% CI: 1–7%) increased risk of having a labor/delivery affected by cardiovascular events including cardiac arrest and stroke. During the warm season (May-September), 1 °C higher during the week prior was associated with a 7% (95% CI: 3–12%) increased risk. These risks translated to 13.4 and 23.9 excess events per 100,000 singleton deliveries during the cold and warm season, respectively. During the warm season, the risks were more pronounced on days closer to delivery and Black women appeared to be more susceptible to the same temperature increase.

Conclusion: Small changes in temperature appear to affect the risk of having cardiovascular events at labor/delivery. Black women had a differentially higher warm season risk. These findings merit further investigation.

1. Background

Cardiovascular events are a leading cause of maternal morbidity and mortality. They are responsible for approximately 15% of all pregnancy-related deaths (Creanga et al., 2015). This proportion has increased in the US from approximately 3% during the years 1987–1990 and has a consistent racial/ethnic disparity over time, with Black women experiencing significantly higher risk (CDC, 2016; Creanga et al., 2015). One factor potentially contributing to this upward trend is the shift in population-level cardiovascular risk factors including maternal age, obesity, and gestational complications (Ferrara, 2007; Lu et al., 2001). Although the incidence of cardiovascular events during labor and delivery is relatively low at 0.3% (Männistö et al., 2015), in addition to being potentially life-threatening, these events have long-term implications for affected women and their families (Sliwa and Bohm, 2014). Consequently, it is critical to identify and understand potentially modifiable risk factors. Our group has published some early evidence on the potential acute association between

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ambient air pollution and the risk of cardiovascular events at labor and delivery (Männistö et al., 2015), but other environment risk factors are largely unknown.

Concurrent with the increase in pregnancy-related cardiovascular events is the steady increase in ambient temperature associated with climate change (NOAA, 2011). Studies have linked extreme ambient temperatures with acute cardiovascular risk in the general population as well as in susceptible subgroups including those with lower socioeconomic status, the elderly, and those with other comorbid conditions (Medina-Ramon and Schwartz, 2007; Wang et al., 2016; Yang et al., 2015). A role for temperature in the pathogenesis of cardiovascular risks is plausible given the oxidative stress and systemic inflammation induced shortly after exposure (Cai et al., 2016; Cheng et al., 2015; Halonen et al., 2010; Hong et al., 2012; Quindry et al., 2013). Since pregnancy itself increases the cardiovascular burden (Ouzounian and Elkayam, 2012), the role of extreme ambient temperature exposure on cardiovascular burden during pregnancy merits attention. To date, no studies have investigated the relationship between ambient temperature and cardiovascular risk among pregnant women.

The aims of this paper were first to examine the acute associations between ambient temperature and the risk of having a labor/delivery affected by cardiovascular events in the US. Second, given the significant racial/ethnic disparity in the risk of pregnancy-related cardiovascular mortality/morbidity (CDC, 2016; Creanga et al., 2015) and evidence of differential temperature health effects by racial/ethnic group (Basu et al., 2012), we sought to investigate whether these associations differ by race/ethnicity. Third, we calculated the excess number of cases potentially attributable to temperature changes in the US.

2. Materials and methods

2.1. Data and study population

The Air Quality and Reproductive Health (AQRH) study estimated environmental exposures in order to evaluate the association of ambient environmental risk factors with reproductive and perinatal outcomes in ongoing studies at the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (Chen et al., 2014). In 2013, the AQRH study linked meteorological data estimated from the Weather Research and Forecasting (WRF) model v3.2.1 to the participants in the Consortium on Safe Labor (CSL) Study. CSL was an observational cohort study with 228,438 deliveries (233,736 newborns) at ≥23 weeks of gestation from 12 clinical centers (19 hospitals and 15 hospital referral regions) across the US from 2002 to 2008 (Zhang et al., 2010) (eFig. 1). Data on maternal demographics; lifestyle; medical history; labor and delivery, obstetric, and neonatal outcomes were obtained from electronic delivery records and discharge summaries. Initially, 686 (0.3%) singleton pregnancies complicated by cardiovascular events at labor/delivery were eligible. Six women had cardiovascular events in more than one pregnancy during the study period, so only their first pregnancy was included, leaving 680 pregnancies in the final analyses. The study was approved by the institutional review boards of all participating institutions. Informed consent was not required since data were anonymized.

2.2. Study design

We used a case-crossover design to assess the risk of a cardiovascular event during a short "hazard period" after exposure to the hypothesized trigger—ambient temperature. The unique feature of the case-crossover design is that each woman serves as her own control. This self-matching feature allows complete control for non-time-varying potential confounders such as genetic factors, consistent characteristics or behavior (e.g., obesity or smoking), or any underlying cardiac susceptibility either known or unknown. This approach essentially holds all time invariant characteristics about a woman and her delivery constant except for the varying temperature or other environmental exposures of interest. As a result, any difference in risk detected after controlling for other varying environmental exposures (e.g., humidity and air pollution) can reasonably be attributed to ambient temperature.

2.3. Exposure assessment

Since the CSL data were anonymized, we used the 15 distinct hospital referral regions as a proxy for maternal residence and local mobility associated with daily activities (e.g., work, errands). Hourly temperature and humidity were obtained from the WRF model and averaged across each hospital referral region. WRF is a state-of-the-art weather prediction system, designed and utilized by many leading research, governmental and academic entities for atmospheric research and forecasting. Its modeling approach and performance have been reported elsewhere (Zhang et al., 2014a).

To assess acute exposure, we first calculated average daily temperature for the following hazard periods: the week prior to delivery, the day of delivery (lag0), and each of the seven days before delivery (lag1-lag7). The week prior to delivery and the days comprising the week prior to delivery were chosen as the hazard periods given evidence suggesting acute cardiovascular effects within seven days in the non-pregnant population (Dahlquist et al., 2016; Wang et al., 2016; Wichmann et al., 2013; Zheng et al., 2016). Temperature during this hazard period was then compared to two control periods: the second week after delivery and the week two full gestational weeks before delivery. A post-event control period may seem counterintuitive because the person is considered no longer at risk after the event. However, studies have shown that this bidirectional control selection method is preferred over the unidirectional method (i.e., selecting control periods only before the event), which is sensitive to time trend bias (Bateson and Schwartz, 1999; Navidi, 1998). This is especially true in studies where exposure has a high seasonal trend and is exogenous to the population under study. We also chose control periods to be relatively close to delivery, so that the seasonal variation in temperature was minimized.

We also obtained concentrations of particulate matter with diameter < 2.5 μm ($PM_{2.5}$) and ozone (O_3) during the same exposure windows using modified Community Multiscale Air Quality models (CMAQ). CMAQ models estimated air pollution levels based on inputs from several sources: local emissions obtained from the National Emission Inventories, local weather obtained from the WRF, and photochemical properties of pollutants (Chen et al., 2014). Air pollutant concentrations were also corrected for measurement errors between modeled and observed levels at local air monitors using inverse distance weighting (Chen et al., 2014).

2.4. Outcome assessment

Our primary outcome of interest was labor/delivery affected by any cardiovascular event consisting of ischemic heart disease, stroke, heart failure, cardiac arrest/failure, and other or unspecified cardiovascular events. Throughout the study time period, these outcomes were identified from labor/delivery discharge summaries using International Classification of Disease, 9th version (ICD-9) codes (eTable 1).

2.5. Statistical analysis

For each woman, we compared a hazard period (lag0, lag1-lag7, or week's average) to the control periods before and after the event. Recognizing that the stress of labor/delivery is a proximal factor increasing risk, this approach modeled the joint event (labor/delivery with cardiovascular event), and tested whether the women with the joint event had exposure to higher or lower temperature during the