ORIGINAL PAPER

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Funding: Funded by the Fogarty International Center, (FIC) the National Institute of Aging (NIA) and the National Institute of Environmental Health Sciences (NIEHS) under the Global Environmental and Occupational Health program award 3U01TW010107-06S2 and 2URTW010114-06.

Conflicts of interest: The authors declare that they have no conflicts of interest.

Ethical considerations: The study protocol was reviewed and approved by the Universidad Peruana Cayetano Heredia IRB, under file 134-11-23 (SIDISI 210818).

Received: 6 October 2023

Accepted: 11 October 2023

Online publication:

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Cite as: Fano-Sizgorich D, Vásquez-Velásquez C, Sernaqué V, Gonzales GF. Maximum apparent temperature is associated with lower birth weight in a population exposed to constant high ambient temperature in Piura, Peru. Rev peru ginecol obstet. 2023;69(4). DOI:

Maximum apparent temperature is associated with lower birth weight in a population exposed to a constant high ambient temperature in Piura, Peru

La temperatura máxima aparente se asocia con un menor peso al nacer, en una población expuesta a una temperatura ambiente alta y constante en Piura, Perú

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DOI:

ABSTRACT
Objective: To evaluate the association between maximum apparent temperature (HImax) during pregnancy with birth weight in newborns in the province of Piura, 2011-2016. Methods: Semi-ecological study in which maternal-perinatal data from Santa Rosa Hospital (N=17,788) and apparent maximum temperature data were evaluated. Four exposure windows were analyzed: the entire pregnancy and each gestational trimester, which were assigned according to date of birth and gestational age, categorized into quartiles. Linear regression models were constructed to evaluate the association between variables. Results: A negative association was found between birth weight and HImax in all exposure windows except in the first trimester. The largest decrease in birth weight was observed in the P95 exposure group in the whole pregnancy (-38.50 95%CI -71.46; -5.53) and third trimester (-70.48 95%CI -102.69; -38.28) exposure windows, but not in the second trimester. Conclusions: HImax during pregnancy is associated with lower birth weight, but with different susceptibility depending on the stage of pregnancy.
Key words: Hot temperature, Heat, Birth weight, Peru, Latin America

RESUMEN
Objetivo. Evaluar la asociación entre la temperatura máxima aparente (HImax) durante el embarazo con el peso al nacer en recién nacidos de la provincia de Piura, 2011 a 2016. Métodos. Estudio semi-ecológico en el que se evaluaron datos materno-perinatales del Hospital Santa Rosa (N=17,788) y datos de temperatura máxima aparente. Se analizaron cuatro ventanas de exposición: todo el embarazo y cada trimestre gestacional, los cuales fueron asignadas según fecha de nacimiento y edad gestacional, categorizados en cuartiles. Se construyeron modelos de regresión lineal para evaluar la asociación entre las variables. Resultados. Se encontró una asociación negativa entre el peso al nacer y el HImax en todas las ventanas de exposición, excepto en el primer trimestre. La mayor disminución del peso al nacer se observó en el grupo de exposición P95 en las ventanas de exposición de todo el embarazo (-38,50 IC95% -71,46 a -5,53) y del tercer trimestre (-70,48 IC95% -102,69 a -38,28), pero no en el del segundo trimestre. Conclusiones. El HImax durante el embarazo se asocia con un menor peso al nacer, pero con diferente susceptibilidad según la etapa del embarazo.
Palabras clave. Temperatura alta, Calor, Peso al nacer, Perú, América latina

Introduction

The National Aeronautics and Space Administration (NASA) has reported an exponential increase in global temperature anomalies from 1920 to the present[1]. In addition, a number of unusual weather events have affected the quality of life of people around the world, posing challenges to the health systems of many countries[2]. For example, rates of diarrhea and vector-borne diseases have increased in tropical locations and warm climate regions[3,4], also affecting the reproductive performance of affected populations[5].

Several studies have provided evidence on the effects of environmental pollutants and other factors on human health[6,7], with infants, the elderly, and pregnant women being the most vulnerable populations[8,9]. Some studies have explored the effects of environmental temperatures on perinatal outcomes, increasing the risk of, among others, low birth weight[10]. A review of the literature found that peaks in low birth weight occur mainly in the summer and winter seasons[11]; however, the greatest effect has been found to be associated with heat stress during exposure to elevated temperatures[12] or in periods of rapidly increasing environmental temperature[13].

During pregnancy, physiological and hormonal changes occur that may influence the body's ability to thermoregulate[14]. In high temperature environments, the functionality of the placenta may be affected, hindering the growth and development of the fetus[15]. This reveals the need to address the effects in understudied equatorial countries, such as Peru, since most research focuses on countries with very marked seasonal temperatures.

Conditions such as low birth weight (LBW) are not only markers of perinatal morbidity and mortality, but can also have repercussions later in life, leading to metabolic syndrome, type 2 diabetes, coronary heart disease[16,17]. All these conditions can affect the economic status and quality of life of individuals. Therefore, it is important to identify the factors that promote the development of these conditions.

The Piura region in northern Peru (latitude W80°37'58.15", longitude S5°11'40.16") is located close to the equator and has some of the highest year-round temperatures in the country. It is possible that in this region exposure to high temperatures is affecting pregnancies and fetal development and increasing the risks of the aforementioned conditions.

Therefore, this study aimed to evaluate the association of maximum apparent temperature (heat index) and birth weight at different stages of pregnancy in the province of Piura, during the period 2011-2016.

Methods

The present study is a retrospective semi-ecological design that seeks to evaluate the association between exposure to high environmental temperatures during pregnancy with birth weight in the province of Piura, during the period 2011-2016.

Piura is located in northern Peru, with coordinates 4º 5' and 6º 22' south latitude and 79º 00' and 81º 7' west longitude, with an altitude of 49 m.a.s.l. The area has a hot, desert, and oceanic climate, with ambient temperatures above the national average due to its proximity to the equator, which is around 30°C.

The study area consists of 10 districts, with a total area of 6,211.61 km2. It has an estimated population of 894,847 inhabitants, of which approximately 190,000 are women of reproductive age (15-45 years old).

A total of 16,247 live births were registered during 2011. This hospital attends the largest number of births in Piura.

The study population is constituted by live births residing in the province of Piura during the years 2011-2016, this being the study period. Maternal-perinatal information is stored in the Perinatal Information System (PIS) of the Santa Rosa Hospital, whose registry began in 2000.

The PIS is a software that allows recording and storing the information corresponding to the mother from her first care in any of the health facilities, such as, for example, the mother's age, district of residence, weight, height, diagnosis of preeclampsia, among others. Similarly, the newborn's information is recorded and linked to the respective mother with a unique identification code, showing information such as gestational age at birth, birth weight and height at birth.

The database obtained from the PIS had records for the years 2000-2017, but only years in which births were reported for all months were considered in the study. Based on this criterion, the period 2011-2016 was eligible for the study.

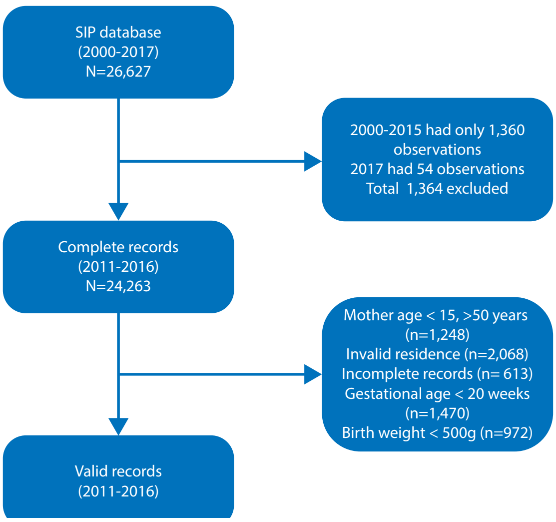
All births occurring at Santa Rosa Hospital were included in the study. Exclusion criteria were maternal age <15 and >50 years, maternal residence outside the province of Piura, neonates weighing less than 500 grams (<500 g), gestational age less than 20 weeks because they were considered spontaneous or induced abortions. Multiple pregnancies and those with missing data on the outcome variables of interest were excluded. Figure 1 shows the flow chart for record selection. A total of 17,788 valid records were included, with no missing values on key variables. The statistical power of each of the models can be found in the Supplementary Material.

Birth weight was defined as the weight assigned to the neonate immediately after birth. The data are expressed in grams, are continuous in nature, and are presented on a ratio scale. Data on birth weight for each newborn are recorded in the PIS database.

Other variables such as maternal age at conception, pregestational body mass index, preeclampsia, gestational diabetes mellitus, employment status, educational level, urinary tract infection (UTI), smoking and sex of the newborn were considered for the analysis.

Maximum temperature and relative humidity (RH) data were obtained through the NASA POWER platform (https://power.larc.nasa.gov/data-access-viewer/), which allows the download of gridded satellite meteorological data.

FIGURE 1. FLOWCHART FOR THE SELECTION OF VALID RECORDS.



The data are processed using the MERRA-2 model, which provides geospatial information from 1980 (https://gmao.gsfc.nasa.gov/reanalysis/MERRA-2/).

The study area is segmented into 4 grids based on the software resolution (0.5° latitude by 0.625° longitude). For each grid, the historical meteorological information corresponding to the period 01/01/2010 - 12/31/2016 was downloaded. Subsequently, the maximum temperature and relative humidity values for each day were averaged. Once the daily average value was obtained, the daily average apparent temperature (HI) of the province was calculated according to the formula indicated by the National Oceanic and Atmospheric Administration (NOAA, https://www.wpc.ncep.noaa.gov/html/heatindex_equation.shtml). For this purpose, temperatures were first transformed to their equivalent in degrees Fahrenheit; then the indicated formula was applied:

$$HI=-42.379+2.04901523*T+10.14333127*RH-0.22475541*T*RH-0.00683783*T*T-0.05481717*RH*RH+0.00122874*T*T*RH+0.00085282*T*RH*RH-0.00000199*T*T*RH*RH$$

Where HI is the apparent temperature, T is the temperature in degrees Fahrenheit, RH is the relative humidity.

Finally, the maximum apparent temperature (HImax) was converted to its equivalent in degrees Celsius, obtaining a daily value.

Four exposure windows were constructed: full pregnancy, third trimester, second trimester and first trimester. For this purpose, HImax was averaged according to the gestational age at birth of the neonate, assigned according to the date of delivery. Exposure was separated into quartiles with an additional level for those above the 95th percentile, giving a total of 5 levels of exposure.

On ethical considerations, the present study did not involve any danger to the identity of the neonates and mothers, since the database provided by the Santa Rosa Hospital was anonymous, identifying the mother-baby dyad by a unique code. In addition, the database did not contain personal information that would allow identification of the study subject, such as home address or telephone number. Only the mother's district of residence was available to select neonates according to inclusion/exclusion criteria.

Residence data were not shared with persons outside the study, thus guaranteeing total confidentiality of the data and anonymity of the study participants.

The study protocol was reviewed and approved by Universidad Peruana Cayetano Heredia IRB, under file 134-11-23 (SIDISI 210818).

Statistical analyses were performed with the STATA v.17 program. First, a description of the sample was made, finding the mean and standard deviation of the quantitative variables if they presented a normal distribution; otherwise, the median and interquartile range were used. For qualitative variables, absolute and relative frequencies expressed as percentages (%) were reported. Exposure was divided and assigned according to HImax groups.

Bivariate analyses were performed between the outcome variables with the different covariates considered. We used t-Student, ANOVA and Spearman regression for birth weight with the different covariates, after evaluation of the assumptions of normality, homoscedasticity, or bivariate normality.

To evaluate the effect of exposure with birth weight, a crude and covariate-adjusted linear regression analysis was performed, evaluating the assumptions of linearity, normality of the residuals and homoscedasticity. Since homoscedasticity was not met, a linear regression model with robust variances was chosen. The evaluation of the linear regression assumptions can be found in the Supplementary Material. A *p* value <0.05 was considered significant.

Results

Table 1 shows the summary statistics of maternal and neonatal characteristics. With respect to the mothers, the mean age was approximately 26 years; and a total of 1,410 women were <18 years old. About 96% of the mothers indicated that they were unemployed, dedicated exclusively to home maintenance, and more than half of them had secondary education. The prevalence of preeclampsia was 6.9%, while the prevalence of gestational diabetes was less than 1%.

Table 1. Description of maternal, neonatal and exposure variables (N=17,788) β.

Variables	N (%)
Mother's age (years)α	**26.1 ± 6.9**
Employment status	
Unemployed	16,896 (95.9)
Employed	713 (4.1)
Educational level	
No education	490 (2.8)
Elementary	3,543 (19.9)
Secondary	10,040 (56.4)
Higher education	3,715 (20.9)
Pregestational BMI (kg/m2)*	
Preeclampsia	
Yes	1,223 (6.9)
No	16,565 (93.1)
Urinary tract infection	
Yes	1,333 (7.5)
No	16,455 (92.5)
Gestational diabetes mellitus	
Yes	57 (0.3)
No	17,731 (99.7)
Smoker	
Yes	860 (4.8)
No	16,928 (95.2)
Newborn sex	
Male	8,517 (47.9)
Female	9,248 (52.1)
Gestational age at birth (weeks)*	**39 (2)**
Entire pregnancy HImax	42.3 ± 2.2
Third trimester HImax	42.6 ± 3.1
Second trimester HImax	42.4 ± 3.3
First trimester HImax	41.9 ± 3.4
Birth weight (grams)	3,235.2 ± 578.5
Low birth weight (%)	**1,299 (7.30)**
Preterm birth (%)	
Yes	1,701 (9.6)
No	16,068 (90.4)

For the variable Employment status, the category 'Employed' considers all pregnant women who expressed that they were dependent or independent workers
For the variable Education, the category 'Higher education' considers both university and technical education
α Mean ± Standard deviation
** Median (interquartile range)*
β Some variables may sum to less than 17,788 due to missing values
BMI=Body mass index

In terms of birth outcomes, female neonates predominated. Mean birth weight was 3,235 grams and mean gestational age at birth was 39 weeks, and there was a 7.30% and 9.6% prevalence of low birth weight and preterm births, respectively. The mean HImax for each of the exposure windows was greater than 40°C.

Table 2. Association between birth weight and covariates.

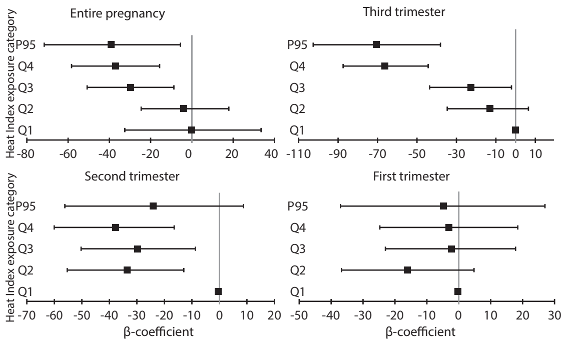
Variables	Birth weight Number (n=17,788) Mean ± SD	p
Mother's age*	0.06	<0.001
Work status		0.416
Unemployed	3,234.3 ± 579.6	
Employed	3,252.3 ± 559.2	
Study levelα		**<0.001**
No studies	3,201.4 ± 574.7	
Elementary	3,171.8 ± 601.8	
Secondary	3,242.3 ± 579.5	
Higher education	3,281.1 ± 547.6	
Pregestational BMI*	**0.15**	**<0.001**
Preeclampsia		<0.001
Yes	3,030.7 ± 609.4	
No	3,250.4 ± 573.3	
Urinary tract infection		**0.152**
Yes	3,257.1 ± 559.7	
No	3,233.5 ± 579.9	
Gestational diabetes mellitus		**0.066**
Yes	3,375.6 ± 874.9	
No	3,234.8 ± 577.3	
Smoker		**0.003**
Yes	3,290.8 ± 559.3	
No	3,232.4 ± 579.3	
Newborn sex		**<0.001**
Male	3,201.9 ± 558.5	
Female	3,267.8 ± 591.5	
Gestational age*	**0.42**	**<0.001**
Entire pregnancy HImaxα		**<0.001**
Q1 (<40.9)	3,260.5 ± 581.2	
Q2 (40.9 – 42.1)	3,255.5 ± 551.5	
Q3 (42.2 – 44.4)	3,217.7 ± 587.9	
Q4 (44.5 – 45.7)	3,240.0 ± 546.9	
P95 (>45.7)	3,079.5 ± 724.4	
Third trimester HImaxα		**<0.001**
Q1 (<40.0)	3,286.3 ± 536.6	
Q2 (40.0 – 42.6)	3,259.1 ± 540.6	
Q3 (42.7 – 44.6)	3,262.8 ± 534.1	
Q4 (44.7 – 47.8)	3,213.7 ± 536.0	
P95 (>47.8)	2,871.4 ± 968.8	
Second trimester HImaxα		**<0.001**
Q1 (<39.7)	3,272.1 ± 560.9	
Q2 (39.7 – 42.6)	3,220.5 ± 595.8	
Q3 (42.7 – 44.7)	3,236.4 ± 561.8	
Q4 (44.8 – 47.7)	3,211.5 ± 588.4	
P95 (>47.7)	3,214.2 ± 609.9	
First trimester HImaxα		**0.029**
Q1 (<39.2)	3,252.4 ± 545.5	
Q2 (39.2 – 42.0)	3,241.2 ± 561.5	
Q3 (42.1 – 44.5)	3,229.4 ± 598.0	
Q4 (44.6 – 47.6)	3,225.7 ± 603.9	
P95 (>47.6)	3,187.9 ± 614.8	

** Spearman correlation analysis*
a Analysis of variance test (ANOVA). For the rest of the variables, the t-Student test was used
BMI (Body mass index)

Table 2 shows a statistically significant association between birth weight and the different covariates, except for delivery status, urinary tract infection (UTI) and gestational diabetes. Regarding the continuous variables (maternal age, pregestational BMI and gestational age), all showed a statistically significant positive monotonic correlation, the coefficient being higher with gestational age. With respect to HImax, an association was found with each of the different exposure windows, suggesting a decrease in birth weight for each level of exposure, with the lowest weight apparently in the P95 group, especially throughout the pregnancy and third trimester window.

Figure 2 shows the results of the adjusted linear regression analysis between birth weight and HImax by exposure window. Throughout the entire pregnancy window, a statistically significant decrease in birth weight is observed from the Q3 onwards (β-coeff=-29.68 95% CI -50.75, -8.60, *p*=0.006), with the largest decrease for the Q4 and P95 exposure groups, -36.86 (95% CI -58.21, -15.45, *p*=0.001) and -38.50 grams (95% CI -71.46 to -5.53, *p*=0.022), respectively. This same association and behavior were maintained for

Figure 2. Forest plot of adjusted linear regression analysis between HImax exposure groups and birth weight in different exposure windows.



the third trimester exposure window, with the largest decrease for P95 at -70.48 grams (95% CI 102.69, -38.28). For the second trimester, the effect of HImax on birth weight was observed in the Q2, Q3 and Q4 groups. The first trimester exposure window showed no statistically significant association. All coefficients can be found in the Supplementary Material.

Discussion

The present study aimed to determine the association between maximum apparent temperature during pregnancy with birth weight in newborns in the province of Piura, 2011-2016. For this purpose, regression models were generated considering four different exposure windows: the entire pregnancy, and for each of the trimesters of gestation.

It was obtained that exposure to the upper quartiles of maximum temperature during the entire pregnancy and the third and second trimester, starting at 40°C, was associated with a decrease in birth weight, this effect being greater during the third trimester, where Q4 and P95 were associated with a reduction of 66.08 and 70.48 grams, suggesting that different stages of pregnancy are more susceptible than others.

A recent meta-analysis[18] found that exposure to high temperature is associated with a decrease in birth weight in a range of (-39.4 to -15.0 grams) similar to our results, however, it is not specified whether normal temperature or apparent temperature was used, as in our case. In a retrospective study conducted in California, USA, in which apparent temperature was evaluated in a manner similar to ours, it was observed that the greatest effect of temperature on term birth weight occurred in the third trimester when exposed to temperatures above 15 °C[19].

It is postulated that one of the mechanisms by which temperature affects pregnancy is by promoting an inflammatory state of the placenta[20]. It is possible that this mechanism is more relevant during the third trimester of gestation, since it is during this stage when the growth rate of the fetus is higher, thus explaining why we found a greater decrease in birth weight in this window of exposure, as in other studies.

It should be noted that most studies have been conducted in countries far from the equator, evaluating Asian, European. and American populations[12,13]. In these regions, environmental temperatures throughout the year would show considerable fluctuations. In addition, the monitoring station only reported the daily minimum and maximum temperature, so it was not possible to evaluate the relationship with the daily mean temperature. To our knowledge, our study is one of the first attempts to evaluate the effect of temperature on calving outcomes in an equatorial country, which helps to establish this area of research that is still novel in our region.

Although our study found significant associations between HImax and birth weight, there are some limitations. The study design only allows us to assess exposure at the population level, which creates an ecological bias. Additionally, there are other factors that could modify exposure to temperature or heat stress, such as having refrigeration equipment at home or at the workplace; or if the pregnant woman migrated to other cities during different stages of pregnancy. Our study only used data from one major hospital in Piura, which may affect the generalizability of the results, especially in areas with higher ambient temperatures. Future studies that evaluate individual exposure to temperature should be conducted. In this way, different temperature variations throughout the day and in different locations can be assessed and monitored.

Since adverse birth outcomes may affect health in adulthood by increasing the risk of metabolic diseases, new methods are needed to assess the effects of temperature and climate variability in pregnancy, such as the novel approach used in the present study to contribute, first, to the understanding of the biological effects and response to exposure and, second, to optimize prenatal controls by considering other variables such as temperature.

Conclusions

Exposure to high maximum temperatures adversely affects fetal growth, especially during the third trimester of gestation. Heat stress resulting from this exposure could be causing deficiencies at the placental level. However, these effects should be explored in future studies given the current climate change situation.

The findings of the present study could help to understand how temperature may affect reproductive health in Piura and in areas of high temperatures, providing new insights into the assessment of temperature exposure during pregnancy, which is during the stage of greatest fetal growth, which could ultimately serve as a new tool for research and evaluation of environmental epidemiology.

Acknowledgments

The authors would like to thank Ms. Paula Flores Sizgorich for her help with the graphic material.

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