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Intrauterine Growth Restriction, Preeclampsia, and Intrauterine Mortality at High Altitude in Bolivia

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ABSTRACT

Infant mortality and stillbirth rates in Bolivia are high and birth weights are low compared with other South American countries. Most Bolivians live at altitudes of 2500 m or higher. We sought to determine the impact of high altitude on the frequency of preeclampsia, gestational hypertension, and other pregnancy-related complications in Bolivia. We then asked whether increased preeclampsia and gestational hypertension at high altitude contributed to low birth weight and increased stillbirths. We performed a retrospective cohort study of women receiving prenatal care at low (300 m, Santa Cruz, $n = 813$) and high altitude (3600 m, La Paz, $n = 1607$) in Bolivia from 1996 to 1999. Compared with babies born at low altitude, high-altitude babies weighed less (3084 ± 12 g *versus* 3366 ± 18 g, $p < 0.01$) and had a greater occurrence of intrauterine growth restriction [16.8%; 95% confidence interval (CI): 14.9–18.6 *versus* 5.9%; 95% CI: 4.2–7.5; $p < 0.01$]. Preeclampsia and gestational hypertension were 1.7 times (95% CI: 1.3–2.3) more frequent at high altitude and 2.2 times (95% CI: 1.4–3.5) more frequent among primiparous women. Both high altitude and hypertensive complications independently reduced birth weight. All maternal, fetal, and neonatal complications surveyed were more frequent at high than low altitude, including fetal distress (odds ratio, 7.3; 95% CI: 3.9–13.6) and newborn respiratory distress (odds ratio, 7.3; 95% CI: 3.9–13.6; $p < 0.01$). Hypertensive complications of pregnancy raised the risk of stillbirth at high (odds ratio, 6.0; 95% CI: 2.2–16.2) but not at low altitude (odds ratio, 1.9; 95% CI: 0.2–17.5). These findings suggest that high altitude is an important factor worsening intrauterine mortality and maternal and infant health in Bolivia. **(*Pediatr Res* 54: 20–25, 2003)**

Abbreviations

PE, preeclampsia
GH, gestational hypertension
IUGR, intrauterine growth restriction
CNS, Caja Nacional de Salud (National Health Care Fund)
BP, blood pressure
IUM, intrauterine mortality
SGA, small-for-gestational age
95% CI, 95% confidence intervals
OR, odds ratio

Bolivia's infant mortality is the highest in the Western Hemisphere, its maternal mortality second only to Haiti (1) and its intrauterine mortality the second highest of 19 South American countries (2). Some 75% of the Bolivian population and 140 million persons worldwide, including an appreciable fraction of the other Andean countries, reside at high altitude (>2500 m) (1, 3, 4). Within Bolivia, neonatal mortality rates rise progressively with increasing altitude, averaging 20 deaths per 1000 live births lower than 2500 m, 33 in the 2500–3500 m region of the country, and 44 higher than 3500 m (4). Maternal mortality also rises with increasing altitude within Bolivia, averaging 110 deaths/100,000 live births at low altitude, 293 in the intermediate altitudes, and 602 in the high regions (5).

A number of factors likely contribute to the altitude-related increase in infant and maternal mortality in Bolivia. A recent retrospective, stratified survey identified lack of schooling, living in a rural location, Altiplano residence, absence of prenatal or perinatal health care, and small size at birth as factors that significantly raised neonatal, infant, and childhood mortality (4). Low birth weight, especially if coupled with

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prematurity, is well known to raise neonatal and infant mortality worldwide (6). High altitude reduces birth weight, averaging a 100-g fall for every 1000-m altitude gain (7). In Colorado the effect of altitude on birth weight is comparable to moderate smoking and greater than parity (7). The reduction in birth weight at altitude is largely attributable to IUGR rather than prematurity in Bolivia (8) as well as in the United States (9).

Not only IUGR but also the maternal complication PE occurs more frequently at high compared with low altitudes in Colorado (16% at 3100 m *versus* 3% at 1260 m) and elsewhere (7, 10–12). To our knowledge, no systematic study of its prevalence has been conducted in Bolivia or other Andean countries. Hypertensive complications of pregnancy also increase IUGR (13), and the two conditions act synergistically in the United States to raise perinatal mortality 3-fold (14). Therefore, we asked whether complications of pregnancy, including IUGR and PE, were increased at high compared with low altitude in Bolivia. We further asked whether an increased frequency of hypertensive complications of pregnancy contributed to the altitude-associated decrease in birth weight and whether hypertensive complications and high altitude together raised IUM in Bolivia.

METHODS

Study sites and design. We used a retrospective cohort design for examining all consecutive, singleton deliveries to women receiving prenatal care at low (300 m, Santa Cruz, $n = 813$) and high altitude (3600 m, La Paz, $n = 1607$). These sites were chosen as the two largest cities in Bolivia with the best and most similar levels of health-care services. The study was conducted in accordance with procedures approved by the Colorado Multiple Institutional Review Board and the Colegio Medico, the ethical oversight group for the Bolivian organizations.

Charts were identified for all births between January 1998 and April 1998 to insured persons at the CNS and from January 1996 to April 1999 in private clinics at each location. The CNS is the largest of the insured sectors of the health-care system in Bolivia and was chosen because it has hospitals in all the metropolitan regions of the country. The private clinics studied were those with the largest obstetrics services in each location. Approximately equal numbers of births were recorded from private clinics, but because fewer births occurred per month, a longer sampling period was used (January 1996 to April 1998). Data were abstracted from the charts of all consecutive deliveries to women with singleton pregnancies and two or more prenatal visits at both the public and private clinics. A minimum of two prenatal visits was required to permit diagnosis of PE or GH (see below).

Study variables. In the CNS hospitals, standardized forms are used for prenatal, labor and delivery, and neonatal medical records throughout the country. Similar information is obtained in the private hospitals, although the forms used are more variable. For each delivery, the following data were abstracted: infant birth weight, gestational age, length, head circumference, sex, Apgar scores, and neonatal complications; and maternal age, parity, gravidity, week at which prenatal care began, number of prenatal visits, altitude of residence, body weight at first and last visit, BP, proteinuria, pregnancy or labor and delivery complications, employment, and past medical history. Gestational age was measured both as weeks from last menstrual period and as a clinical estimate based on newborn physical examination. Values reported are the weeks from last menstrual period except when these differed by more than 2 wk from those determined by physical examination, in which case the clinical estimate was reported. Altitude of residence was recorded for the mother's place of residence. Maternal weight gain was calculated as the difference between weight at the first prenatal visit and at time of delivery.

Definitions. Babies born at less than 37 wk were considered preterm. IUGR was defined as birth weight less than the 10th percentile, adjusted for gestational age and sex using a large sea-level study validated with perinatal mortality criteria (15). Maternal hypertensive complications of pregnancy were considered as either GH or PE. In both cases, hypertension was defined as two or more BP readings in rested seated subjects at least 6 h apart $\geq$ 140/90 mm Hg or a $\geq$ 30/15 mm Hg rise above values recorded at the first prenatal visit in a woman whose BP was $<$ 140/90 mm Hg before week 20 or postpartum. GH was defined as hypertension during pregnancy without proteinuria and PE as hypertension with proteinuria as measured qualitatively or in a 24-h collection (16). Quantification of proteinuria varies in Bolivia, even within a hospital laboratory, and is not reported consistently using the plus (+) system. Therefore, we used the presence of any proteinuria to distinguish between PE and GH. Women were classified as having PE or GH (PE/GH) if no proteinuria determinations were made. Severe PE was defined as women with PE and BP $>$ 160/110 mm Hg, and all others were classified as mild. Women were considered normal who were without PE or GH, or who had a single elevated BP with or without proteinuria. To distinguish women with GH who presented late from those with chronic hypertension, women were classified as chronic hypertension if both their presenting and discharge BPs were elevated. A small number of women ($n = 40$) had chronic hypertension with ($n = 12$) or without superimposed PE or GH and are reported separately in the analyses of PE/GH. Four women diagnosed with gestational diabetes were excluded from all analyses.

The maternal prenatal complications reported were bleeding at any time during pregnancy, premature rupture of membranes, preterm labor requiring treatment, oligohydramnios or polyhydramnios, and placental abruption or previa. Newborn complications were intrauterine demise, fetal distress (including meconium staining of amniotic fluid), nuchal cord, congenital anomalies, and newborn respiratory distress. Newborn respiratory distress was considered for all babies in whom the medical record documented one or more of the following: treatment with oxygen at time of birth, respiratory distress, apnea, respiratory depression, pulmonary hypertension, hyaline membrane disease, or newborn hypoxia as a discharge diagnosis. This may include a wide range of other etiologies, such as perinatal asphyxia or depression, transient tachypnea of the newborn, surfactant deficiency, and congenital pneumonia.

All reported intrauterine deaths occurred after 20 wk gestational age.

Statistical analysis. Data are reported as the mean ± SEM or as proportions with 95% CI (in parentheses). Maternal and neonatal characteristics were compared between altitudes using two-sample t tests for continuous variables and χ^2 tests for categorical variables (StatView 5.01, 1998; SAS Institute Inc, Cary, NC, U.S.A.). IUM rates were calculated as the number of intrauterine deaths per 1000 live births for all women and for defined subsets. A contingency table approach was used to calculate ORs with confidence intervals for IUM rates, and to compare IUM rates between altitudes. A stepwise logistic regression approach was used to examine the influence of (*i.e.* the risk associated with or protection afforded by) altitude on the occurrence of PE or GH. ANOVA was used to examine the effects of altitude, hypertensive complications, gestational age, parity, and maternal weight at delivery on birth weight. These latter analyses were implemented with SAS statistical software (SAS STAT, Version 8.1, 2000; SAS Institute, Inc.).

RESULTS

A slightly higher proportion of women were studied from the CNS than from the private-practice sector at low than at high altitude (Table 1). Women at high altitude (La Paz) were older, taller, and more likely to have secondary or higher education or to smoke than the low-altitude (Santa Cruz) women although few smoked at either location (Table 1). Although weight gain was similar in both groups, women at high altitude weighed less at delivery than low-altitude women. Women at high altitude also had more prenatal visits than the low-altitude women and began their prenatal care earlier. Similar proportions of women had manual labor occupations at both altitudes (Table 1), but more fathers were engaged in manual labor at low than high altitude (44%; 95% CI: 36–51 *versus* 31%; 95% CI: 28–33, respectively; $p < 0.01$).

Babies at high altitude weighed less at birth, were 1 cm shorter, had slightly smaller head circumferences, and had greater occurrence of IUGR (OR, 3.2; 95% CI: 2.3–4.5; Table 2). Although the gestational age at birth was 0.4 wk or 2.8 d shorter at high altitude, there was no difference in the percentage of preterm births (Table 2).

More women developed PE and GH at high than low altitude (Fig. 1). However, because many women (n =1376; 57%) had no urine protein determinations made during pregnancy and this proportion of women was greater at low than high altitude (95% *versus* 37%, respectively; $p < 0.01$), we combined the categories of PE and GH. Together, PE and GH were more common at high than at low altitude (OR, 1.7; 95% CI: 1.3–2.3), especially among primiparous women (OR, 2.2; 95% CI: 1.4–3.5; Fig. 1). There was no difference in the proportion of women with chronic hypertension at low and high altitude (1.7% *versus* 0.8%; NS), and the frequency of PE or GH among chronically hypertensive women did not differ at the two altitudes (0%; 95% CI: 0–0 at low *versus* 0%; 95% CI: 0–0 at high altitude; NS).

Using stepwise logistic regression with hypertensive complications as the dependent variable, we found that hypertensive complications remained 1.8 times (95% CI: 1.3–2.3; $p < 0.01$) more common at high than low altitude when comparisons were controlled for differences between the two groups in the proportion of women who were primiparous, at the extremes of maternal age (<18 or >35 y), and weight at delivery. Among primiparous women, PE or GH also remained more common at high *versus* low altitude (OR, 2.1; 95% CI: 1.3–3.3; $p < 0.01$) when controlled for extremes of maternal age (<18 or >35 y) and weight at delivery.

Both residence at high altitude (Table 2) and hypertensive complications of pregnancy reduced birth weight (Fig. 2). Women with hypertensive complications had smaller babies than normotensive women (3085 ± 31 g *versus* 3210 ± 11 g, respectively; $p < 0.01$). When women with hypertensive complications were excluded, women at high altitude still had smaller babies than their low-altitude counterparts (3110 ± 14 g, n = 1183 at high altitude *versus* 3384 ± 19 g, n = 647 at low altitude; $p < 0.001$). We used ANOVA to examine the effect of altitude and hypertensive complications of pregnancy on birth weight while controlling for gestational age, parity, and maternal weight at delivery (Fig. 2). Both high altitude and hypertensive complications significantly reduced birth weight.

Table 1. *Maternal characteristics*

	Low altitude (n = 812)	High altitude (n = 1608)
Altitude (m)	300	3600
CNS (%)	59 (56–63)	53 (51–55)*
Age (y)	28 ± 0.2	30 ± 0.1*
Gravidity (no. of pregnancies)	2.8 ± 0.1	2.7 ± 0
Height (cm)	152 ± 0.3	156 ± 0.3*
Weight at delivery (kg)	70.7 ± 0.4	67.8 ± 0.2*
Pregnancy weight gain (kg)	8.0 ± .2	8.3 ± 0.2
Secondary or higher education (%)	75 (72–78)	86 (85–88)*
Smoker (%)	0 (0–0)	4 (3–5)*
Manual labor (%)	45 (41–49)	44 (41–46)
Prenatal visits (no.)	5.7 ± 0.1*	7.4 ± 0.1*
Week of first prenatal visit	19 ± 0.2*	16 ± 0.3*
Cesarean delivery (%)	58.4 (55.0–61.8)	42.4 (40.0–44.8)
Normotensive, n (%)	666 (86.9)	1189 (81.1)
PE/GH, n (%)	87 (11.4)	265 (17.6)*

Values are mean ± SEM or proportions with 95% CI in parentheses unless otherwise noted.
* $p < 0.01$.

Table 2. *Newborn characteristics*

	Low altitude (n = 775)	High altitude (n = 1575)
Birth weight (g)	3363 ± 18	3084 ± 12*
Length (cm)	50.3 ± 0.1	48.7 ± 0.1*
Head circumference (cm)	34.4 ± 0.1	34.2 ± 0.0*
Gestational age (wk)	38.9 ± 0.1	38.7 ± 0.1†
Preterm (%)	8.8 (6.8–10.8)	10.5 (9.0–12.1)
IUGR (%)	5.9 (4.2–7.5)	16.8 (14.9–18.6)*

Values are mean ± SEM or proportions with 95% CI in parentheses.
* $p < 0.01$; † $p < 0.05$.

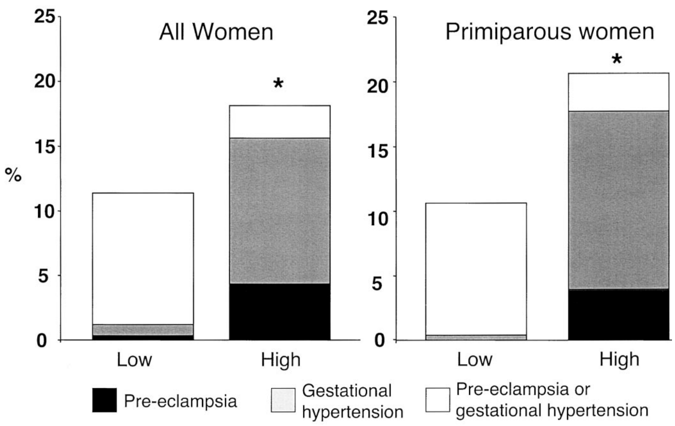

Figure 1. Hypertensive complications of pregnancy at low and high altitude. More women develop hypertensive complications of pregnancy (PE, GH, or unable to distinguish because of missing protein data; PE/GH) at high than low altitude (18.1%; 95% CI: 16.1–20.0 *vs* 11.4%; 95% CI: 9.1–13.6, respectively) especially when primiparous (20.6%; 95% CI: 17.0–24.2 *vs* 10.6%; 95% CI: 6.8–14.4, respectively). Total sample sizes were 753 (n = 87, PE, GH, and PE/GH) and 1454 (n = 265, PE, GH, and PE/GH) for all women, and 255 (n = 28, PE, GH, and PE/GH) and 485 (n = 102, PE, GH, and PE/GH) among primiparous women at low and high altitude, respectively. *$p < 0.01$.

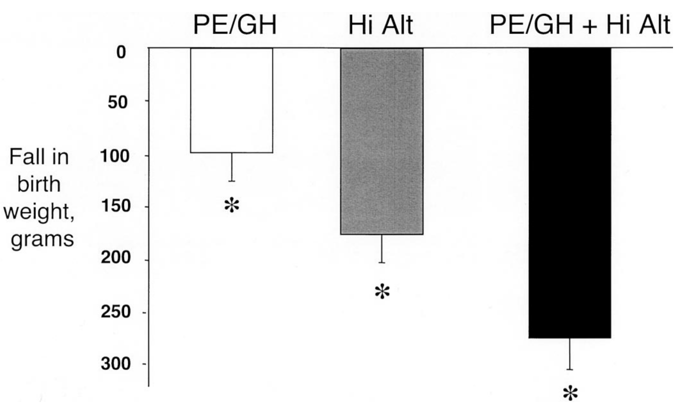

Figure 2. High altitude and PE decrease birth weight. Contributions of hypertensive complications of pregnancy and altitude to reduction in birth weight in grams, controlling for gestational age, parity, and maternal weight. *$p < 0.01$.

Their combined effects were additive, not multiplicative, as demonstrated by the absence of a significant interaction term.

All pregnancy-related maternal, fetal, and neonatal complications surveyed were more common at high than low altitude (Table 3). The most frequent complications were fetal distress and newborn respiratory distress, both of which were markedly more common at high than low altitude. Fetal distress also occurred more often among babies born to hypertensive women when compared with babies of normotensive women (10.2%; 95% CI: 7.1–13.4 *versus* 5.6%; 95% CI: 4.5–6.6; $p < 0.01$), as did newborn respiratory distress (15.9%; 95% CI: 12.1–19.7 *versus* 8.2%; 95% CI: 7.0–9.4; $p < 0.01$).

IUM rates did not differ by altitude (NS by t test; Table 4). PE or GH raised the risk of intrauterine death at high altitude but not at low altitude (OR, 5.9; 95% CI: 2.2–16.1 at high altitude *versus* OR, 1.9; 95% CI: 0.2–17.5 at low altitude). At high altitude, 21% of all intrauterine deaths occurred in women with severe PE, and these women had the greatest occurrence of stillbirth (Table 4). Documented congenital anomalies accounted for two (8%) of the intrauterine deaths. Compared with previously reported IUM rates for Latin America, IUM in our study subjects with hypertensive complications at high altitude was higher than in Latin America overall (35.7/1000 live births *versus* 17.6/1000; $p < 0.05$) but similar (NS) to the 44.3/1000 live births value reported for Bolivia (2). IUM rates among babies born to women with hypertensive complications at low altitude were similar to the Latin American value of 17.6 deaths/1000 livebirths (Table 4). Among normotensive women at either altitude, IUM rates were lower than in Latin America overall (5.9 *versus* 17.6 deaths/1000 live births at high altitude; $p < 0.01$; and 6.1 *versus* 17.6 deaths/1000 live births at low altitude; $p < 0.05$).

DISCUSSION

Our results confirmed that infant birth weight was lower and that the percentage of babies with IUGR was greater at high than at low altitude in Bolivia. Hypertensive complications of pregnancy (PE or GH) were also more common and were associated with a dramatic increase in IUM at high altitude. The high incidence of stillbirths in high- compared with low-altitude women with hypertensive complications of pregnancy suggests that these factors have a greater impact on fetal well-being at high than low altitude. In addition, fetal distress and newborn respiratory distress occurred more frequently at high than low altitude. These results suggest that strategies to improve maternal and child health in Bolivia (and perhaps in other high-altitude communities) should take into account the importance of altitude on maternal well-being and pregnancy outcomes.

Table 3. *Maternal, fetal, and neonatal complications*

	Low altitude	n	High altitude	n
Bleeding first–third trimester (%)	0.1 (−0.1 to 0.4)	1476	3.1 (2.2–4.0)*	801
Premature rupture of membranes (%)	0.4 (0.0–0.8)	1518	4.0 (3.0–4.9)*	802
Preterm labor (%)	3.6 (2.3–4.8)	1494	6.5 (5.3–7.7)*	765
Oligo- or polyhydramnios (%)	0.2 (−0.1 to 0.6)	1488	2.2 (1.6–3.0)*	800
Placental abruption or previa (%)	0.4 (0.0–0.8)	1494	1.7 (1.1–2.3)*	800
Fetal distress (%)	1.6 (0.7–2.5)	1275	13.2 (11.6–14.9)*	787
Nuchal cord (%)	0.4 (0.0–0.8)	1275	3.4 (2.5–4.2)*	787
Newborn respiratory distress (%)	1.4 (0.6–2.1)	1518	9.1 (7.7–10.5)*	802
Congenital anomalies (%)	0.1 (−0.1 to 0.4)	1499	1.4 (0.8–2.0)*	801

Values are mean ± SEM or proportions with 95% CI (in parentheses).
* $p < 0.01$ compared with low altitude.

Table 4. *Incidence of and mortality rate among stillbirths*

	Low altitude	High altitude
All women		
n	6	19
Mortality rate	7.4	11.8
Normotensive women		
n	4	7
Mortality rate	6.1	5.9
PE or GH women		
n	1	11.8
Mortality rate	11.8	34.1*
Severe PE women		
n	1	3
Mortality rate	200	375
Mild PE women		
n	0	6
Mortality rate	0	15.6

n = number of intrauterine deaths.

* $p < 0.01$ compared with normotensive at high altitude, all other comparisons NS.

The total number of intrauterine deaths in normotensive and PE/GH women do not add up because of stillbirths in women who could not be classified as normotensive or PE/GH owing to missing data.

Although we sampled a large number of persons at both altitudes, these data may not be representative of the entire Bolivian population, given that all our subjects received prenatal care and delivered in hospitals whereas only 43% of all Bolivian births are attended by trained personnel and a smaller number receive prenatal care (1). The high- and low-altitude groups differed in respect to maternal age, indices of socioeconomic, and health-care status, but these differences should be to the advantage of the high-altitude women. The difference in number of prenatal visits between high and low altitude was small and not likely to be clinically significant. Moreover, these factors are likely to decrease IUGR (17) and PE or GH (18) and therefore bias against our hypothesis that IUGR and hypertensive complications were increased at high altitude. Finally, none of these was found to be significant in our stepwise regression models for birth weight or PE. We therefore concluded that the higher rates of IUGR and PE/GH observed at high compared with low altitude in Bolivia were owing to altitude rather than differences in other sample characteristics.

We observed a reduction in birth weight at high altitude in Bolivia consistent with that first reported by Lichty *et al.* (9) and subsequently confirmed in a large number of studies in the United States, South America, Asia [reviewed in Niermeyer *et al.* (3)], and Bolivia (8). The reduction in birth weight is accompanied by little or no decrease in gestational age, indicating that IUGR rather than shortened gestation is responsible. In the present study, gestational age was significantly but only very modestly (2.8 d) lower, and the percentage of preterm deliveries did not differ. Newborn length and head circumference were also diminished, with the reduction in length being greater than that in head circumference, further supporting the occurrence of fetal growth restriction at high altitude. Inasmuch as there is no agreed on standard for assessing IUGR in different populations with different birth weight characteristics (19), we used IUGR criteria from a large sea-level study that had been validated with reference to perinatal mortality data.

Risk factors for PE/GH in Latin America are similar to those in North America and Europe (20), but the effect of altitude on PE or GH in Latin American women has not previously been reported. Finding an increased frequency of PE at high altitude is consistent with our previous studies in Colorado (7, 12) and others in Saudi Arabia (11). In Colorado we observed a 3.6-fold increase in PE at 3100 m compared with a sociodemographically matched 1300-m community (12). In Bolivia and other developing countries, the overall prevalence of hypertensive complications is higher than that reported in the developed world (5% in Latin America overall *versus* 2.6% in the United States) (20, 21). A higher prevalence in Bolivia, the poorest country in South America (1), may contribute to the relatively smaller altitude-associated increase in Bolivia than in Colorado.

We defined PE based on clinical classification; namely, two or more BPs at least 6 h apart ≥ 140/90 mm Hg or a ≥ 30/15 mm Hg rise above values recorded at the first prenatal visit in a woman whose BP was < 140/90 mm Hg before wk 20 or postpartum with proteinuria (16). The American College of Obstetrics and Gynecology has recommended dropping the use of a BP rise in pregnancy from the definition of PE (22). However, we chose to include BP rise in our definition for several reasons. First, this is the definition used in Bolivia. Furthermore, the studies showing no adverse outcomes in women with the BP rise compared with women with absolute BP > 140/90 mm Hg have all been done in the United States and European countries (13, 23), where socioeconomic, nutritional, and lifestyle conditions are quite different from those in Bolivia. Thus, we thought a broader definition would be more useful for studying the impact of a disease in which the functional sequelae are still not well understood, particularly in our population.

Owing to the absence of routine proteinuria determinations in Bolivia, our ability to distinguish between PE and GH was limited in many women. Despite collecting data from centers that have more complete health-care services than most facilities in Bolivia, most women had no protein determinations at any time during pregnancy, and only 10% had more than one protein measurement during their entire pregnancy. Twenty-four–hour urine protein determinations were done rarely (six cases). In most cases urine protein determination was not performed at the time the patient had elevated BP, and therefore many of the women with GH are likely to have actually had PE. Tests for other indicators of systemic disease in PE, such as renal insufficiency or liver disease (24), were rarely performed in our study sample and thus we could not use them to distinguish between PE and GH. We therefore grouped the categories of GH and PE together as hypertensive complications.

Whether the distinction between PE and GH is important in terms of fetal outcome remains controversial. In a study by North *et al.* (13) GH and PE were both associated with increased SGA infants and preterm births. Outcomes such as perinatal mortality and SGA are likely to be worse in women with proteinuria and PE than in hypertensive women without proteinuria (25). However, women with GH were twice as likely as normotensive women to have SGA infants (25). Buchbinder (26) compared preterm delivery, birth weight, and perinatal outcome and found worse outcomes in women with severe GH without proteinuria than those with mild PE, defined as BPs > 140/90 mm Hg and proteinuria. Given that pregnancy-induced hypertension with and without proteinuria adversely impacts birth outcomes, we considered it valid to group women with GH and PE together to assess the impact on birth weight, IUGR, IUM, and the influence of altitude.

The IUM rate of 10.6 deaths per 1000 live births observed in the combined low- and high-altitude samples is high by standards in developed countries, for example 6.7 per 1000 live births in the United States (27), but lower than the previously reported value for Bolivia of 44.3 deaths per 1000 live births, the second highest among 19 Latin American countries (2). Whereas we surveyed only facilities with insured or private patient populations in the two largest cities with the most extensive health-care services in Bolivia, the 44.3 IUM rate was calculated from data from all over Bolivia, including small cities and rural areas where IUM is likely higher. Interestingly, the IUM rate among babies born to women with hypertensive complications at high altitude in our study was similar to the 44.3 value. Inasmuch as 75% of the Bolivian population resides at high altitude (4), this suggests that an altitude-related effect on raising the frequency of PE or GH may contribute to the high IUM rates observed in the country as a whole.

The combined effects of altitude and hypertensive complications of pregnancy on IUM in Bolivia suggest the need for improved monitoring for PE/GH during pregnancy. The lack of testing for proteinuria during pregnancy is one possible target for future intervention for improving the identification and treatment of PE. Another potential intervention that could be initiated in Bolivia is dietary supplementation with the antioxidants vitamin E and vitamin C, which have been shown to decrease the incidence of PE in at-risk women (28). Increased use of fetal monitoring in women with hypertensive complications of pregnancy might also reduce IUM, especially in women who require antihypertensive therapy. Further, the high rate of fetal distress associated with high altitude, hypertensive disorders of pregnancy, and IUGR calls for increased preparation for neonatal resuscitation.

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