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Is ambient temperature associated with risk of infant mortality? A multi-city study in Korea

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ABSTRACT

Background: Although numerous studies have shown increased risk of mortality from elevated temperatures for adults, limited studies have examined temperature's effect on mortality for infants. Our study investigated the city-specific and overall effects of ambient temperature on infant mortality in seven major cities in Korea, 2004–2007.

Methods: Birth cohort using a linked birth and death records included 777,570 births with 557 all-cause deaths. We estimated city-specific hazard ratios for each city using an extended Cox proportional hazards model with time-dependent covariates. Then we combined city-specific hazard ratios to generate overall hazard ratio across the seven cities using a Bayesian hierarchical model. Stratified analyses were conducted by cause of death (total and SIDS), exposure period (whole gestation, each trimester, lifetime, 1 month before death, and 2 weeks before death), sex, and maternal characteristics.

Results: Overall across the cities, we found significantly positive associations between ambient temperature during 1 month before death or 2 weeks before death and infant mortality from total or SIDS. The overall hazard ratio of infant mortality from total deaths and SIDS for a 1 °C increase during 1 month before death was 1.52 (95% CI, 1.46–1.57) and 1.50 (95% CI, 1.35–1.66), respectively. We also found suggestive evidence that some factors such as mother's age may modify the association.

Conclusions: Our findings have implications for establishment of policy to reduce the risk of infant mortality from high ambient temperature under climate change.

1. Introduction

Numerous studies conducted in many parts of the world have demonstrated associations between ambient temperature and mortality (Goggins et al., 2015; Vardoulakis et al., 2014; Wang et al., 2015; Yang et al., 2015). Moreover, significantly raised risks of heat- and cold-related mortality are anticipated under climate change (Hajat et al., 2014). Given that climate change is expected to result in more severe weather patterns with overall warming in the future, it is important to investigate the impacts of temperature on health outcomes and establish appropriate strategies for potential high risk populations.

Previous studies reported variability in vulnerability to temperature-related health effects by sub-population. People with low socioeconomic status, the elderly, and children are often reported to be at greater risk from high ambient temperature (Basu and Malig, 2011; Basu and Ostro, 2008; Basu and Samet, 2002a). Baccini et al. (2008) reported stronger associations between heat and mortality in the elderly (≥ 75) than other age groups. Other studies investigating temperature and mortality also suggest that the elderly are particularly vulnerable (Hajat et al., 2007; Medina-Ramón et al., 2006; Stafoggia et al., 2006). Another study reported that very young children, especially infants, are particularly vulnerable to heat-related deaths (Xu et al., 2012). Although a few studies reported that infants are more susceptible to heat-related mortality (Basagaña et al., 2011; Basu et al., 2015; Basu and Ostro, 2008), most studies focused on the general population or the elderly and limited studies exist for temperature's mortality effect on infants.

Possible biological mechanisms of heat exposure with mortality include decreased blood circulation to the heart and vital organs resulting from changes in blood composition such as increased platelet and red blood cell counts, blood viscosity, and plasma cholesterol levels due to heat stress (Bouchama and Knochel, 2002; Keatinge et al., 1986). In particular, infants' vulnerability to high temperature may be related to thermal instability. Infants may be especially vulnerable to heat due to several physiologic differences such as increased ratio of body surface area to body mass and metabolic rate, higher sweating threshold,

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smaller blood volume and their immaturity of thermoregulatory mechanisms, and lack of self-care ability from heat stress (Basagaña et al., 2011; Guntheroth and Spiers, 2001; Xu et al., 2012).

Of the few studies that investigated temperature and mortality for infants, most focused on a single city. Temperature effects may differ by area because of different regional characteristics such as climatic characteristics, use of air conditioning, and individual behaviors (e.g., spend time outdoors) or other characteristics. Thus, more studies in various locations and study populations are needed.

We investigated the city-specific and overall effects of ambient temperature on infant mortality in seven major cities in Korea. We considered several timeframes of heat exposure on infant mortality and effect modification by infant sex and mother's age and education.

2. Material and methods

2.1. Data

We obtained linked birth and death records for 2004–2007 from the Korean National Statistical Office for seven major cities in Korea (Seoul, Busan, Incheon, Daegu, Daejeon, Gwangju, and Ulsan). Linked data included residential address, sex, birth weight, gestational age, birth order, date of birth, mother's age, mother's education, date of death, age at death, and cause of death. We excluded subjects with incomplete data for covariates for infant's sex, gestational age, birth weight, and maternal characteristics (i.e., mother's age or education). We restricted study subjects to singleton births with 37–44 weeks of gestation. Also, we excluded infants who died prior to the postneonatal period (i.e., those who died in the first 27 days after birth) to consider only deaths more plausibly related with exposure of our interest because death before the postneonatal period tended to occur from pregnancy complications (Woodruff et al., 2006). The study includes 777,570 births with 557 all-cause deaths. We considered total mortality as all causes of death except external causes (International Classification of Diseases, ICD-10, A00-R99), and sudden infant death syndrome (SIDS; ICD-10, R95).

Hourly measurements of ambient temperature for each city were obtained from the National Meteorological Administration, Republic of Korea. We calculated 24-hr average values for each city. We considered long-term exposures for ambient temperature for each study subject for: (1) gestational exposure from conception to birth, (2) exposure for each trimester, (3) lifetime exposure from birth to death or end of eligibility for outcome (1 year of age), (4) 1 month before death, and (5) 2 weeks before death. Trimesters were defined as 1–13 weeks, 14–26 weeks, and 27 weeks to birth. As a sensitivity analysis, we performed analysis with and without air pollution exposure adjustment. We obtained hourly PM_{10} concentration for each city for the study period from the Department of Environment, Republic of Korea. $PM_{2.5}$ data were not available. We calculated daily values (i.e., 24-hr averages) for each city and considered exposures for the gestation period, each trimester, lifetime and 1 month or 2 weeks before death.

2.2. Statistical analysis

At the first stage, we estimated city-specific hazard ratios for each city. We applied an extended Cox proportional hazards model with time-dependent covariates to estimate the association between long-term exposure to ambient temperature and infant mortality. This model assumes that the effect of a time-dependent variable $X_i(t)$ (in this case ambient temperature) on the hazard at time t depends on the values of this variable at that same time t, and not on the value at an earlier or later time. This approach allowed us to examine the effects relative to other subjects for the same follow-up interval. This is similar to the matching used in other studies to compare the exposure levels between the deceased and surviving subjects until the time of death (Woodruff et al., 2006). We analyzed separate models for each cause of death (total and SIDS) and exposure period (whole gestation, each trimester, lifetime, 1 month before death, and 2 weeks before death). For each cause of death and exposure period, we fitted a time-dependent Cox proportional hazards model:

$$h_i(t) = h_0(t) \exp [ß_1 X_i + ß_2 X_i(t)] \quad (1)$$

where $h_0(t)$ is the unspecified baseline hazard function, X_i is the vector of time-independent variables (sex, birth weight, gestational age, mother's age, mother's educational level, and season of birth) for subject i, $X_i(t)$ is the vector of the time-dependent variable (temperature), and $ß_j$ ($j = 1, 2$) are vectors of model parameters. We categorized mother's age (< 25, 25–30, 30–35, and ≥ 35 years) and mother's education (≤ 12, > 12 years). As a next step, we combined city-specific hazard ratios to generate an overall hazard ratio across the seven cities using a Bayesian hierarchical model that incorporates with-city and between-city variances.

To examine the critical exposure window to heat exposure for infant mortality, first we conducted analysis for Seoul, which has the largest population of any city in Korea. We estimated hazard ratios based on different exposure timeframes (whole gestation, each trimester, lifetime, 1 month before death, and 2 weeks before death) for Seoul. We then estimated city-specific and overall hazard ratios for exposure timeframes for which we observed associations. To estimate heat exposure, many environmental health studies have used several measures to consider combined exposure of several weather conditions such as heat index. Thus, we performed sensitivity analysis using a heat index which is a function of air temperature and relative humidity instead of ambient temperature for Seoul. We used a heat index algorithm by the U.S. National Weather Service (NWS) (NWS, 2016). We estimated hazard ratios of infant mortality for total deaths and SIDS for exposure timeframes for which we observed associations and then compared with original findings using an ambient temperature. We also conducted sensitivity analyses to consider: (1) the long-term time trend and seasonality; and (2) temperature variation for Seoul. We estimated hazard ratios of total infant mortality for exposure timeframes for which we observed associations and then compared results with original findings.

We assessed nonlinear associations between continuous temperature and the hazard of infant mortality via restricted cubic splines. We considered 3 (10th, 50th, and 90th temperature percentiles) and 5 knots (10th, 25th, 50th, 75th and 90th temperature percentiles) for splines. Results of the analysis suggested a linear association between increased temperature and risk of infant mortality. Stratified analyses were conducted by characteristics (i.e., infant's sex, mother's age and education level). All analyses were conducted with SAS (version 9.4; SAS Institute Inc., Cary, NC, USA) and R 3.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

Table 1 and Table S1 provide summary statistics of key study variables and distribution of daily ambient temperature for the seven major cities in Korea. The number of all-cause deaths ranged from 34 in Gwangju to 233 in Seoul. Average daily mean temperatures were generally similar across the seven cities, ranging from 12.7 °C in Incheon to 14.8 °C in Ulsan. Most infants for all cities were male and had a mother who was 25–30 or 30–35 years of age at time of birth. Mother's education level for all cities except for Incheon averaged more than 12 years, which ranged from 53.6% to 66.3% for a given city.

Table 2 shows hazard ratios for a 1 °C increase based on various exposure windows in Seoul, Korea. We conducted separate analysis by cause of death and exposure timeframe. We found that heat exposure during 1 month before death or 2 weeks before death was associated with infant mortality. The hazard ratio of infant mortality for total deaths and SIDS for a 1 °C increase during 1 month before death was 1.46 (95% confidence interval (CI), 1.44–1.47) and 1.44 (95% CI,