

Maximum Apparent Temperature Lowers Birth Weight And Increase Hazards Of Preterm Birth In A Constant High Ambient Temperature Exposed Population In Piura, Peru

Diego Fano-Sizgorich (✉ Diego.fano.s@upch.pe)

Universidad Peruana Cayetano Heredia

Cinthya Vásquez-Velásquez

Universidad Peruana Cayetano Heredia

Vanessa Vásquez

Universidad Peruana Cayetano Heredia

Vilma Tapia

Universidad Peruana Cayetano Heredia

José Chauca

Universidad Peruana Cayetano Heredia

Víctor Sernaqué

Hospital Nacional Cayetano Heredia

Gustavo F. Gonzales

Universidad Peruana Cayetano Heredia

Research Article

Keywords: Apparent Temperature, Heat Index, Birth Outcomes, Peru, Latin America

Posted Date: March 11th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1432107/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Introduction: Exposure to high environmental temperature during pregnancy has been associated with lower birth weight, and an increased risk of preterm birth (PTB). The province of Piura is a region with a higher environmental temperature than the rest of the country; however, it is unknown how temperature would be impacting reproductive health in populations exposed to high basal temperatures.

Objective: To determine the association between maximum apparent temperature (Hlmax) during pregnancy with birth weight and preterm birth in newborns in the province of Piura, 2011-2016.

Methods: Semi-ecological study, where maternal-perinatal data from Santa Rosa Hospital (N=17,788); and maximum apparent 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. The association with birth weight was assessed by linear regression; and Cox regression for PTB.

Results: A negative association was found between birth weight and Hlmax in all exposure windows, except for the first trimester, the effect being greater during the third trimester. As for preterm birth, higher Hlmax increased the hazard of PTB, with the highest effect seen in the P95 exposed group in every exposure window; nonetheless, the first and second trimester being the most temperature-sensitive exposure windows.

Conclusion: Hlmax during pregnancy is related to lower birth weight and higher PTB hazards, but with different susceptibility according to the stage of pregnancy.

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 hot climate regions (3, 4), also affecting the reproductive output of affected populations (5).

Several studies have provided evidence on the effects of environmental contaminants 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, particularly birth weight and gestational age, indicating that elevated temperature may increase the risks of preterm birth (PTB) (10). A review of the literature found that peaks in low birth weight and preterm birth occurred 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 can influence the body's ability to thermoregulation (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 very marked seasonal temperatures.

Conditions such as low birth weight (LBW) are not only markers of perinatal morbidity and mortality, but may also have repercussions in later life, leading to metabolic syndrome, type 2 diabetes, coronary heart disease (16, 17), cancers, and reproductive, brain, or neurodegenerative disorders (18). All these conditions have the potential to 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 determine the effect of temperature and climate variability during the last eight weeks of gestation on perinatal outcomes in Piura, an area located near the equator, during the period 2011–2016.

Materials And Methods

Design and Area of Study

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

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

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

During 2011, a total of 16,247 live births were registered in the province of Piura, while the rest of the provinces in the region reported between 2000–6000 births. Births are mainly attended at the Santa Rosa de Piura Hospital (MINSA), located in the district of Castilla. This is a teaching hospital which attends the largest number of births in the province of Piura along with the Cayetano Heredia Hospital (EsSalud).

Study Population

The study population is composed of live births residing in the province of Piura during the years 2011–2016. Maternal-perinatal information of neonates is stored in the Perinatal Informatics System (SIP) of the Santa Rosa Hospital, whose registration begins in 2000.

The SIP 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, etc. Likewise, the information of the newborn is registered and nested to its respective mother, finding information such as birth weight, gestational age at birth, birth weight and height at birth.

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

Other inclusion criteria were single deliveries, maternal age range of 15 to 45 years, and maternal residence in the province of Piura. Neonates weighing less than 500 grams, gestational age less than 20 weeks were excluded as these are considered miscarriages or abortion, twin deliveries, and those with missing data on the outcome variables of interest. Figure 1 shows the flow chart for the selection of records.

Variables

Maternal and Neonatal variables

Birth Weight is defined as the weight assigned to the neonate immediately after birth. The data are expressed in grams, are continuous in nature and on a ratio scale.

Preterm Birth is defined as the birth of the newborn prior to 37 completed weeks of gestation. The variable is a qualitative, dichotomous, nominal variable. For its creation, information on gestational age at birth was used according to the date of the last menstrual period registered in the SIP.

Other variables such as mother's age at conception, pregestational body mass index, pre-eclampsia, gestational diabetes mellitus, work status, study level, urinary tract infection (UTI), smoking and newborn sex were considered for the analysis.

Maximum environmental heat index

Maximum temperature and relative humidity (RH) data were obtained through NASA's POWER platform (<https://power.larc.nasa.gov/data-access-viewer/>), which allows the download of gridded satellite meteorological data. The data are produced using the MERRA-2 model, which provides geospatial information starting in 1980 (<https://gmao.gsfc.nasa.gov/reanalysis/MERRA-2/>).

The province of Piura is segmented into 4 grids, each with a resolution of 0.5° latitude by 0.625° longitude. Historical meteorological information for the period 01/01/2010–31/12/2016 was downloaded from each grid. Subsequently, the maximum temperature and relative humidity values were averaged for each day. Once the daily average value was obtained, we proceeded to calculate the daily average apparent temperature (HI) of the province, according to the formula indicated by the National Oceanic and Atmospheric Administration (NOAA) (https://www.wpc.ncep.noaa.gov/html/heatindex_equation.shtml). To do so, the 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 (HI_{max}) was converted to its equivalent in degrees Celsius, obtaining a daily value.

Four exposure windows were constructed: whole pregnancy, third trimester, second trimester and first trimester. For this purpose, the HI_{max} 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 above percentile 95, giving a total of 5 levels of exposure.

Ethical considerations

The present study did not represent any danger or harm to the neonates and mothers in the study, since the database provided was anonymized, identifying the mother-infant dyad by means of a unique code. Likewise, the database did not contain personal information that would allow the identification of the study subject. Only the district of residence of the mother was available to select the neonates according to the inclusion/exclusion criteria.

The data on residence were not shared with persons outside the study, thus guaranteeing complete confidentiality of the data and anonymity of the study participants.

Statistical Analysis

Statistical analyses were carried out using STATA v.17 software. First, a description of the sample was made, reporting the mean and standard deviation of quantitative variables if they showed normal distribution; otherwise, the median and interquartile range were reported. For qualitative variables,

absolute and relative frequencies expressed as percentages (%) were reported. Exposure was divided and assigned according to Hlmax quartiles.

Bivariate analysis was performed between the outcome variables with the different covariates considered; t-Student, ANOVA and Spearman regression were used for Birth Weight with the different covariates, after evaluation of the assumptions of normality, homoscedasticity, or bivariate normality, while Chi-square and U-Mann Whitney and t-Student were used for Preterm Birth with the different covariates.

To evaluate the effect of exposure with birth weight, a crude linear regression analysis and adjusted for covariates was performed, evaluating the assumptions of linearity, normality of residuals and homoscedasticity; if the latter was not met, the modification of the model with robust variances was used. For Preterm birth, this outcome was considered as a time-to-event variable, determining gestational age in weeks as the follow-up time, whose maximum follow-up value was 37 weeks (gestational age at which a neonate is no longer considered preterm). A crude and adjusted Cox regression was performed. The assumption of proportionality of hazards was assessed using Schoenfeld residuals analysis, while the assumption of linearity of the model with the numerical variables was assessed using Martingale residuals. A p-value < 0.05 was considered significant.

Results

Table 1 shows the summary statistics of maternal and newborn characteristics. With respect to the mothers, the average age was approximately 26 years. About 96% of the mothers indicated that they did not have a job, dedicating themselves exclusively to home maintenance; and more than half of them had a high school education. The prevalence of preeclampsia was 6.9%, while the prevalence of gestational diabetes was less than 1%. Regarding birth outcomes, female neonates predominated; the average birth weight was 3235 grams, and the median gestational age at birth was 39, and there was a 9.6% prevalence of preterm birth. The mean Hlmax for each of the exposure windows was greater than 40°C.

Table 1
Maternal, neonatal and exposure variables description (N = 17,788)^β

Variables	N (%)
Mother's age (years) ^α	26.1 ± 6.9
Work status	
Unemployed	16,896 (95.9)
Employed	713 (4.1)
Study 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/m ²)*	25.22 (4.4)
Pre-eclampsia	
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)
Smoke	

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.

^αMean ± Standard deviation

* Median (interquartile range)

^β Some variables may add up to less than 17,788 due to missing values.

Variables	N (%)
Yes	860 (4.8)
No	16,928 (95.2)
Newborn sex	
Masculine	8,517 (47.9)
Femenine	9,248 (52.1)
Gestational age at birth (weeks)*	39 (2)
Entire pregnancy Hlmax	42.3 ± 2.2
Third trimester Hlmax	42.6 ± 3.1
Second trimester Hlmax	42.4 ± 3.3
First trimester Hlmax	41.9 ± 3.4
Birth Weight (grams)	3235.2 ± 578.5
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.	
^a Mean ± Standard deviation	
* Median (interquartile range)	
^β Some variables may add up to less than 17,788 due to missing values.	

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

Table 2
Association between birth weight and covariates

Variables	Birth Weight	p
	No (n = 17,788)	
	Mean ± SD	
Mother's age*	0.06	< 0.001
Work Status		0.416
Unemployed	3234.3 ± 579.6	
Employed	3252.3 ± 559.2	
Study level ^a		< 0.001
No studies	3201.4 ± 574.7	
Elementary	3171.8 ± 601.8	
Secondary	3242.3 ± 579.5	
Higher education	3281.1 ± 547.6	
Pregestational BMI*	0.15	< 0.001
Pre-eclampsia		< 0.001
Yes	3030.7 ± 609.4	
No	3250.4 ± 573.3	
UTI		0.152
Yes	3257.1 ± 559.7	
No	3233.5 ± 579.9	
Gestational diabetes mellitus		0.066
Yes	3375.6 ± 874.9	
No	3234.8 ± 577.3	
Smoke		0.003
Yes	3290.8 ± 559.3	
No	3232.4 ± 579.3	

*Spearman correlation analysis.

^a Analysis of Variance test (ANOVA). For the rest of the variables, the t-Student test was used.

Variables	Birth Weight	p
	No (n = 17,788)	
	Mean ± SD	
Newborn sex		< 0.001
Masculine	3201.9 ± 558.5	
Femenine	3267.8 ± 591.5	
Gestational age*	0.42	< 0.001
Entire pregnancy Hlmax ^α		< 0.001
Q1 (< 40.9)	3260.5 ± 581.2	
Q2 (40.9–42.1)	3255.5 ± 551.5	
Q3 (42.2–44.4)	3217.7 ± 587.9	
Q4 (44.5–45.7)	3240.0 ± 546.9	
P95 (> 45.7)	3079.5 ± 724.4	
Third trimester Hlmax ^α		< 0.001
Q1 (< 40.0)	3286.3 ± 536.6	
Q2 (40.0–42.6)	3259.1 ± 540.6	
Q3 (42.7–44.6)	3262.8 ± 534.1	
Q4 (44.7–47.8)	3213.7 ± 536.0	
P95 (> 47.8)	2871.4 ± 968.8	
Second trimester Hlmax ^α		< 0.001
Q1 (< 39.7)	3272.1 ± 560.9	
Q2 (39.7–42.6)	3220.5 ± 595.8	
Q3 (42.7–44.7)	3236.4 ± 561.8	
Q4 (44.8–47.7)	3211.5 ± 588.4	
P95 (> 47.7)	3214.2 ± 609.9	
First trimester Hlmax ^α		0.029

*Spearman correlation analysis.

^α Analysis of Variance test (ANOVA). For the rest of the variables, the t-Student test was used.

Variables	Birth Weight	p
	No (n = 17,788)	
	Mean ± SD	
Q1 (< 39.2)	3252.4 ± 545.5	
Q2 (39.2–42.0)	3241.2 ± 561.5	
Q3 (42.1–44.5)	3229.4 ± 598.0	
Q4 (44.6–47.6)	3225.7 ± 603.9	
P95 (> 47.6)	3187.9 ± 614.8	
*Spearman correlation analysis.		
^a Analysis of Variance test (ANOVA). For the rest of the variables, the t-Student test was used.		

Regarding preterm birth, in Table 3, there was no statistical significance with employment status, diagnosis of UTI, pregestational BMI and smoking. It was observed that the highest proportion of preterm births occurred in the group of mothers with lower educational level; likewise, pre-eclampsia and gestational diabetes were shown to be factors strongly associated with preterm birth. As for Hlmax, no statistically significant association was obtained with the third trimester exposure window, although this can be considered marginal ($p = 0.059$); however, a slight trend is seen in terms of an increase in the prevalence of preterm birth the higher the quartile of exposure of interest, and with a evident highest prevalence for the P95 group.

Table 3
Association between preterm birth and covariates

Variable	Preterm Birth		p
	No (n = 16,565)	Yes (n = 1,223)	
	n (%)	n (%)	
Mother's age*	25 (11)	25 (12)	< 0.001
Work status			0.191
Unemployed	15,260 (93.4)	1,626 (9.6)	
Employed	653 (91.8)	58 (8.2)	
Study level			0.001
No studies	428 (88.6)	55 (11.4)	
Elementary	3,141 (88.8)	398 (11.25)	
Secondary	9,121 (90.9)	915 (9.12)	
Higher education	3,378 (91.0)	333 (9.0)	
Pregestational BMI ^a	25.2 ± 4.5	25.2 ± 4.8	0.759
Pre-eclampsia			< 0.001
Yes	1,008 (82.4)	215 (17.6)	
No	15,060 (91.0)	1,486 (9.0)	
UTI			0.405
Yes	1,214 (91.1)	119 (8.9)	
No	14,854 (90.4)	1,582 (9.6)	
Gestational diabetes mellitus			< 0.001
Yes	38 (66.7)	19 (33.3)	
No	16,030 (90.5)	1,682 (9.5)	
Smoking			0.791
Yes	779 (90.7)	80 (9.3)	

*Median (interquartile range), U-Mann Whitney test.

^a Mean ± SD, t-Student.

For the analysis between qualitative variables, the Chi-square test was used.

Variable	Preterm Birth		p
	No (n = 16,565)	Yes (n = 1,223)	
	n (%)	n (%)	
No	15,289 (90.4)	1,621 (9.6)	
Newborn sex			0.032
Masculine	7,740 (91.0)	769 (9.0)	
Femenine	8,315 (90.0)	922 (10.0)	
Entire pregnancy Hlmax			0.024
Q1 (< 40.9)	4,013 (90.3)	430 (9.7)	
Q2 (40.9–42.1)	4,068 (91.5)	376 (8.5)	
Q3 (42.2–44.4)	4,002 (90.1)	438 (9.9)	
Q4 (44.5–45.7)	3,251 (91.5)	303 (8.5)	
P95 (> 45.7)	734 (72.7)	154 (17.3)	
Third trimester Hlmax			0.059
Q1 (< 40.0)	4,032 (91.4)	379 (8.6)	
Q2 (40.0–42.6)	4,008 (90.9)	400 (9.1)	
Q3 (42.7–44.6)	4,050 (91.8)	361 (8.2)	
Q4 (44.7–47.8)	3,204 (90.9)	322 (9.1)	
P95 (> 47.8)	774 (76.4)	239 (23.6)	
Second trimester Hlmax			< 0.001
Q1 (< 39.7)	4,071 (91.6)	372 (8.4)	
Q2 (39.7–42.6)	3,980 (89.6)	462 (10.4)	
Q3 (42.7–44.7)	4,407 (91.1)	398 (8.9)	
Q4 (44.8–47.7)	3,178 (89.6)	368 (10.4)	
P95 (> 47.7)	792 (88.7)	101 (11.3)	
First trimester Hlmax			< 0.001
*Median (interquartile range), U-Mann Whitney test.			
^a Mean ± SD, t-Student.			
For the analysis between qualitative variables, the Chi-square test was used.			

Variable	Preterm Birth		p
	No (n = 16,565)	Yes (n = 1,223)	
	n (%)	n (%)	
Q1 (< 39.2)	4,041 (90.9)	406 (9.1)	
Q2 (39.2–42.0)	4,096 (92.1)	350 (7.9)	
Q3 (42.1–44.5)	3,974 (89.5)	464 (10.5)	
Q4 (44.6–47.6)	3,196 (90.1)	353 (9.9)	
P95 (> 47.6)	761 (85.6)	128 (14.4)	
*Median (interquartile range), U-Mann Whitney test.			
^a Mean ± SD, t-Student.			
For the analysis between qualitative variables, the Chi-square test was used.			

Figure 2 shows the results of the adjusted linear regression analysis between birth weight and Hlmax by exposure window. In the entire pregnancy window, it can be seen a statistically significant decrease in birth weight as from Q3 (β -coeff=-29.68 95%CI -50.75, -8.60, $p = 0.006$), with the biggest decrease for Q4 and P95 exposure groups, -36.86 (95%CI -58.21, -15.45, $p = 0.001$) and - 38.50 grams (95%CI -71.46, -5.53, $p = 0.022$), respectively. This same association and behavior held for the third trimester exposure window, with the greatest decrease for P95 with - 70.48 grams (95%CI -102.69, -38.28). For the second trimester the effect of Hlmax over birth weight is seen in Q2, Q3 and Q4 groups. The first trimester exposure window did not show any statistically significant association. All coefficients can be found in **Supplementary Table 1**.

Figure 3 shows the association between Hlmax and the hazard of preterm birth, showing that for exposure during the entire pregnancy and the third trimester, only those exposed to the P95 Hlmax considerably increased the hazard for preterm birth HR = 1.93 (95%CI 1.58, 2.37, $p < 0.001$) and 2.76 (95%CI 2.30, 3.31, $p < 0.001$), respectively. Second trimester exposure window showed an increase of preterm birth hazard in Q2 (HR = 1.36 95%CI 1.16, 1.59, $p < 0.001$), Q4 (HR = 1.36 95%CI 1.16, 1.61, $p < 0.001$) and P95 (HR = 1.47 95%CI 1.16, 1.86, $p = 0.001$). For the first trimester, all Hlmax groups, except for Q2, showed increased hazards for preterm birth, with the highest effect in the P95 (HR = 1.76 95%CI 1.42, 2.18, $p < 0.001$). All coefficients can be found in **Supplementary Table 2**.

Discussion

The present study aimed to determine the association between maximum apparent temperature during pregnancy with birth weight and preterm birth in newborns in the province of Piura, 2011–2016. For this

purpose, regression models were generated considering 4 different exposure windows: entire pregnancy, and for each of the trimesters of gestation.

It was obtained that exposure to 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 was associated with a reduction of 66.08 and 70.48 grams, meaning that different stages of pregnancy progression are more susceptible than others.

A recent meta-analysis (19) 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 ambient temperature or apparent temperature was used, as in our case. In a retrospective study performed in California, United States, where apparent temperature was evaluated similar to ours, it was found that the greatest effect of temperature on birth weight at term occurred in the third trimester when exposed to temperatures higher than 15°C (20).

It is postulated that one of the mechanisms by which temperature affects pregnancy is by promoting an inflammatory state of the placenta (21). It is possible that this mechanism is more relevant during the third trimester of gestation, since it is during this stage that the growth rate of the fetus is higher, thus explaining why we found a greater decrease in birth weight in this window of exposure, like other studies.

Regarding preterm birth, we found that there Hlmax affected overall gestation increasing in 93% the risk for preterm birth when exposed to temperatures > 45.7°C (P95); but there is a greater susceptibility during the first two trimesters of gestation since almost all groups of exposure showed increased hazard for preterm birth, but the greater effect of Hlmax was found in P95 in the third trimester. In a study conducted in Sabzevar, Iran, where maximum temperatures similar to ours were observed, the hazard of preterm birth was found to increase with temperatures above 30°C (22). On the other hand, the greater susceptibility found in the first 2 trimesters agrees with those obtained in a study performed in China where more than 1 million records were evaluated, finding that exposure to temperatures above 24°C was associated with a 78% increase in the hazard of preterm birth in the first trimester, and a 41% increase in the second trimester; while in the third trimester this effect was diluted (23). This increased susceptibility during the first trimesters of gestation seems to be a characteristic mainly given in areas with a higher basal temperature, since in an evaluation conducted in China (24), provinces considered as hot areas showed a greater increase in preterm birth hazard during this period, as well as during the first week of the third trimester of gestation.

It is possible that this increased susceptibility during the first trimesters of gestation is due to heat stress impacting placental formation, as suggested by a model in pigs (25). The inflammatory state would cause deficiencies in blood vessel formation, leading to inadequate oxygenation, and thus a constant oxidative environment incapable of sustaining a pregnancy to term (26). However, it has been observed that the risk of placental abruption associated with environmental heat stress occurs mainly in pregnant women at term (27); therefore, the mechanism could be different.

Although our study found significant associations between Hlmax birth weight and preterm birth, there are some limitations. The study design only allows us to assess exposure at the population level, creating an ecological bias. To avoid these biases, future studies should include individual measurements. 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.

On the other hand, several studies have shown how pollutants, especially particulate matter (PM) < 10 and 2.5 µm and nitrogen oxides (NOx) significantly increase the risk of adverse birth outcomes (28–30); however, for the present study no information could be obtained regarding air pollutants. Likewise, social and urban factors may play an important role in terms of thermal sensation, as socioeconomic status and density of green areas interact with temperature effects (31).

On the other hand, 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 daily minimum and maximum temperature, so it was not possible to evaluate the relationship with mean daily temperature. To our knowledge, our study is one of the first attempts to evaluate the effect of temperature on birth outcomes in an equatorial country, which helps to establish this area of research that is still novel in our region.

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

Exposure to high maximum temperatures negatively affects fetal growth, especially during the third trimester of gestation; while it affects the duration of pregnancy mainly when exposure occurs during the first two trimesters. The thermal stress resulting from this exposure could be causing deficiencies at the placental level, both in the formation and functioning of the organ; however, these effects need to be explored in future studies given the current situation of climate change.

The findings of this study could help to understand how temperature may affect reproductive health in Piura, be useful to anticipate and adapt hospital obstetric services during periods of high heat; and promote public health initiatives and campaigns that could help improve the impact of temperature stress on birth outcomes. Finally, this study provides new insight 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 environmental epidemiology research and evaluation.

Declarations

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by Universidad Peruana Cayetano Heredia IRB under document number 638-21-17.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The dataset supporting the conclusions of this article is available in the Science Data Bank repository, <https://www.scidb.cn/en/detail?dataSetId=caa782c509bf4b4e8bd3f991b55e0e68>.

COMPETING INTERESTS

The authors declares that they have no competing interests.

FUNDING

Research reported in this publication was supported by the National Institutes of Health Fogarty International Center, National Institutes of Environmental Health Sciences, National Cancer Institute, Centers for Disease Control and Prevention and the NIH under Award Number for research Grant U01 TW0101 07.

AUTHORS' CONTRIBUTION

Diego Fano-Sizgorich: Conceptualization, Methodology, Formal Analysis, Investigation, Data Curation, Writing - Original Draft, Writing – Review & Editing, Visualization. Cinthya Vásquez-Velásquez: Formal Analysis, Writing – Original Draft, Writing – Review & Editing. Vanessa Vásquez: Investigation, Project Administration. Vilma Tapia: Formal Analysis, Writing – Review & Editing. José Chauca: Conceptualization, Methodology, Formal Analysis, Data Curation. Víctor Sernaqué: Investigation. Gustavo F Gonzales: Conceptualization, Methodology, Writing – Review & Editing, Supervision, Project Administration, Funding Acquisition.

ACKNOWLEDGEMENTS

The authors thank Ms. Paula Flores Sizgorich for helping with the artwork.

References

1. NASA. Global Temperature | Vital Signs – Climate Change: Vital Signs of the Planet. 2019. Available from: <https://climate.nasa.gov/vital-signs/global-temperature/>

2. Rossati A. Global warming and its health impact. Vol. 8, International Journal of Occupational and Environmental Medicine. NIOC Health Organization; 2017. p. 7–20.
3. Kurane I. The Effect of Global Warming on Infectious Diseases. Vol. 1, Osong Public Health and Research Perspectives. Elsevier; 2010. p. 4–9.
4. Musengimana G, Mukinda FK, Machekano R, Mahomed H. Temperature variability and occurrence of diarrhoea in children under five-years-old in Cape Town metropolitan sub-districts. *Int J Environ Res Public Health*. 2016 Sep 1;13(9).
5. Boland MR, Fieder M, John LH, Rijnbeek PR, Huber S. Female Reproductive Performance and Maternal Birth Month: A Comprehensive Meta-Analysis Exploring Multiple Seasonal Mechanisms. *Sci Rep*. 2020 Dec 1;10(1):1–13.
6. Analitis A, De' Donato F, Scortichini M, Lanki T, Basagana X, Ballester F, et al. Synergistic effects of ambient temperature and air pollution on health in Europe: Results from the PHASE project. *Int J Environ Res Public Health*. 2018 Sep 1;15(9).
7. Bose S, Romero K, Psoter KJ, Curriero FC, Chen C, Johnson CM, et al. Association of traffic air pollution and rhinitis quality of life in Peruvian children with asthma. *PLoS One*. 2018;13(3):e0193910.
8. Levy BS, Patz JA. Climate Change, Human Rights, and Social Justice. *Ann Glob Heal*. 2015;81(3):310.
9. Potts M, Henderson CE. Global warming and reproductive health. *Int J Gynecol Obstet*. 2012;119(SUPPL.1).
10. Kuehn L, McCormick S. Heat exposure and maternal health in the face of climate change. Vol. 14, International Journal of Environmental Research and Public Health. MDPI AG; 2017.
11. Strand LB, Barnett AG, Tong S. The influence of season and ambient temperature on birth outcomes: A review of the epidemiological literature. Vol. 111, Environmental Research. Academic Press; 2011. p. 451–62.
12. Zhang Y, Yu C, Wang L. Temperature exposure during pregnancy and birth outcomes: An updated systematic review of epidemiological evidence. Vol. 225, Environmental Pollution. Elsevier Ltd; 2017. p. 700–12.
13. Carolan-Olah M, Frankowska D. High environmental temperature and preterm birth: A review of the evidence. *Midwifery*. 2014 Jan;30(1):50–9.
14. Charkoudian N, Hart ECJ, Barnes JN, Joyner MJ. Autonomic control of body temperature and blood pressure: influences of female sex hormones. Vol. 27, Clinical Autonomic Research. Dr. Dietrich Steinkopff Verlag GmbH and Co. KG; 2017. p. 149–55.
15. Soultanakis-Aligianni HN. Thermoregulation during exercise in pregnancy. *Clin Obstet Gynecol*. 2003 Jun;46(2):442–55.
16. Smith CJ, Ryckman KK, Barnabei VM, Howard B V, Isasi CR, Sarto GE, et al. The impact of birth weight on cardiovascular disease risk in the Women's Health Initiative. *Nutr Metab Cardiovasc Dis*. 2016;26(3):239–45.

17. Valente MH, Gomes FM da S, Benseñor IJM, Brentani AVM, Escobar AM de U, Grisi SJFE. Relation between Birth Weight, Growth, and Subclinical Atherosclerosis in Adulthood. *Biomed Res Int.* 2015;2015:1–10.
18. Tchernitchin AN, Gaete L. Influence of environmental pollutants on human gestation: Cause of adult pathologies. *Rev Chil Pediatr.* 2018 Nov 1;89(6):761–5.
19. Chersich MF, Pham MD, Areal A, Haghighi MM, Manyuchi A, Swift CP, et al. Associations between high temperatures in pregnancy and risk of preterm birth, low birth weight, and stillbirths: systematic review and meta-analysis. *BMJ.* 2020;371.
20. Basu R, Rau R, Pearson D, Malig B. Temperature and Term Low Birth Weight in California. *Am J Epidemiol.* 2018 Nov 1;187(11):2306–14.
21. Kumar P, Rathore B, Saxena AK, Purohit DC, Mathur N, Paul BN. Role of TNF- α in prenatal alterations in dams of mice under thermal stress. *Lab Anim.* 2006;40(2):172–9.
22. Mohammadi D, Naghshineh E, Sarsangi A, Sakhvidi MJZ. Environmental extreme temperature and daily preterm birth in Sabzevar, Iran: a time-series analysis. *Environ Health Prev Med.* 2019;24(5).
23. Wang YY, Li Q, Guo Y, Zhou H, Wang QM, Shen HP, et al. Ambient temperature and the risk of preterm birth: A national birth cohort study in the mainland China. *Environ Int.* 2020 Sep 1;142:105851.
24. Guo T, Wang Y, Zhang H, Zhang Y, Zhao J, Wang Y, et al. The association between ambient temperature and the risk of preterm birth in China. *Sci Total Environ.* 2018 Feb 1;613–614:439–46.
25. Zhao W, Liu F, Bell AW, Le HH, Cottrell JJ, Leury BJ, et al. Controlled elevated temperatures during early-mid gestation cause placental insufficiency and implications for fetal growth in pregnant pigs. *Sci Rep.* 2020;10(1).
26. Alijotas-Reig J, Esteve-Valverde E, Ferrer-Oliveras R, Llorba E, Gris JM. Tumor Necrosis Factor-Alpha and Pregnancy: Focus on Biologics. An Updated and Comprehensive Review. Vol. 53, *Clinical Reviews in Allergy and Immunology.* Humana Press Inc.; 2017. p. 40–53.
27. He S, Kosatsky T, Smargiassi A, Bilodeau-Bertrand M, Auger N. Heat and pregnancy-related emergencies: Risk of placental abruption during hot weather. *Environ Int.* 2018;111:295–300.
28. Arroyo V, Díaz J, Salvador P, Linares C. Impact of air pollution on low birth weight in Spain: An approach to a National Level Study. *Environ Res.* 2019 Apr 1;171:69–79.
29. Guo LQ, Chen Y, Mi BB, Dang SN, Zhao DD, Liu R, et al. Ambient air pollution and adverse birth outcomes: a systematic review and meta-analysis. *J Zhejiang Univ Sci B.* 2019 Mar 1;20(3):238–52.
30. Klepac P, Locatelli I, Korošec S, Künzli N, Kukec A. Ambient air pollution and pregnancy outcomes: A comprehensive review and identification of environmental public health challenges. Vol. 167, *Environmental Research.* Academic Press Inc.; 2018. p. 144–59.
31. Son JY, Lee JT, Lane KJ, Bell ML. Impacts of high temperature on adverse birth outcomes in Seoul, Korea: Disparities by individual- and community-level characteristics. *Environ Res.* 2019 Jan 1;168:460–6.

Figures

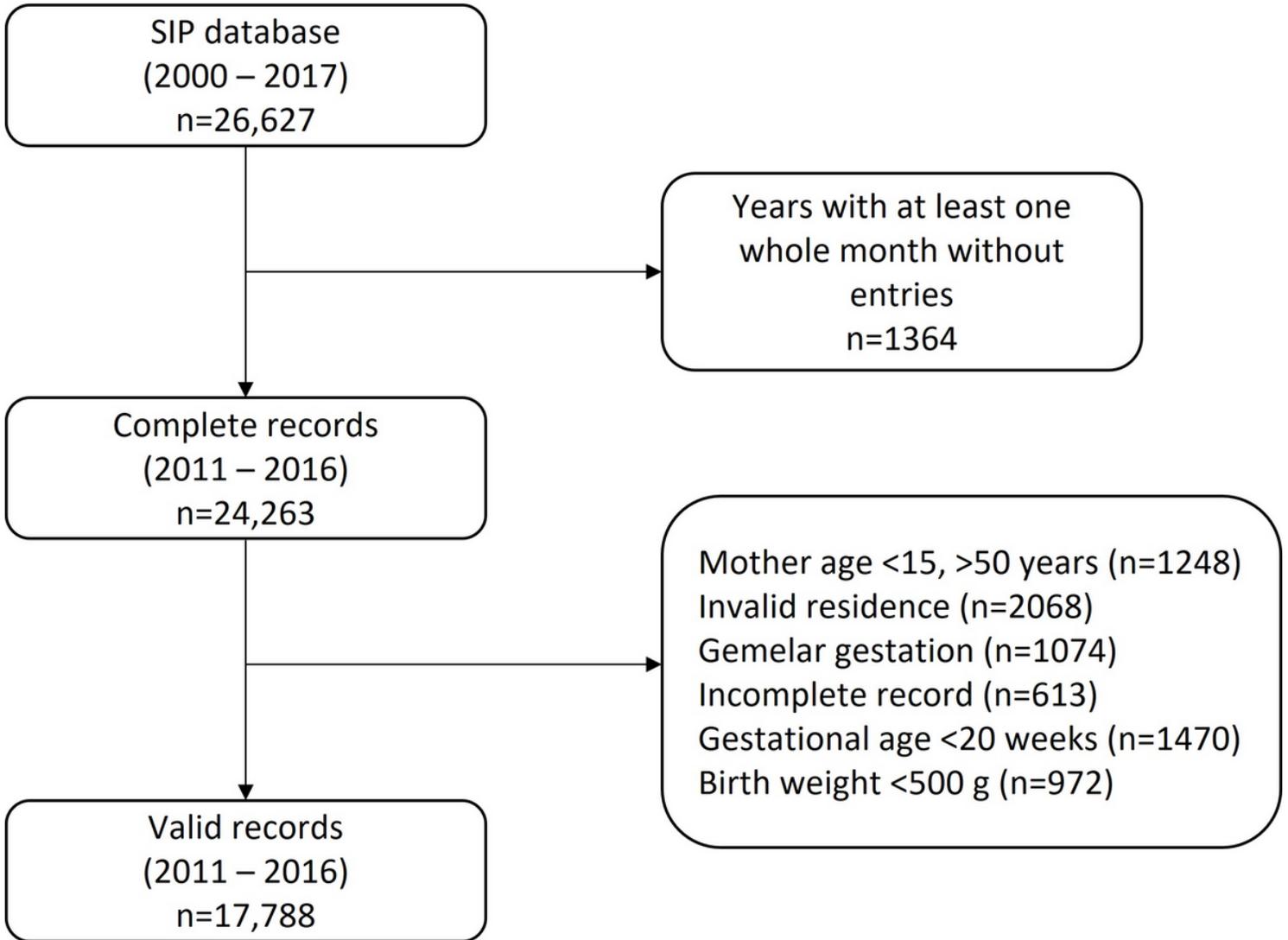


Figure 1

Flow diagram for valid registries selection

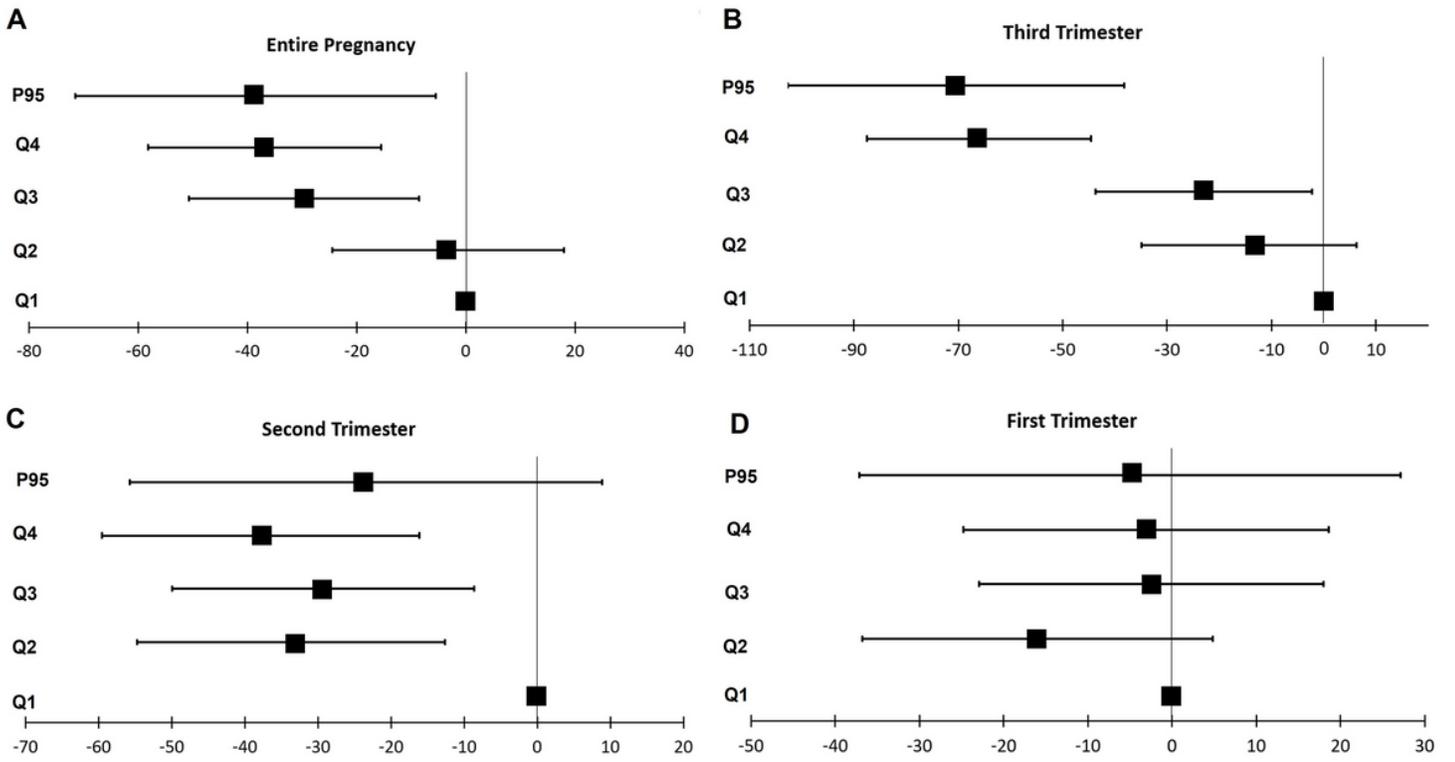


Figure 2

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

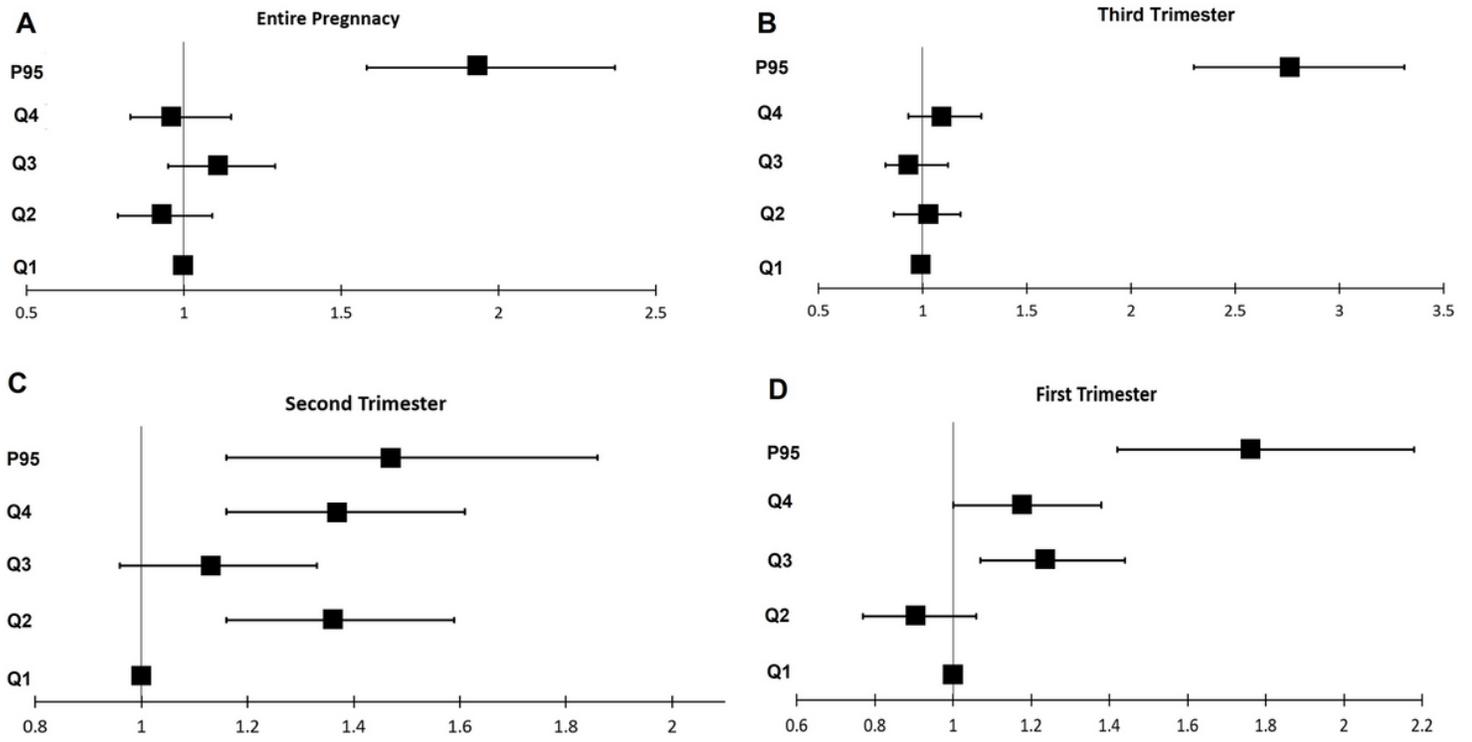


Figure 3

Forest plot of adjusted Cox regression analysis between Hlmax exposure groups and preterm birth in different exposure windows.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryTable1.docx](#)
- [SupplementaryTable2.docx](#)