Perinatal Outcomes at High Altitude: Analysis of Birth Weight, Low Birth Weight, and Small for Gestational Age in Relation to Maternal Factors. Catamarca, Northwestern Argentina

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Abstract: This study compared birth weight (BW) and associated gestational and maternal determinants among newborns from high- and low-altitude regions in Catamarca, northwestern Argentina. A retrospective population-based analysis was conducted using vital records from 1990 to 2010, including 485 births from high-altitude areas (HA; 3,323 m above sea level) and 65,538 births from low-altitude areas (LA; 520 m above sea level). Neonatal outcomes were classified according to international standards: low birth weight (LBW; <2,500 g) and small for gestational age (SGA; <10th percentile). Mann–Whitney U tests, chi-square tests, generalized linear models, and logistic regression was used. Newborns from HA exhibited significantly lower BW and a higher frequency of LBW and SGA compared with those from LA. BW was strongly influenced by gestational age, with preterm birth being the main predictor of reduced weight; the altitude–prematurity interaction showed a partial attenuation of this effect in HA newborns. LBW was associated with preterm pregnancy and younger maternal age, whereas high altitude and post-term pregnancy were associated with SGA. Additionally, younger maternal age and low educational level increased the risk of SGA. These findings demonstrate the combined influence of altitude, fetal maturation, and sociodemographic factors on neonatal outcomes and underscore the need for targeted perinatal strategies in high-altitude populations.

Keywords: Fetal growth, Geographical altitude, Intrauterine growth restriction, Neonatal health, Puna, Sociodemographic factors.

INTRODUCTION

Birth weight is a critical indicator of intrauterine growth and neonatal health, and it is associated with risks of infant morbidity and mortality as well as short-, medium-, and long-term metabolic consequences [1, 2]. Its variability is influenced by multiple biological and social determinants, including maternal, environmental, geographical, and healthcare-related conditions [2].

In high-altitude regions, hypobaric hypoxia resulting from reduced barometric pressure constitutes the main environmental factor affecting fetal development [3]. During pregnancy, this hypoxia decreases uteroplacental blood flow and compromises the transfer of oxygen and nutrients, thereby increasing the risk of intrauterine growth restriction, low birth weight, and reduced neonatal length [4, 5]. However, the underlying causal mechanisms are not yet fully understood [6].

It is estimated that approximately 6% of the global population resides permanently at high altitudes [7], where physiological responses to hypoxia interact with socioterritorial factors that influence perinatal outcomes. These include rurality, geographic dispersion, unequal healthcare infrastructure, and disparities in access to prenatal care, as documented in several countries by international organizations [8-10]. Thus, exposure to hypoxia does not operate in isolation but within a broader framework of social determinants that shape neonatal risk [11].

In South America, the principal high-altitude areas correspond to the Andean region, including the Argentine–Chilean Puna, characterized by low atmospheric pressure, extreme temperature variation, low humidity, high solar radiation, and heterogeneous access to healthcare services [7, 12, 13].

Previous studies in Argentina and the Andean region have consistently documented the association between altitude, chronic hypoxia, and low birth weight [14], as well as a higher proportion of small for gestational age (SGA) and low birth weight (LBW) newborns [15-18]. However, few studies analyze other maternal sociodemographic variables in the northwestern highlands [19, 20].

Within this framework, this study aims to compare birth weight, low birth weight, and small size for gestational age among newborns from the highlands and lowlands of the province of Catamarca, analyzing for the first time its association with maternal characteristics over a 20-year period in a poorly studied region of the Argentine Puna. Providing contextualized evidence on how territory and living conditions influence neonatal outcomes may contribute to the

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development of public policies sensitive to the specific challenges of pregnancy at high altitude.

MATERIALS AND METHODS

Study Area

The province of Catamarca, located in northwestern Argentina (NOA) alongside the provinces of Tucumán, Santiago del Estero, Salta, and Jujuy, has a population of 429,562 inhabitants and an average population density of 4.2 inhabitants/km² [21]. Administratively, it is divided into sixteen departments.

The Capital Department covers an area of 399 km², with 186,947 inhabitants and a population density of 469 inhabitants/km². With an average elevation of 520 meters above sea level, it constitutes the main political, economic, and administrative center of the province and concentrates approximately 70% of the urban population. Its administrative head town is San Fernando del Valle de Catamarca.

In contrast, the Department of Antofagasta de la Sierra, located in the Puna region in the northwest of the province, exhibits distinct demographic and territorial characteristics. Covering 28,109 km², it is the least populated department, with only 2,022 inhabitants and a density of 0.05 inhabitants/km², at an average elevation of 3,323 meters above sea level (National Geographic Institute). It comprises four main localities (Antofagasta de la Sierra, El Peñón, Los Nacimientos, and Antofalla) and 19 dispersed rural settlements.

Marked contrasts exist between both departments in ethnic ancestry, socioeconomic level, and structural poverty. Provincial records indicate that 19,668 people self-identified as Indigenous or Indigenous descendants; among them, 4,049 (≈2%) reside in the Capital Department and 313 (≈15%) in Antofagasta de la Sierra [21]. According to the 1991 Census, 41.5% of households in Antofagasta de la Sierra and 19.2% in the Capital Department exhibited Unmet Basic Needs (UBN). Although these values decreased substantially by 2010, inequalities persisted: Antofagasta reported 213 individuals with UBN (17.5%), whereas the Capital Department reported 18,372 (11.6%) [22].

Study Design

A retrospective, descriptive, and comparative population-based study was conducted using birth records from 1990 to 2010. Data was obtained from vital statistics compiled by the Provincial Bureau of Statistics and Census of Catamarca.

A total of 148,137 births were recorded during the study period, of which 623 corresponded to Antofagasta de la Sierra and 68,678 to the Capital Department.

Data Inclusion and Cleaning Criteria

The analysis included singleton births between 35 and 42 weeks of gestation, with complete information for the following variables: birth weight, gestational age, sex of the newborn, maternal age, maternal educational level and marital status.

A total of 138 records from Antofagasta de la Sierra and 3,140 from the Capital Department were excluded for not meeting these criteria.

The final sample consisted of 485 births from High-Altitude Areas (Antofagasta de la Sierra) and 65,538 births from Low-Altitude Areas (Capital).

All data were dissociated from personal identifiers to ensure participant anonymity, in compliance with the Argentine Personal Data Protection Law (Law No. 25.326/2000).

Neonatal variables included sex, gestational age, and birth weight, classified as follows:

Sex: male, female

Gestational age: preterm (<37 weeks), term (37–41 weeks), post-term (>41 weeks)

Birth weight: Low Birth Weight (LBW), <2,500 g), Normal Weight (2,500–3,999 g), and High Birth Weight (>3,999 g)

Size-for-gestational-age categories: Small for Gestational Age (SGA) (<P10), Appropriate for Gestational Age (AGA) (P10–P90), and Large for Gestational Age (LGA) (>P90), according to Intergrowth-21st standards [23].

Maternal variables included maternal age, marital status, and educational level, categorized as follows:

Maternal age: <20 years, 20–35 years, >35 years

Marital status: cohabiting, non-cohabiting

Educational level: primary, secondary, tertiary

Statistical Analysis

The distribution of birth weight was assessed using the Kolmogorov–Smirnov test with Lilliefors correction.

Group comparisons were performed using the Mann–Whitney U test for non-parametric continuous variables and the Chi-square test for categorical variables.

To evaluate the association between birth weight (in grams) and maternal/neonatal predictors, a multivariate generalized linear model (GLM) with Gamma distribution and log link was applied, given the positive skewness of the birth weight distribution. Parameters were estimated using maximum likelihood. Categorical variables were dummy coded using physiologically normative reference categories. Results were reported as β coefficients with 95% confidence intervals, Wald statistics, and p-values. Statistical significance was set at $p < 0.05$. Analyses were performed using IBM SPSS Statistics version 27.

To assess associations between maternal, neonatal, and contextual factors and the outcomes Low Birth Weight (LBW) and Small for Gestational Age (SGA), independent multivariate binary logistic regression models were constructed. Categorical variables were dummy-coded, using physiological or socially normative reference categories (*i.e.*, low altitude, term gestation, mothers aged 20–35 years, highest educational level, cohabiting married status, and female newborn).

Explanatory variables included altitude of residence, gestational age, maternal age, maternal educational level, marital status, and newborn sex. All covariates were entered simultaneously to estimate independent effects.

Results were expressed as odds ratios (OR) with 95% confidence intervals and p-values, with statistical significance set at $p < 0.05$.

RESULTS

Neonatal Characteristics

Table **1** presents the distribution of neonatal characteristics according to altitude of residence. No statistically significant differences were observed in the distribution of newborn sex between High-Altitude Areas (HA) and Low-Altitude Areas (LA) ($p = 0.350$). In contrast, gestational age differed significantly between groups: HA showed a higher proportion of both preterm and post-term births compared with LA ($p < 0.001$), indicating greater variability in pregnancy duration at high-altitude.

Birthweight distributions also differed significantly between regions. In High-Altitude Areas, the median birth weight was 3050 g (IQR: 2750–3350; range: 1300 to 4608 g). In Low-Altitude Areas, the median was significantly higher (3300 g, IQR: 3050–3550; range: 950 to 4550 g), with a Mann-Whitney U test confirming a significant difference between groups ($p < 0.001$). Although variability was greater in LA (IQR= 556 g) than in HA (IQR=415 g), values remained consistently lower at high altitude.

Adverse neonatal outcomes were also more frequent in HA. The prevalence of Small for Gestational Age (SGA) was 21.0% in HA compared with 8.9% in LA ($p = 0.010$). Similarly, Low Birth Weight (LBW) was more common at high altitude (8.2% vs. 3.3%; $p = 0.001$).

Maternal Characteristics

Table **2** summarizes maternal characteristics according to altitude. Significant differences were

Table 1: Neonatal and Gestational Characteristics by Altitude (Chi-Square Tests)

Variable	Category	High Altitude n (%)	Low Altitude n (%)	Chi²	*p*-value
Sex	Female	234 (48.2)	32572 (40.7)	0.149	0.350
	Male	251 (51.8)	32966 (50.3)		
Gestational age	Preterm	91 (18.8)	5702 (8.7)	91.673	<0.001**
	Term	317 (65.3)	58067 (88.6)		
	Post-term	77 (15.9)	1770 (2.7)		
Birth weight	Low	40 (8.2)	2163 (3.3)	14.240	0.012*
	Appropriate	432 (89.1)	59967 (91.5)		
	High	13 (2.7)	3408 (5.2)		
Size for gestational age	Small	102 (21.0)	5833 (8.9)	27.741	<0.001**
	Appropriate	353 (72.8)	53938 (82.3)		
	Large	30 (6.2)	5767(8.8)		

*Significant at p<0,05; **Significant at <0,001
Chi-square corresponds to the overall comparison across categories within each variable.

Table 2: Maternal Characteristics by Altitude (Chi-Square Tests)

Variable	Category	High Altitude n (%)	Low Altitude n (%)	Chi²	*p*-value
Maternal age	<20 years	112 (23.0)	12452 (19.0)	3.630	0.163
	20-35 years	323 (66.6)	47384 (72.3)		
	>35 years	50 (10.4)	5702 (8.7)		
Marital status	Cohabiting	403 (83.0)	59050 (90.1)	5.042	0.017*
	Non-cohabiting	82 (17.0)	6488 (9.9)		
Maternal education	Primary	417 (85.9)	24708 (37.7)	71.899	<0.001**
	Secondary	54(11.2)	29361 (44.8)		
	Tertiary	14 (2.9)	11469(17.5)		

*Significant at p<0,05; **Significant at p<0,001
Chi-square corresponds to the overall comparison across categories within each variable.

observed across several sociodemographic and obstetric variables. In High-Altitude Areas, a higher proportion of single/non-cohabiting mothers was recorded ($p = 0.017$). Maternal educational level also differed significantly: women from HA had a higher prevalence of primary education ($p < 0.001$). Conversely, maternal age showed no statistically significant differences between regions, with the 20–35 years age group predominating in both settings.

Birth Weight

Table **3** presents the results of the generalized linear model assessing predictors of birth weight.

Altitude was significantly associated with lower neonatal weight: newborns from high-altitude regions had reduced estimated birth weight compared with those from low altitude ($\beta = -0.038$; 95%CI: −0.071 to −0.005; $p = 0.024$). Preterm birth was strongly associated with decreased birth weight ($\beta = -0.243$; 95%CI: −0.328 to −0.158; $p < 0.001$). Maternal age <20 years was also associated with lower birth weight ($\beta = -0.050$; 95%CI: −0.083 to −0.017; $p = 0.003$). Maternal educational level, marital status, and newborn sex showed no significant associations (all $p > 0.05$).

A significant interaction was observed between high altitude and preterm birth ($\beta = 0.195$; 95%CI:

Table 3: Association of Altitude and Maternal–Perinatal Characteristics with Birth Weight: Generalized Linear Model (Gamma log-link)

Variable	Category	B	SE	95% CI	Wald χ²	*p*-value
Altitude	Low§	—	—	—	—	—
	High	−0.038	0.0169	−0.071, −0.005	5.104	.024*
Sex	Female§	—	—	—	—	—
	Male	−0.016	0.0133	−0.042, 0.010	1.532	.216
Gestational age	Term§	—	—	—	—	—
	Post-term	0.013	0.0228	−0.032, 0.058	0.331	.565
	Preterm	−0.243	0.0435	−0.328, −0.158	31.250	<.001**
Maternal age	20–35 years§	—	—	—	—	—
	>35 years	−0.032	0.0203	−0.071, 0.008	2.447	.118
	<20 years	−0.050	0.0169	−0.083, −0.017	8.853	.003*
Maternal education	Tertiary §	—	—	—	—	—
	Secondary	0.023	0.0619	−0.099, 0.114	0.133	.716
	Primary	−0.005	0.0212	−0.047, 0.036	0.061	.806
Marital status	Cohabiting§	—	—	—	—	—
	Non-cohabiting	0.025	0.0195	−0.014, 0.063	1.586	.208
Interaction	High altitude × Preterm	0.195	0.0503	0.096, 0.293	14.994	<.001**

§ Reference category. *p < .05; **p<.001.

0.096–0.293; p < 0.001), indicating that the negative impact of prematurity on birth weight is partially attenuated in high-altitude environments.

Table **4** summarizes the logistic regression results for Low Birth Weight (LBW) and Small for Gestational Age (SGA).

Low Birth Weight (LBW)

Altitude was not significantly associated with LBW (OR = 0.45; 95%CI: 0.17–1.23; p = 0.120). Gestational age showed strong effects: preterm newborns had markedly higher odds of LBW (OR = 5.20; 95%CI: 1.88–14.39; p = 0.002), whereas post-term births not associated with LBW (p = 0.211). Mothers <20 years had a higher likelihood of delivering LBW infants (OR = 2.41; 95%CI: 1.02–5.70; p = 0.045), whereas mothers older than 35 years showed no significant association. Maternal education, marital status, and newborn sex showed no significant associations.

Small for Gestational Age (SGA)

High altitude was significantly associated with a higher odd of SGA (OR = 2.29; 95%CI: 1.20–4.38; p = 0.011). Post-term birth also increased the likelihood of SGA (OR = 3.36; 95%CI: 1.40–8.07; p = 0.006), whereas preterm birth showed no significant association. Maternal age <20 years increased the risk of SGA (OR = 1.96; 95%CI: 1.05–3.65; p = 0.036). Additionally, low maternal educational (Primary) was associated with higher odds of SGA (OR = 2.12; 95%CI: 1.13–3.97; p = 0.019). Marital status and newborn sex were not significant predictors.

DISCUSSION

This study examined differences in birth weight and its association with gestational and geographical determinants among newborns from highlands (HL) and lowlands (LL) in the province of Catamarca. Our findings indicate that newborns from HL exhibited significantly lower birth weights and a higher frequency of low birth weight (LBW) and small-for-gestational-age (SGA) compared with those born in LL. However, although the prevalence of low birth weight (LBW) was higher in HL in the descriptive analysis, this difference did not remain significant after multivariate adjustment (p = 0.120), suggesting that the apparent excess of LBW is primarily explained by variation in gestational age rather than by altitude itself.

The magnitude of these differences is consistent with international evidence documenting a progressive decline in birth weight with increasing altitude [2, 15, 24, 25], with an estimated reduction of approximately 54.7 g per 1000 m of elevation [26].

However, this trend is not uniform across populations. Comparative studies report similar birth weight values among Tibetans and low-altitude populations, whereas Andean and North American groups with more recent settlement at high altitude exhibit significantly lower birthweight than their low-altitude counterparts [18, 24, 25, 27]. These

Table 4: Association of Altitude and Maternal–Perinatal Characteristics with LBW and SGA: Multivariable Logistic Regression

Variable	Category	Low Birth Weight OR (95% CI)	*p*-value	Small for Gestational Age OR (95% CI)	*p*-value
Altitude	Low§	—	—	—	—
	High	0.45 (0.17–1.23)	.120	2.29 (1.20–4.38)	.011*
Sex	Female§	—	—	—	—
	Male	1.32 (0.60–2.93)	.491	1.12 (0.78–1.61)	.676
Gestational age	Term§	—	—	—	—
	Post-term	2.34 (0.62–8.92)	.211	3.36 (1.40–8.07)	.006*
	Preterm	5.20 (1.88–14.39)	.002*	0.63 (0.27–1.45)	.331
Maternal age	20–35 years§	—	—	—	—
	>35 years	0.97 (0.26–3.63)	.963	1.57 (0.73–3.38)	.241
	<20 years	2.41 (1.02–5.70)	.045*	1.96 (1.05–3.65)	.036*
Maternal education	Tertiary§	—	—	—	—
	Secondary	1.79 (0.35–9.13)	.484	0.77 (0.26–2.26)	.636
	Primary	1.58 (0.41–6.07)	.502	2.12 (1.13–3.97)	.019*
Marital status	Cohabiting§	—	—	—	—
	Non-cohabiting	0.54 (0.12–2.43)	.421	0.99 (0.46–2.14)	.990

§ Reference category. *p < .05.

differences have been linked to multigenerational adaptive processes that modulate maternal–fetal oxygenation, supporting the notion that the response to altitude depends not only on the environment but also on population history. In fact, certain multigenerational high-altitude populations, particularly those of Andean and Tibetan ancestry, exhibit placental, hematological, and vascular physiological adaptations that mitigate the effects of hypoxia on fetal growth [28-29]. This evidence suggests an evolutionary process that differentiates risk profiles between populations with recent versus long-term residence at high altitude.

In this context, the differences observed in Catamarca are consistent with previous reports for historically exposed Andean populations, although their magnitude varies among regions [9, 30].

The observed interaction between geographic altitude and prematurity could be explained by the physiological effects of chronic hypobaric hypoxia during gestation. Exposure to reduced oxygen availability can induce alterations in placental function, activation of the hypothalamic-pituitary-adrenal axis, and increased inflammatory signaling—all mechanisms involved in the onset of labor. While in high-altitude populations the predominant adaptation is usually fetal growth restriction with term pregnancies, in contexts where adaptive capacity is exceeded, these mechanisms could contribute to an increased risk of preterm birth [18, 31, 32].

Among maternal factors, age <20 years was associated with lower neonatal weight and a higher risk of LBW and SGA, whereas marital status showed no association, and low educational level specifically increased the risk of SGA, reflecting biological and socioeconomic vulnerabilities in fetal growth.

Finally, the observed prevalence of LBW and SGA fell within intermediate values compared with Asian and South American high-altitude populations [19, 20, 33-36], reinforcing that interregional differences are influenced not only by altitude but also by population-specific characteristics, including duration of residence at high altitude. Similarly, the association identified between SGA and post-term pregnancy in HL, comparable to findings by Ogah *et al*. (2024) [36], suggests a potential functional limit in placental transfer beyond 40 weeks under chronic hypoxic conditions, warranting targeted investigation in the Andean region.

Low birth weight is a composite indicator that may result from prematurity, fetal growth restriction, or both, and is strongly associated with increased neonatal morbidity and mortality, particularly respiratory, metabolic, and infectious complications in the early postnatal period [37]. In contrast, small for gestational age more specifically reflects impaired intrauterine growth and is closely linked to altered postnatal growth trajectories, including delayed or excessive catch-up growth, as well as increased risk of neurodevelopmental difficulties and long-term cardiometabolic disorders [38,39]. Distinguishing between these outcomes is particularly relevant in high-altitude settings, where growth restriction at term may be more frequent than prematurity due to chronic hypobaric hypoxia and placental adaptive constraints [32].

Overall, these findings demonstrate that in Catamarca, birth weight is strongly determined by geographical elevation and gestational age, as well by specific maternal characteristics such as adolescent maternity and low education attainment, whose effects likely reflect both biological and socioeconomic mechanisms. This scenario is further complicated by climate change, as environmental and thermal variability have been associated with increased perinatal complications, preterm birth, and low birth weight [40, 41]. This combined exposure -altitude and climate change- places pregnancies at high altitude in a particularly vulnerable situation, demanding integrated approaches to perinatal health. However, there is a scarcity of studies simultaneously addressing physiological components and socioterritorial inequalities in rural high-altitude areas of northwestern Argentina, where accessibility, healthcare organization, and geographical conditions play key roles [1, 10, 42].

In populations residing at high altitude, perinatal care and pediatric follow-up of newborns with low birth weight or small for gestational age require specific strategies that acknowledge both physiological adaptations to hypoxia and the increased clinical vulnerability of these infants. Neonatal monitoring should prioritize early metabolic and cardiorespiratory assessment, together with intensive support for breastfeeding and planned neonatal discharge. Adapting neonatal care at high altitude does not imply more interventions, but rather smarter and context-specific ones.

Future research integrating individual socioeconomic indicators and maternal–fetal biomarkers is required to more accurately assess the relative contributions of environmental, obstetric, and adaptive factors in high-altitude pregnancy.

LIMITATIONS AND STRENGTHS

A major strength of this study is the analysis, conducted for the first time, of a large series of births occurring among populations residing at high altitude in the province of Catamarca, which provides original information within a geographic context that remains scarcely studied in the country. The use of key neonatal indicators, such as low birth weight and small for gestational age, allowed for a more precise characterization of maternal–infant outcomes associated with altitude.

An important limitation of this study is the lack of information on several maternal and clinical variables known to influence birth outcomes, including parity, adequacy of prenatal care, smoking status, maternal anemia, pre-pregnancy body mass index, and pregnancy-related complications. As a result, residual confounding cannot be entirely ruled out, and the findings should be interpreted as associative rather than causal.

The study period (1990–2010) spans years during which changes in obstetric care, maternal nutrition, and neonatal management may have occurred. Although these temporal factors could not be explicitly accounted for due to data limitations, the extended time frame provides a broad perspective on birth outcomes in the study population.

Finally, the smaller proportion of births at high altitude reflects the demographic distribution of the province. While this imbalance may reduce the precision of estimates for the high-altitude group, it does not invalidate the observed associations.

CONCLUSIONS

Overall, the results of this study—including lower birth weight and higher prevalence of LBW and intrauterine growth restriction at high altitude—confirm the vulnerability of populations residing under hypobaric hypoxia. The most relevant finding is the observed association between being small for gestational age and post-term pregnancy, which contributes an additional element for understanding the complex interaction among altitude, fetal maturation, and duration of gestation. These findings highlight the need for context-specific perinatal strategies in high-altitude regions and emphasize the importance of strengthening perinatal information systems to support early detection and timely intervention.

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CONFLICTS OF INTEREST

The authors declare that there are no relevant financial or non-financial competing interests to report.

AUTHORS' CONTRIBUTION

Both authors contributed equally to this work.

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