Original Contribution

High Ambient Temperature and the Risk of Preterm Delivery

Rupa Basu*, Brian Malig, and Bart Ostro

*Correspondence to Dr. Rupa Basu, Air Pollution Epidemiology Section, California Office of Environmental Health Hazard Assessment, 1515 Clay Street, 16th Floor, Oakland, CA 94612 (e-mail: rbasu@oehha.ca.gov).

Initially submitted November 23, 2009; accepted for publication May 11, 2010.

With temperatures expected to increase because of climate change, it is essential to study the health outcomes of elevated temperature in vulnerable populations, such as expectant mothers. In this study, the authors estimated the association between heat and humidity, as measured by apparent temperature, and preterm delivery. They conducted a case-crossover analysis of almost 60,000 births spanning 16 counties in California that occurred from 1999 to 2006 between May and September. The authors identified cases of preterm birth from a state registry of births, which were combined with meteorologic and air pollution monitoring data based on residential zip code. High ambient temperature was significantly associated with preterm birth for all mothers, regardless of maternal racial/ethnic group, maternal age, maternal education, or sex of the infant. Results indicated that an 8.6% increase (95% confidence interval: 6.0, 11.3) in preterm delivery was associated with a 10°C increase in weekly average (lag06) apparent temperature. Greater associations were observed for younger mothers, blacks, and Asians. These associations were independent of air pollutants. Given the significant associations for apparent temperature and preterm delivery found in this study, more large-scale studies of temperature and preterm delivery are warranted.

Abbreviations: CI, confidence interval; PM2.5, particulate matter less than 2.5 μm in aerodynamic diameter.

Editor’s note: An invited commentary on this article appears on page 1118, and the authors’ response is published on page 1121.

Preterm delivery of an infant before 37 gestational weeks occurred in 12.8% of all livebirths in the United States in 2006 (1). Preterm infants are more likely to experience adverse health outcomes, such as death (2), respiratory distress during hospitalization, and hospital readmission after birth (3). Families of preterm infants also bear a substantial economic burden, including inpatient hospital costs (4) and long-term health care costs during the first year (5) and through early childhood (6, 7). Infants born preterm can suffer lifelong impacts including decreased motor and cognitive functioning, increased behavioral disorders, and lower educational attainment in adulthood when compared with those born at full term (8, 9). Thus, researchers need to identify risk factors for preterm delivery and work toward prevention.

The etiology of the majority of preterm births remains unknown. Maternal risk factors that have been identified include chronic infections and hypertension (10). More recently, preterm delivery has been linked to environmental factors such as air pollution and traffic exposure (11–16). In a recent investigation of preterm delivery, a peak was observed in August and September (17). Only a few studies have focused on the associations between temperature or other meteorologic variables and preterm delivery, and the findings from these studies have been inconclusive (18, 19).

We studied the association between elevated ambient temperature and preterm delivery during the warm season in California from 1999 to 2006. In addition, several demographic subgroups were examined.
MATERIALS AND METHODS

Exposure classification

Meteorologic data consisting of daily mean, maximum, and minimum temperatures and relative humidity were provided by the California Irrigation Management Information System (20) and the US Environmental Protection Agency Air Quality System (21) for the warm season, designated as May 1 to September 30, from 1999 to 2006. Temperatures in California generally rise sharply in May and June, level off in July and August, and start to decline in September. Apparent temperature was calculated using the following formula: \(-2.653 + (0.994 \times \text{temperature in } °C) + 0.0153 \times (\text{dew-point temperature in } °C)^2\). Each mother was assigned the resulting apparent temperature value from the weather monitor closest to the reported residential zip code centroid at the time she gave birth. Only those cases residing in zip codes with centroids located within 10 km of a weather monitor, as identified by Hawth’s Tools for ArcGIS 9.3 (22), were eligible for this study.

Since previous investigators have reported an association between preterm delivery and several air pollutants, such as particulate matter less than 2.5 μm in aerodynamic diameter (PM\(_{2.5}\)) (15), sulfur dioxide (13), and carbon monoxide (12), potential confounding or effect modification by these pollutants was considered. Nitrogen dioxide was also examined, since traffic measures were found to be associated with preterm delivery in some studies (16, 23), and nitrogen dioxide serves as a proxy for traffic (16). Potential confounding or effect modification by ozone was assessed, since ozone levels are generally elevated during the warm season in California, and ozone has been found to be associated with intrauterine growth retardation (24).

Mean daily data from air pollution monitors were provided by the California Air Resources Board (25). The pollution monitor closest to each mother’s residential zip code centroid was used to assign exposure, restricting cases to those residing within 10 km of an air pollution monitor. The daily 1-hour maximum was used for all pollutants except PM\(_{2.5}\), which was based on a 24-hour average.

Outcome measure

California’s Office of Vital Records supplied information on infants born between 1999 and 2006 (26). To focus on heat exposures, births were restricted to those occurring from May 1 to September 30. Length of gestation was abstracted from birth certificate data, with preterm delivery defined as births from 20 to 36 gestational weeks. Other variables collected from the birth certificate included date of infant’s birth, infant’s sex, mother’s age, mother’s years of completed education, mother’s race/ethnicity, and mother’s residential zip code at the time she gave birth. Only singleton births in counties with at least 20 preterm births for which data on the demographic variables of interest were available were included in the analyses. Deliveries induced prematurely because of pregnancy complications were excluded. Births at an improbable gestational age and/or birth weight were also excluded, using cutoffs as described previously (27).

Statistical analysis

The case-crossover method, a statistical technique ideally suited to examine short-term exposures with acute outcomes, was used for the analysis. The case-crossover study is a modification of the matched case-control study, where each person serves as his or her own control so that known and unknown time-invariant confounders, such as body mass index, are inherently adjusted for by study design. In this study, exposures for up to 1 week before a birth were compared with exposures for the same mother at other times in the infant’s birth month and year. Confining the control periods to the month of birth reduces the influence of long-term time trends. Control periods were also limited to the same day of the week as for the case to adjust for day of the week. Consequently, there could be a maximum of 4 control periods per case occurring a minimum of 7 days and a maximum of 28 days before or after the case period.

Two sampling schemes using single-day lags are demonstrated in Figure 1. If a case of preterm delivery occurred in the middle of the month, control periods would have occurred both before and after the case period, as shown in the first example. In the second scenario, a case of preterm delivery occurred at the end of the month, so that all control periods occurred prior to the case. Similarly, if a case of preterm delivery occurred at the beginning of the month, all control periods would be selected after the case. If a case occurred on the first of the month, the lag period could be selected from the last week of the previous month. This sampling scheme is known as the time-stratified design, the most current methodology used in studies with the case-crossover design; bidirectional and unidirectional sampling of control days may introduce bias (28). For the time-stratified design to be valid, it is essential for control periods to be selected at random with respect to when the case of preterm delivery occurred. As mentioned above, this design may use postevent control periods, even though a pregnant woman is theoretically no longer at risk of giving birth. However, any bias from using control periods after the risk period is small if the event is rare (29). In our birth cohort, giving birth on a specific gestational
day was a rare occurrence, never exceeding a 4% probability.

A linear term for apparent temperature was included in a conditional logistic regression model, and the log(odds) of preterm delivery (yes/no) served as the outcome measure. Nonlinear associations at higher temperatures were explored (i.e., adding a term for the 90th percentile for apparent temperature to the model), but such terms were not significant and were excluded from subsequent analyses. All analyses were performed in 2 steps: first, we calculated the county-level estimate based on residential zip codes; second, we combined the county-level estimates to produce an overall estimate using meta-analytical techniques (30). In this paper, all estimates are reported as percent change per 10°F (5.6°C) increase in apparent temperature with corresponding 95% confidence intervals. Estimates with 95% confidence intervals that do not include zero are considered statistically significant. PROC PHREG in SAS version 9.1 software (31) was used to conduct the first stage of the analysis, and version 2.6.2 of the R program (32) was used for the meta-analyses.

Several lag periods of mean, maximum, and minimum apparent temperature were examined to determine which metric demonstrated the best model fit according to $t$ tests. The exposure periods tested included same-day lag (lag 0), 6 single-day lags (lag 1, lag 2, lag 3, lag 4, lag 5, and lag 6), and 3 cumulative average lag periods (lag01, lag03, lag06). The single-day lags referred to apparent temperature on the previous day (lag 1), 2 days prior (lag 2), and so forth, whereas the cumulative lag periods were averages of several days, such as the exposure on the same day and the previous 3 days (lag03).

We used the apparent temperature metric and lag period with the best model fit to examine potentially vulnerable subgroups of high ambient temperature and preterm delivery. In separate models, we stratified by maternal racial/ethnic group (non-Hispanic white, non-Hispanic black, Hispanic, non-Hispanic Asian), maternal age (<20, <25, 25–34, ≥35 years), infant’s sex (male, female), and highest level of maternal education completed at the time of giving birth (high school graduation or less vs. some college). We also examined whether effect estimates differed between earlier (20–33 gestational weeks) and later (34–36 gestational weeks) preterm births, for all full-term births between earlier (20–33 gestational weeks) and later (34–36 gestational weeks) preterm births, for all full-term births (37–44 gestational weeks), and specifically for 37 and 38 gestational weeks. Differential impacts among demographic groups were evaluated using $t$ tests (33).

We assessed the potential confounding or effect modification of the apparent temperature and preterm delivery association by air pollutants. Bivariate models with a weekly average of each air pollutant considered in addition to the weekly average apparent temperature term were used to assess potential confounding. An interaction term incorporating apparent temperature and each air pollutant was added when assessing potential effect modification.

Effect estimates were compared by month and by year to examine whether any month or year influenced the overall estimate. For the same reason, we also compared effect estimates between inland (Fresno, Kern, Merced, Riverside, Sacramento, San Bernardino, San Joaquin, Tulare) and coastal (Alameda, Contra Costa, Los Angeles, Orange, San Diego, Santa Clara, Solano, Ventura) areas and between northern and southern (designated as Kern and San Bernardino counties and below) California. Finally, we restricted the control periods to 2 weeks instead of 1 month since baseline risk for preterm delivery changes by gestational week.

Before this study was conducted, the research protocol was approved by the California Department of Public Health Internal Review Board.

**RESULTS**

The study population included 58,681 preterm births throughout 16 counties in California from May to September, 1999–2006 (Table 1). Mothers who were Hispanic (55%), who were between 25 and 34 years of age (47%), or whose educational attainment had not exceeded high school (62%) constituted most of the study population. In Table 2, the overall study mean, 5th percentile, and 95th percentile values for case mean apparent temperature (overall mean: 70.4°F (1°F = 0.56°C), case maximum apparent temperature (88.7°F), case minimum temperature (57.6°F), carbon monoxide (1.0 ppm), nitrogen dioxide (37 ppb), PM$_{2.5}$ (15.3 μg/m³), ozone (63 ppb), and sulfur dioxide (5 ppm) are listed by county. The ranges for mean and maximum apparent temperature were larger than those for minimum apparent temperature. Although the probability of birth rises with increasing gestation, the design is valid if the probability of giving birth does not change throughout the month at the aggregate level. We found that approximately the same number of births occurred every week (21% the first week, 22% the second week, 22% the third week, and 25% the fourth week).

The cumulative average weekly lag (lag 06) provided the best model fit for mean, minimum, and maximum apparent temperatures (Figure 2), although all temperature metrics were associated with significant elevated risks. Mean and minimum apparent temperature had higher per-unit effect estimates than maximum apparent temperature, although ranges for these metrics varied. Scaling by the difference between the 5th and 95th percentiles in each metric yielded virtually identical excess risks. Because mean apparent temperature consistently supplied the best overall model fit, this temperature metric with lag06 was used in subsequent analyses.

Figure 3 is a map of California with county-level estimates for the 16 counties studied. As shown, most counties had elevated risks, except for Merced and Solano, the 2 smallest, which had nonsignificant negative risks. In meta-analyses, northern California (12.1%, 95% confidence interval (CI): 7.5, 16.8) had a higher association than southern California (6.9%, 95% CI: 3.7, 10.1) ($P = 0.07$ for the difference), whereas coastal (7.9%, 95% CI: 4.1, 11.9) and inland (8.7%, 95% CI: 5.5, 13.1) areas had similar associations ($P = 0.72$). When considering associations by month of exposure, we found that the months May–July were associated with elevated risks, whereas August and September were not. We did not find a significant differential impact by year.

As demonstrated in Figure 4, all racial/ethnic groups analyzed had significantly elevated risks for weekly apparent
temperature and preterm delivery. Black mothers had the highest risk, followed by Asians, Hispanics, and whites. Differences between the estimates for any racial/ethnic group were not significant ($P = 0.17$ between blacks and whites).

Elevated risk was found across all maternal age group categories (Figure 5). A slightly higher risk was found for the younger age groups, specifically for mothers less than 20 years of age ($P = 0.04$ compared with mothers at least 35 years of age). A significant risk was also found for mothers between the ages of 25 and 34 years, whereas mothers who were at least 35 years of age had a slightly elevated but nonsignificant risk.

No significant differences were found by either infant’s sex or maternal education. Female infants (10.1%, 95% CI: 5.9, 14.4 per 10°C increase in apparent temperature) had a slightly more elevated risk, but it was not significantly different from that for male infants (7.8%, 95% CI: 4.2, 11.6; $P = 0.44$). Mothers who completed at most a high school education yielded slightly higher estimates (9.7%, 95% CI: 6.2, 13.2) than mothers who had some college education (7.0%, 95% CI: 2.7, 11.6), but this difference was not significant ($P = 0.36$).

For a sufficient number of cases, nitrogen dioxide and ozone data were available for all 16 counties, as in the primary analysis. However, some counties did not have enough cases with carbon monoxide, sulfur dioxide, or PM$_{2.5}$ data for analysis, and these counties were excluded (refer to Table 2 for counties with missing data). No significant confounding was found for any pollutant examined; the estimates for apparent temperature did not decrease with any air pollutant in the model (not shown). In the same models, no pollutant demonstrated an independently significant positive association with preterm delivery. There was also no consistent significant interaction between apparent temperature and any air pollutant.

In the analysis of preterm delivery by gestational week, the strongest impacts were observed for preterm births from 34 to 36 gestational weeks (13.5%, 95% CI: 10.2, 16.9). For earlier preterm births, however, the association was significantly negative ($-5.2\%$, 95% CI: $-9.9$, $-0.4$). When the data were limited to only full-term births, a relatively small but significant association (1.8%, 95% CI: 0.8, 2.7) was found for the same-day lag of mean daily apparent temperature. No association was found for full-term births when weekly apparent temperature was considered (0.0%, 95% CI: $0.9$, $0.9$). A significantly negative association was found for both gestational weeks 37 and 38.

**DISCUSSION**

A significant positive association was found between apparent temperature and preterm delivery during the warm season in California. Mean, maximum, and minimum apparent temperatures all had significantly elevated associations for lag days up to 1 week. When we considered vulnerable subgroups, all studied showed increased risks regardless of maternal age, racial/ethnic group, level of educational attainment, or infant’s sex. A stronger association observed earlier in the warm season could be explained by different conception patterns. Temperatures earlier in the season may also have greater impacts than those later in the season because of acclimatization.

<table>
<thead>
<tr>
<th>County</th>
<th>No. of Preterm Births</th>
<th>Maternal Race/Ethnicity</th>
<th>Maternal Age, Years</th>
<th>Maternal Education</th>
<th>Infant Sex Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alameda</td>
<td>2,812</td>
<td>19</td>
<td>23</td>
<td>32</td>
<td>24</td>
</tr>
<tr>
<td>Contra Costa</td>
<td>1,107</td>
<td>40</td>
<td>6</td>
<td>35</td>
<td>14</td>
</tr>
<tr>
<td>Fresno</td>
<td>3,100</td>
<td>24</td>
<td>10</td>
<td>54</td>
<td>7</td>
</tr>
<tr>
<td>Kern</td>
<td>2,570</td>
<td>24</td>
<td>8</td>
<td>63</td>
<td>4</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>20,900</td>
<td>13</td>
<td>10</td>
<td>65</td>
<td>11</td>
</tr>
<tr>
<td>Merced</td>
<td>422</td>
<td>23</td>
<td>5</td>
<td>61</td>
<td>6</td>
</tr>
<tr>
<td>Orange</td>
<td>3,560</td>
<td>20</td>
<td>2</td>
<td>58</td>
<td>18</td>
</tr>
<tr>
<td>Riverside</td>
<td>2,828</td>
<td>27</td>
<td>6</td>
<td>61</td>
<td>4</td>
</tr>
<tr>
<td>Sacramento</td>
<td>3,165</td>
<td>43</td>
<td>15</td>
<td>26</td>
<td>12</td>
</tr>
<tr>
<td>San Bernardino</td>
<td>4,869</td>
<td>21</td>
<td>15</td>
<td>58</td>
<td>5</td>
</tr>
<tr>
<td>San Diego</td>
<td>6,006</td>
<td>32</td>
<td>9</td>
<td>41</td>
<td>13</td>
</tr>
<tr>
<td>San Joaquin</td>
<td>2,240</td>
<td>22</td>
<td>11</td>
<td>45</td>
<td>18</td>
</tr>
<tr>
<td>Santa Clara</td>
<td>1,231</td>
<td>30</td>
<td>2</td>
<td>36</td>
<td>29</td>
</tr>
<tr>
<td>Solano</td>
<td>474</td>
<td>31</td>
<td>19</td>
<td>33</td>
<td>14</td>
</tr>
<tr>
<td>Tulare</td>
<td>998</td>
<td>24</td>
<td>2</td>
<td>67</td>
<td>5</td>
</tr>
<tr>
<td>Ventura</td>
<td>2,399</td>
<td>31</td>
<td>2</td>
<td>55</td>
<td>7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>58,681</td>
<td>22</td>
<td>10</td>
<td>55</td>
<td>11</td>
</tr>
</tbody>
</table>
Table 2. Exposure Metrics for Weekly Average (Lag06) Apparent Temperature and Air Pollutants, by California County, May–September, 1999–2006

<table>
<thead>
<tr>
<th>County</th>
<th>Case Mean Apparent Temperature, °F (5th, 95th Percentile)</th>
<th>Case-Control Difference in Mean Apparent Temperature, °F</th>
<th>Case Maximum Apparent Temperature, °F (5th, 95th Percentile)</th>
<th>Case Minimum Apparent Temperature, °F (5th, 95th Percentile)</th>
<th>Case Mean O3 Level, ppb (5th, 95th Percentile)</th>
<th>Case Mean CO Level, ppm (5th, 95th Percentile)</th>
<th>Case Mean NO2 Level, ppb (5th, 95th Percentile)</th>
<th>Case Mean SO2 Level, ppb (5th, 95th Percentile)</th>
<th>Case Mean PM2.5 Level, μg/m³ (5th, 95th Percentile)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alameda</td>
<td>61.3 (53.2, 68.0)</td>
<td>2.5</td>
<td>77.9 (64.7, 91.7)</td>
<td>50.2 (43.6, 55.5)</td>
<td>35 (19, 52)</td>
<td>0.7 (0.4, 1.3)</td>
<td>23 (12, 36)</td>
<td>3 (1, 6)</td>
<td>10.6 (6.3, 16.4)</td>
</tr>
<tr>
<td>Contra Costa</td>
<td>64.0 (54.2, 74.3)</td>
<td>2.9</td>
<td>84.8 (68.1, 100.5)</td>
<td>49.5 (42.5, 55.0)</td>
<td>51 (37, 71)</td>
<td>0.5 (0.3, 0.8)</td>
<td>17 (10, 28)</td>
<td>5 (1, 12)</td>
<td>12.1 (8.3, 16.2)</td>
</tr>
<tr>
<td>Fresno</td>
<td>75.7 (62.5, 87.5)</td>
<td>4.4</td>
<td>95.9 (78.4, 109.1)</td>
<td>57.9 (47.6, 68.4)</td>
<td>80 (57, 104)</td>
<td>0.6 (0.2, 1.1)</td>
<td>28 (16, 44)</td>
<td>3 (1, 5)</td>
<td>10.6 (6.3, 16.4)</td>
</tr>
<tr>
<td>Kern</td>
<td>76.9 (62.3, 89.3)</td>
<td>4.4</td>
<td>93.8 (75.6, 107.7)</td>
<td>61.1 (48.6, 73.6)</td>
<td>79 (60, 98)</td>
<td>1 (0.5, 1.6)</td>
<td>40 (19, 58)</td>
<td>5 (3, 7)</td>
<td>12.1 (8.3, 16.2)</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>70.3 (59.7, 80.6)</td>
<td>2.9</td>
<td>87.6 (70.7, 104.3)</td>
<td>59.0 (49.9, 66.6)</td>
<td>60 (40, 85)</td>
<td>1.2 (0.5, 2.1)</td>
<td>46 (27, 73)</td>
<td>6 (1, 14)</td>
<td>18.1 (10, 27.9)</td>
</tr>
<tr>
<td>Merced</td>
<td>69.9 (58.5, 81.4)</td>
<td>3.3</td>
<td>95.0 (79.2, 107.7)</td>
<td>49.6 (42.2, 58.3)</td>
<td>79 (57, 99)</td>
<td>23 (13, 36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orange</td>
<td>70.3 (59.6, 80.2)</td>
<td>2.5</td>
<td>86.2 (70.6, 99.6)</td>
<td>59.4 (50.4, 68.4)</td>
<td>62 (46, 78)</td>
<td>0.7 (0.3, 1.4)</td>
<td>27 (14, 44)</td>
<td>3 (1, 6)</td>
<td>14.4 (9, 21.5)</td>
</tr>
<tr>
<td>Riverside</td>
<td>77.1 (61.3, 94.4)</td>
<td>3.9</td>
<td>98.9 (78.8, 113.7)</td>
<td>59.9 (48.0, 76.0)</td>
<td>82 (58, 105)</td>
<td>1.1 (0.3, 2.3)</td>
<td>33 (16, 56)</td>
<td>4 (0, 11)</td>
<td>24.9 (14.2, 38.3)</td>
</tr>
<tr>
<td>Sacramento</td>
<td>71.6 (59.9, 82.0)</td>
<td>4.1</td>
<td>93.6 (75.7, 107.4)</td>
<td>55.3 (47.1, 63.0)</td>
<td>64 (46, 86)</td>
<td>0.7 (0.3, 1.5)</td>
<td>24 (12, 43)</td>
<td>4 (1, 9)</td>
<td>8.5 (4.9, 14.6)</td>
</tr>
<tr>
<td>San Bernardino</td>
<td>73.9 (59.7, 85.6)</td>
<td>3.8</td>
<td>96.2 (75.4, 111.6)</td>
<td>57.7 (47.9, 67.5)</td>
<td>84 (57, 109)</td>
<td>1 (0.4, 1.7)</td>
<td>50 (32, 70)</td>
<td>3 (1, 7)</td>
<td>23.7 (13.6, 37.7)</td>
</tr>
<tr>
<td>San Diego</td>
<td>68.4 (58.3, 78.0)</td>
<td>2.4</td>
<td>83.4 (67.3, 101.5)</td>
<td>58.4 (48.2, 66.9)</td>
<td>52 (38, 67)</td>
<td>1 (0.5, 1.7)</td>
<td>25 (15, 37)</td>
<td>6 (2, 12)</td>
<td>12.9 (7.6, 18.1)</td>
</tr>
<tr>
<td>San Joaquin</td>
<td>70.7 (59.0, 81.2)</td>
<td>3.8</td>
<td>91.9 (75.2, 104.3)</td>
<td>54.6 (45.1, 64.0)</td>
<td>58 (43, 78)</td>
<td>0.7 (0.4, 1.2)</td>
<td>27 (17, 43)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Santa Clara</td>
<td>63.9 (53.6, 71.5)</td>
<td>2.7</td>
<td>83.0 (67.4, 96.5)</td>
<td>50.7 (41.5, 56.6)</td>
<td>43 (26, 66)</td>
<td>1.1 (0.6, 1.6)</td>
<td>33 (19, 50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solano</td>
<td>65.1 (55.7, 74.9)</td>
<td>2.9</td>
<td>86.4 (70.7, 100.7)</td>
<td>49.8 (41.8, 55.3)</td>
<td>46 (34, 61)</td>
<td>0.6 (0.3, 0.9)</td>
<td>17 (10, 26)</td>
<td>3 (1, 6)</td>
<td>10.6 (6.3, 16.4)</td>
</tr>
<tr>
<td>Tulare</td>
<td>74.4 (60.7, 85.5)</td>
<td>4.1</td>
<td>96.8 (77.7, 110.1)</td>
<td>55.6 (45.2, 65.4)</td>
<td>80 (59, 100)</td>
<td>0.7 (0.3, 1.2)</td>
<td>31 (20, 48)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventura</td>
<td>65.0 (56.6, 73.4)</td>
<td>2.5</td>
<td>77.7 (65.6, 91.7)</td>
<td>54.6 (46.8, 62.1)</td>
<td>59 (43, 84)</td>
<td>0.6 (0.3, 1.3)</td>
<td>21 (13, 38)</td>
<td>3 (0, 11)</td>
<td>10.6 (6.3, 16.4)</td>
</tr>
<tr>
<td>Overall</td>
<td>70.4 (58.1, 83.1)</td>
<td>3.1</td>
<td>88.7 (70.2, 106.7)</td>
<td>57.6 (47.1, 67.2)</td>
<td>63 (37, 95)</td>
<td>1.0 (0.3, 1.9)</td>
<td>37 (15, 65)</td>
<td>5 (1, 12)</td>
<td>15.3 (7.5, 26.7)</td>
</tr>
</tbody>
</table>

Abbreviations: CO, carbon monoxide; NO2, nitrogen dioxide; O3, ozone; PM2.5, particulate matter less than 2.5 μm in aerodynamic diameter; SO2, sulfur dioxide.

*a 1°F = 0.56°C.
No significant difference by infant’s sex or maternal education was observed. Although a distinction by infant’s sex was not expected, maternal education was used as a proxy for socioeconomic status. Maternal race/ethnicity and maternal age may have served as better markers of socioeconomic status, since younger mothers had greater risks. Younger mothers are generally of lower socioeconomic status, have completed less education, and exhibit more risky behavioral patterns (34), particularly mothers of preterm infants (35–37). Our findings were significant across all racial/ethnic groups, with the strongest associations for black and Asian mothers. Previous investigators have also indicated disparities in birth outcomes by race/ethnicity for black (38–40), Hispanic (39), and Native American (41) infants.

Among preterm births, the effect estimates were all significantly elevated for up to 6 days, with a weekly average of apparent temperature being the best predictor. The same magnitude of association and statistical significance was not found for full-term births at 37–44 gestational weeks. The estimates tapered off after the first day for the full-term births and became significantly negative after a few days,

Figure 2. Map of California showing county-level estimates for the estimated percent change associated with a 10°F (5.6°C) increase in weekly average apparent temperature (lag06) and preterm birth, May–September, 1999–2006. For each county, 95% confidence intervals are given in parentheses.
suggestive of a harvesting pattern not observed in the preterm delivery analysis. Harvesting refers to the phenomenon by which an exposure merely accelerates the occurrence of an outcome by a few days. In other analyses, we found that preterm births occurring later in the pregnancy had greater associations with apparent temperature than those occurring earlier. However, there may have been some misclassification of gestational age, since it was based on the date of the last menstrual period, which may be unknown for some women. A broader definition for preterm delivery such as 20–36 weeks, as used in our main analyses, is subject to less error.

Much of the prior evidence for preterm delivery from environmental exposures has been based on air pollutants.
In this study, temperature was found to be associated with preterm delivery independent of air pollutants. Because this analysis was restricted to the warm season and short-term associations of up to 1 week, any association with air pollutants may have been masked by ambient heat exposure. Air pollutants, on the other hand, may have had a larger impact if longer-term exposure windows, such as trimester averages, were considered (14, 42).

To our knowledge, only 2 previous investigations have focused on preterm labor or delivery and ambient temperature (18, 19). In a large time-series study recently conducted in London, United Kingdom, no associations were reported between preterm delivery and short-term meteorologic or air pollution variables (18). In a preliminary analysis in New York examining heat-humidity index, an association with preterm labor was found, but not with preterm delivery (19). With only a few cases in the study, it is possible that potentially small associations may have been missed. Investigators from both studies found that a weekly lag, as used in our study, was most relevant in terms of preterm delivery. Single dates could result in misclassification bias since labor may last more than 1 day, or a mother may not be admitted until a day following the high heat-humidity index (19). These 2 previous studies did not analyze specific subgroups. Health effects from ambient temperature are based primarily on studies of mortality (43, 44).

Since preterm delivery has multiple etiologies, a clear biologic mechanism or cause is unknown. One possible explanation may be increased dehydration with heat exposure, which could decrease uterine blood flow and increase pituitary secretion of antidiuretic hormone and oxytocin to induce labor (45). Pregnant women may not be able to thermoregulate efficiently. When body temperatures rise, the body generally shifts blood flow from the vital organs to the skin’s surface in an effort to cool down (46). Thus, thermoregulation may be inadequate when too much blood is diverted from the vital organs of the mother and the developing fetus (46). Increased blood viscosity, elevated cholesterol levels associated with higher temperatures, and a higher sweating threshold have also been reported in susceptible subgroups (47).

There are several limitations to this study. We relied on ecologically monitored data rather than on individual monitoring to assign exposure. By limiting the study to mothers whose residential zip codes were within 10 km of a meteorologic monitor, we minimized exposure misclassification, but it still could have been a problem, especially in coastal areas. We had to rely on data provided on the birth certificates, and we did not have information on several characteristics, such as individual income level, to adjust for socioeconomic status more efficiently than relying on maternal age and racial/ethnic group. We also did not have information on occupational address or air conditioning status, so we could not account for these variables in our analysis. For most cases, utilizing the zip code for the residential address reported on the birth certificate should be sufficient to characterize exposure for the week prior to birth.

This is the first known large-scale, population-based epidemiologic study of ambient temperature and preterm delivery in the United States covering an extensive time period. It is also the first study known to find significant positive associations and to examine potentially vulnerable subgroups. All demographic subgroups examined had elevated risks, although some differences were found between groups. This study focused on high ambient temperature, and the association during a heat wave is likely to be substantially greater, as was found in a recent mortality study (48). The Intergovernmental Panel on Climate Change...
states that hot days and nights, as well as heat waves, have become more frequent in recent years, and their duration and intensity are likely to increase in the future (49). Given the significant associations for apparent temperature and preterm delivery found in this study, more large-scale studies of temperature and preterm delivery are warranted. Biologic acclimatization and susceptible subgroups should be considered.

ACKNOWLEDGMENTS

Author affiliation: California Office of Environmental Health Hazard Assessment, Air Pollution Epidemiology Section, Oakland, California (Rupa Basu, Brian Malig, Bart Ostro).

The opinions expressed in this article are solely those of the authors and do not represent the policy or position of the state of California or the California Environmental Protection Agency.

Conflict of interest: none declared.

REFERENCES

12. Wilhelm M, Ritz B. Local variations in CO and particulate air pollution and adverse birth outcomes in Los Angeles County, California, USA. Environ Health Perspect. 2005;113(9):1212–1221.


