OBSTETRICS

Preterm birth risk at high altitude in Peru

Lisa D. Levine, MD, MSCE; Gustavo F. Gonzales, MD, PhD; Vilma L. Tapia, MPH; Manuel Gasco, MSc; Mary D. Sammel, ScD; Sindhu K. Srinivas, MD, MSCE; Jack Ludmir, MD

OBJECTIVE: High altitude has been implicated in a variety of adverse pregnancy outcomes including preeclampsia and stillbirth. Smaller studies show conflicting data on the association between high altitude and preterm birth (PTB). The objective of this study was to assess the association between altitude and PTB.

STUDY DESIGN: A retrospective cohort study was performed using data from the Perinatal Information System, which includes deliveries from 43 hospitals in Peru from 2000 through 2010. Altitude was classified into the following categories: low (0-1999 m), moderate (2000-2900 m), and high (3000-4340 m). The primary outcome was PTB (delivery <37 weeks). Secondary outcomes were cesarean delivery and small for gestational age (SGA). Deliveries less than 23 weeks are not included in the database. χ^2 analyses were performed to compare categorical variables, and a logistic regression was used to calculate the odds ratios and control for confounders. Clustering by hospital was accounted for using generalized estimating equations.

RESULTS: A total of 550,166 women were included (68% low, 15% moderate, 17% high altitude). The overall PTB rate was 5.9%, with no difference in the PTB rate among the 3 altitudes (5.6%, 6.2%, 6.8%, $P = .13$). There was a significant difference in cesarean rates (28.0%, 26.6%, 20.6%, $P < .001$) with a 34% decreased risk at high vs low altitude adjusted for confounders (adjusted odds ratio, 0.66; 95% confidence interval, 0.51−0.85). There was a difference in SGA (3.3%, 3.6%, 5.0%, $P = .02$) with a 51% increased risk at high vs low altitude adjusted for confounders (adjusted odds ratio, 1.49; 95% confidence interval, 1.14−1.93).

CONCLUSION: High altitude is not associated with PTB. At high altitude, the cesarean rate was reduced and the SGA rate was increased.

Key words: cesarean delivery, high altitude, Peru, preterm birth, small for gestational age

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Preterm birth (PTB) is a leading cause of perinatal morbidity and mortality worldwide.[1-4] The reality of neonatal morbidity and health care costs associated with PTB are well known and are a major public health concern both nationwide and worldwide. In developing countries, PTB is a known contributor to neonatal mortality. In 2000, the United Nations held a summit to create goals for improving the world's health and poverty. The fourth Millennium Development Goal is to reduce the child mortality rate by two thirds from 1990 to 2015.[5] Among child mortality, neonatal deaths are a major contributor, with a large proportion of neonatal deaths being from complications of prematurity.

In developing countries, in which there are fewer resources, fewer hospitals, and fewer health care providers trained in caring for a preterm infant, the neonatal mortality rate (NMR) remains incredibly high.[6] In Latin America, the PTB rate is estimated to be 6%,[5] with an NMR of 15 per 1000 live births, which is 3 times as high as the United States.[1,2] These rates are even higher in the country of Peru in which the PTB rate ranges from 6% to 18% and the NMR is 20 per 1000 live births, with large variations, depending on geographical location.[2-4]

There are many identifiable risk factors for PTB[7-14]; however, to date, there are conflicting data on the association between high altitude and PTB.[15-17] More than 140 million people live at high altitude in North, Central, and South America, East Africa, and Asia.[18] Peru is a country of more than 30 million people. The country is divided

From the Maternal and Child Health Research Program, Department of Obstetrics and Gynecology (Drs Levine, Srinivas, and Ludmir), and Department of Biostatics and Epidemiology, Center for Clinical Epidemiology and Biostatistics (Dr Sammel), Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, and Department of Biological and Physiological Sciences (Dr Gonzales and Mr Gasco) and Instituto de Investigaciones de la Altura (Dr Gonzales and Ms Tapia), Universidad Peruana Cayetano Heredia, Lima, Peru.

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Corresponding author: Lisa D. Levine, MD, MSCE. lisa.obgyndoc@gmail.com

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into 3 regions: the coastal area at sea level, the Andean region at high altitudes, and the Amazonian jungle region at low altitude. Approximately 9 million people live at moderate or high altitude in the Andean regions.[3,4]

High altitude has been associated with decreased uterine artery blood flow, increased uteroplacental resistance, alterations in the expression of placental factors, chronic hypoxia, and changes in vascularity and has been implicated in a variety of adverse pregnancy outcomes including intrauterine growth restriction, low birthweight infants, intrauterine fetal demise, and preeclampsia.[15,19-24] Some of these same physiological changes have been observed and linked specifically with PTB.[25-27] Previous studies that have evaluated the impact of high altitude on PTB have not been designed or powered to specifically evaluate the PTB outcome.[15-17] Therefore, the objective of this study was to evaluate the association between PTB and high altitude in Peruvian pregnant women.

Materials and Methods

A retrospective cohort study was performed using data from the Perinatal Information System (PIS) database, which includes deliveries from 43 urban, public hospitals belonging to the Ministry of Health in Peru. Institutional Review Board approval was obtained from the University of Pennsylvania and the Universidad Peruana Cayetano Heredia prior to this study.

The PIS database was developed by the Latin American Centre for Perinatology/Women and Reproductive Health (CLAP/SMR) in Uruguay and has become a well-established national Peruvian database in which individual hospitals report information on all obstetric patients. The database includes maternal demographic information, medical history, and labor and delivery information from the 43 hospitals included. The altitude of these hospitals ranges from 29 m to 4340 m above sea level.

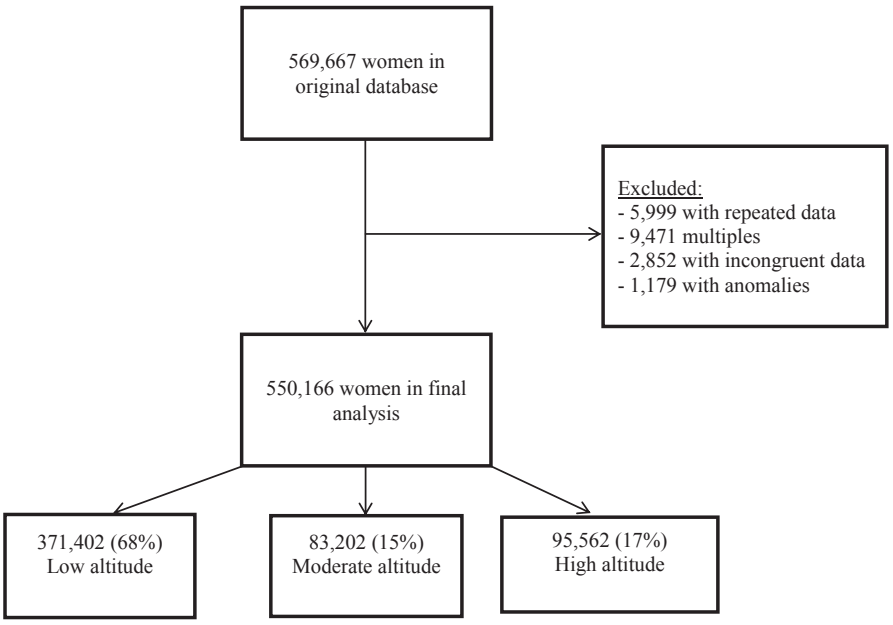
Data were collected from 2000 through 2010. The hospitals included health centers, community hospitals, and tertiary care referral hospitals. A quality assessment of the PIS database has been previously performed.[23] During this assessment, Gonzales et al[23] validated the database in 3 ways: (1) computer checks to reduce the risk of typing errors, (2) computer review of records for missing or aberrant data, and (3) review of a random sample of records to compare with other sources of information. For the record review, records were randomly sampled and compared with other sources of information (ie, a birth registry in a delivery room or records of neonatal services provided along with a review of the clinical record) to assure the reliability of the information in the database.

Data are grouped according to altitude of residency: low altitude (0-1999 m), moderate altitude (2000-2999 m), and high altitude (3000-4340 m). The unexposed patients are those living at low altitude and include 22 hospitals. The exposed patients are those living at moderate altitude (8 hospitals) and high altitude (13 hospitals). The altitude at the hospital site of delivery was used to define the altitude of residency. Almost all women deliver in close proximity to their place of residency, thereby making the hospital site altitude an acceptable way to classify this exposure.[15]

Our primary outcome was PTB, which was defined by delivery less than 37 weeks' gestation and included both spontaneous PTB (sPTB) and medically indicated PTB. Our secondary outcomes were PTB less than 34 weeks' gestation, sPTB less than 37 weeks, preeclampsia/eclampsia, small for gestational age (SGA), stillbirth, Apgar less than 6 at 5 minutes, and cesarean delivery rate. SGA was defined as birthweight below the 10th percentile for gestational age using the CLAP standard. The birthweights for Peru are similar to those derived by CLAP.[27] Stillbirth was defined as birth of a fetus 22 weeks or longer with no signs of life after birth.

Gestational age of delivery was determined by the last menstrual period or ultrasound and confirmed by physical examination. Those who did not have 2 forms of gestational age and those with incongruent data (for example, listed a gestational age of 24 weeks and birthweight of 4000 kg) were not included in the analysis (0.5% of cases) because of possible inaccuracies when sites input that data. Deliveries less than 23 weeks are not included in the

FIGURE 1
Flow diagram of patients included in the analysis



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