Arch Argent Pediatr 2024;122(2):e202310051

Birth weight in the Northwest region of Argentina. Comparison with a national reference and an international standard

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ABSTRACT

Introduction. Size at birth is subject to genetic and environmental influences; altitude is highly influential. Birth weight (BW) is the most widely used indicator to assess size at birth; different standards and references are available. Due to the variability in BW distribution in relation to altitude in the province of Jujuy (Argentina), the purpose of this study is to analyze the percentile distribution of BW in the highlands (HL) and the lowlands (LL) of Jujuy based on gestational age (GA) and sex and compare it with a national reference and the INTERGROWTH-21st (IG-21) international standard.

Population and methods. The records of 78 524 live births in Jujuy in the 2009–2014 period were analyzed. Using the LMS method, the 3rd, 10th, 50th, 90th, and 97th percentiles of BW/GA by sex were estimated for the HL (≥ 2000 MASL), the LL (< 2000 MASL), and the total for Jujuy, and compared with the Argentine population reference by Urquía and the IG-21 standard using growth charts. The statistical significance was established using the Wilcoxon test.

Results. BW in Jujuy showed a heterogeneous distribution, with statistically significant differences ($p < 0.05$) between the LL and the HL. When compared with the national reference and the IG-21 standard, differences in terms of altitude were observed, mainly in the 90th and 97th percentiles for both regions and the 3rd and 10th percentiles in the HL compared with the international standard.

Conclusions. BW distribution varied in association with altitude; therefore, to assess intrauterine growth, it is critical to include GA and the environment in which the pregnancy takes place.

Keywords: *birth weight; growth charts; altitude; Jujuy.*

doi: http://dx.doi.org/10.5546/aap.2023-10051.eng

To cite: Revollo GB, Dipierri JE, Díaz MP, Alfaro Gómez EL. Birth weight in the Northwest region of Argentina. Comparison with a national reference and an international standard. *Arch Argent Pediatr* 2024;122(2):e202310051.

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Funding*: Project "Anthropometric profile and altitude in pediatric and adolescent populations of Jujuy" (Perfil antropométrico y altura geográfica en poblaciones infanto-juveniles jujeñas). SECTER – UNJu (2016–2019 period).*

Conflict of interest: *None.*

Received*: 3-30-2023*
Accepted*: 7-6-2023*

INTRODUCTION

Human growth is subject to genetic and environmental influences; their expression varies based on time, magnitude, and duration of exposure, and is characterized by extraordinary plasticity and intra- and inter-population heterogeneity.[1,2] Among the environmental factors, altitude is one of the most relevant determinants of size at birth; there are numerous precedents that confirm its reverse association with birth weight (BW), even in developed countries and regions of the same country with similar socioeconomic conditions.[3–8] It is therefore worthy studying the variation of BW in the province of Jujuy, due to its location on the Andean foothills, with ecoregions located on an altitudinal gradient (between 400 and 4000 MASL) and their own differential demographic, socioeconomic, and cultural characteristics.

The size of a newborn (NB) infant is the result of all growth, from conception to birth, that depends both on the duration of gestation and the growth rate of the fetus. BW is the most common indicator used for its assessment. Different standards and references have been developed to assess it according to the NBs gestational age (GA). On the one side, references are descriptive in nature, showing or describing how most healthy children in a country grow up. On the other side, standards are prescriptive, showing how children should grow in an environment with optimal conditions according to their nutritional status and level of maturation.[9,10]

In Argentina, the references by Lejarraga and Fustiñana[11] were used until 2017 for the assessment of size; as of that year, the Committee on Fetal and Neonatal Studies (Comité de Estudios Fetoneonatales, CEFEN) of the Sociedad Argentina de Pediatría[12] proposed an update of the anthropometric assessment of preterm NBs using the reference by Fenton and Kim.[13] However, in 2011, Urquía et al. published a BW reference for the Argentine population, which was representative of the recent Argentine population and included all births occurred between 2003 and 2007.[14] In 2008, the multinational project for the development of prescriptive standards for fetal growth, newborn size, and postnatal growth of preterm infants was developed (INTERGROWTH-21st).[15] In 2020, the CEFEN, together with the National Secretariat of Health, agreed to recommend the replacement of the curves by Fenton and Kim[13] with the INTEGROWTH-21st (IG-21) standard for the assessment of size at birth and postnatal growth of preterm newborns in Argentina.[16]

Since the province of Jujuy presents variability in the distribution of BW in relation to altitude, this study analyzes the percentile distribution of BW for the highlands and lowlands of Jujuy based on GA and sex (2009–2014) and compares it with the reference by Urquía et al.[14] and the IG-21 standard.[15]

POPULATION AND METHODS

This was a descriptive, retrospective, eco-epidemiological, cross-sectional, time-series study. The data were obtained from the certificates of live births in the province of Jujuy from 2009 to 2014, provided by the Health Statistics and Information Department of the National Ministry of Health of Argentina. Exclusion criteria were records with missing data (weight, sex, GA), BW < 500 g, GA < 24^{+0} and > 42^{+6} weeks, multiple pregnancy, and those where the mother‘s place of residence was outside the province of Jujuy.

Statistical analysis

BW/GA percentiles by sex for the 2009–2014 period for the total of Jujuy, the highlands (HL ≥ 2000 MASL), and the lowlands (LL < 2000 MASL) were estimated. The LMS method was used, which summarizes the changing distribution of anthropometric measurements as a function of GA by means of L (lambda, asymmetry), M (mu, median), and S (sigma, coefficient of variation). The L, M, and S parameters were estimated using the maximum penalized likelihood procedure. Based on the L, M, and S values and using the LMS ChartMaker Pro software (The Institute of ChildHealth, London), the 3rd, 10th, 50th, 90th, and 97th percentiles were estimated,[17,18] which were selected taking into account those existing for the national reference[14] and the international standard.[15] The percentiles estimated for each sex in the HL and the LL were compared using growth charts with their corresponding values in the Argentine population reference by Urquía and the IG-21 standard, using the STATA V15 software. The differences for each GA and sex were established as follows:[19]

100 log* (reference percentile/estimated percentile)

The differences between the estimated percentiles and the selected parameters and their statistical significance were calculated using the Wilcoxon test.[20]

Ethical considerations

This study was conducted in accordance with the Declaration of Helsinki,[21] law no. 25326 on Personal Data Protection, resolution no. 1480/2011 by the National Ministry of Health, and resolution no. 012565 by the Ministry of Health of the province of Jujuy, and has been approved by the Provincial Health Research Ethics Committee of the Ministry of Health of Jujuy under resolution no. 2872-S-2018.

RESULTS

Once the selection criteria were applied, 78 524 live births in the province of Jujuy were included in the analysis (*Figure 1*). BW in Jujuy showed a heterogeneous distribution, with statistically significant differences between the LL and the HL. As shown in *Figure 2*, the percentile distribution of BW in the LL was consistent with that of the total for Jujuy, for both sexes. Births in the HL had a higher BW than in the LL between

Figure 1. Flow chart of data selection

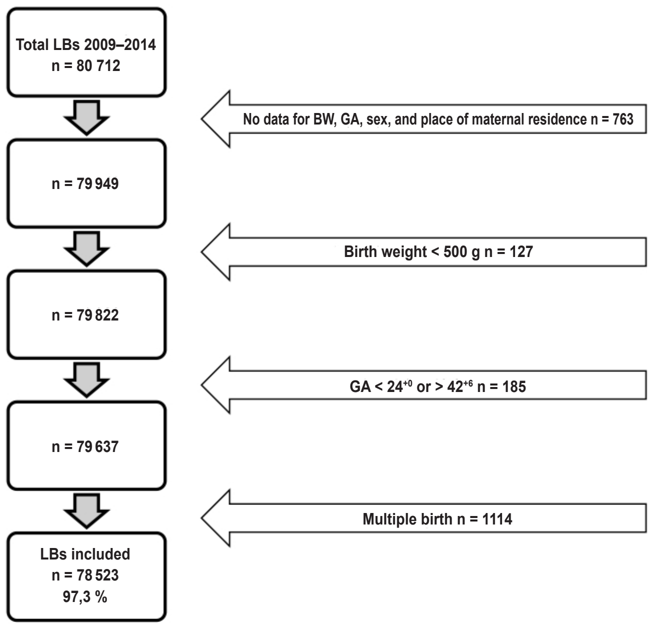
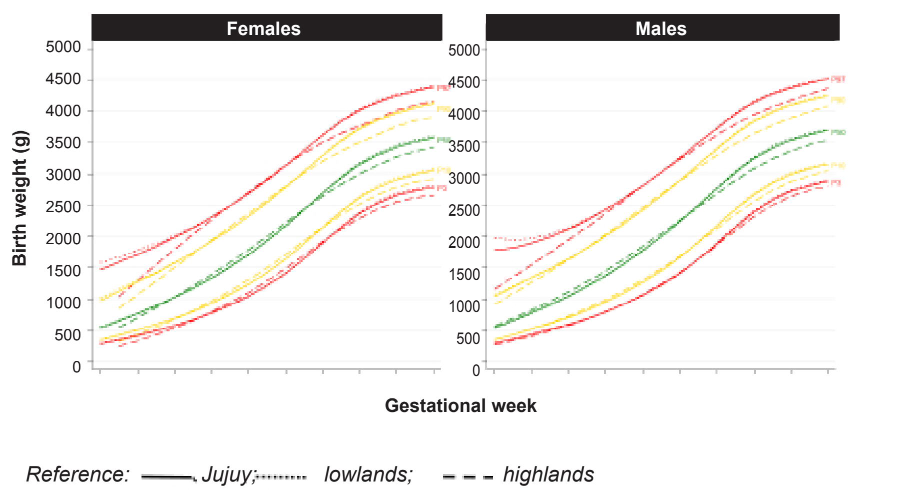


Figure 2. Percentile distribution of birth weight by gestational age and sex, total for Jujuy, the highlands, and the lowlands



30 and 34 weeks of GA, with a similar behavior in both sexes, although more marked differences were observed in males after 24 weeks of GA at the 10th and 50th percentiles (*Figure 2* and *Tables 1 and 2*). The differences were statistically significant only at the 90th and 97th percentiles in both sexes.

When comparing the percentile distribution

Table 1. Birth weight percentiles (grams) by gestational age of females in the highlands, the lowlands, and total for Jujuy. 2009–2014

GA	HIGHLANDS					LOWLANDS					TOTAL FOR JUJUY				
	P3	P10	P50	P90	P97	P3	P10	P50	P90	P97	P3	P10	P50	P90	P97
24	-	-	-	-	-	296	354	548	1016	1579	286	344	534	974	1465
25	247	327	541	844	1034	359	430	659	1158	1670	351	422	649	1125	1590
26	335	435	699	1066	1296	424	509	773	1294	1768	418	504	766	1271	1712
27	431	550	860	1284	1546	495	595	893	1433	1878	492	592	889	1417	1839
28	539	676	1028	1501	1790	575	691	1023	1581	2003	574	690	1023	1571	1978
29	659	815	1205	1720	2030	667	800	1168	1742	2146	668	802	1171	1738	2132
30	793	966	1391	1938	2264	773	925	1329	1918	2307	776	929	1334	1918	2302
31	940	1129	1583	2153	2487	895	1068	1507	2109	2486	901	1074	1514	2112	2486
32	1102	1305	1783	2367	2703	1039	1231	1704	2316	2682	1045	1238	1711	2321	2685
33	1285	1499	1994	2585	2918	1207	1420	1922	2539	2895	1215	1427	1928	2544	2900
34	1487	1710	2216	2805	3132	1406	1636	2162	2781	3127	1413	1642	2166	2784	3130
35	1700	1929	2437	3014	3330	1637	1881	2424	3039	3374	1642	1884	2423	3037	3374
36	1913	2143	2644	3201	3501	1894	2147	2695	3300	3624	1892	2142	2687	3291	3616
37	2113	2342	2831	3363	3645	2155	2410	2954	3543	3854	2144	2396	2937	3525	3837
38	2291	2517	2995	3502	3767	2387	2640	3174	3741	4038	2367	2618	3149	3717	4015
39	2438	2666	3138	3630	3884	2563	2813	3336	3885	4169	2538	2787	3309	3859	4145
40	2555	2791	3270	3761	4010	2681	2933	3452	3992	4268	2657	2908	3428	3969	4248
41	2621	2866	3358	3852	4098	2754	3011	3536	4072	4345	2729	2987	3512	4051	4325
42	2657	2913	3416	3910	4154	2810	3074	3605	4139	4408	2783	3047	3579	4117	4387

GA: gestational age.

Table 2. Birth weight percentiles (grams) by gestational age of males in the highlands, the lowlands, and total for Jujuy. 2009–2014

GA	HIGHLANDS					LOWLANDS					TOTAL FOR JUJUY				
	P3	P10	P50	P90	P97	P3	P10	P50	P90	P97	P3	P10	P50	P90	P97
24	270	347	566	911	1151	297	350	534	1063	1980	298	353	541	1042	1775
25	337	431	693	1089	1355	364	430	652	1207	1929	365	433	659	1192	1817
26	410	522	824	1264	1550	433	514	773	1347	1959	434	517	781	1337	1891
27	489	620	963	1442	1744	508	604	901	1490	2031	509	607	909	1485	1990
28	578	728	1112	1628	1943	591	704	1041	1645	2137	592	708	1049	1644	2112
29	679	850	1274	1823	2150	686	819	1197	1816	2273	687	823	1206	1818	2260
30	794	986	1450	2030	2365	794	949	1370	2003	2433	795	954	1379	2007	2429
31	924	1137	1639	2244	2586	916	1096	1560	2203	2611	918	1101	1568	2210	2613
32	1071	1304	1838	2462	2808	1057	1263	1768	2418	2807	1059	1266	1774	2425	2812
33	1237	1486	2044	2679	3024	1221	1453	1994	2649	3021	1222	1454	1997	2653	3026
34	1424	1684	2255	2891	3233	1413	1668	2240	2893	3250	1412	1666	2238	2894	3253
35	1634	1897	2468	3096	3431	1638	1912	2503	3149	3492	1634	1905	2495	3144	3490
36	1861	2122	2683	3295	3619	1893	2178	2776	3410	3739	1884	2165	2761	3398	3730
37	2096	2350	2892	3482	3794	2161	2447	3040	3655	3970	2146	2429	3019	3637	3956
38	2317	2560	3079	3643	3942	2407	2690	3267	3859	4160	2388	2667	3242	3837	4142
39	2502	2735	3234	3776	4063	2601	2878	3438	4007	4294	2580	2853	3411	3984	4276
40	2643	2873	3363	3894	4174	2738	3010	3560	4115	4393	2718	2988	3536	4094	4377
41	2737	2969	3463	3995	4275	2828	3101	3646	4192	4465	2810	3079	3624	4175	4453
42	2804	3041	3543	4083	4367	2901	3174	3716	4255	4523	2882	3152	3695	4241	4514

GA: gestational age.

in the Jujuy regions with the national reference[14] and the IG-21 standard,[15] differences were observed in terms of altitude. BW values in the LL in both sexes were lower with most GA periods at the 3rd and 10th percentiles. As of the 50th percentile, the pattern reversed, with a higher BW as of week 27 of GA in females and as of week 30 of GA in males (*Figure 3*). Differences were always statistically significant ($p < 0.05$) at the 90th and 97th percentiles, with a more heterogeneous behavior across the other percentiles by sex. In the case of males, a statistical significance was recorded at the 3rd percentile compared with both the national reference and the international standard, and only at the 10th percentile compared with the national reference, while, in females, the differences were only significant in the comparison of the 50th percentile with the international standard.

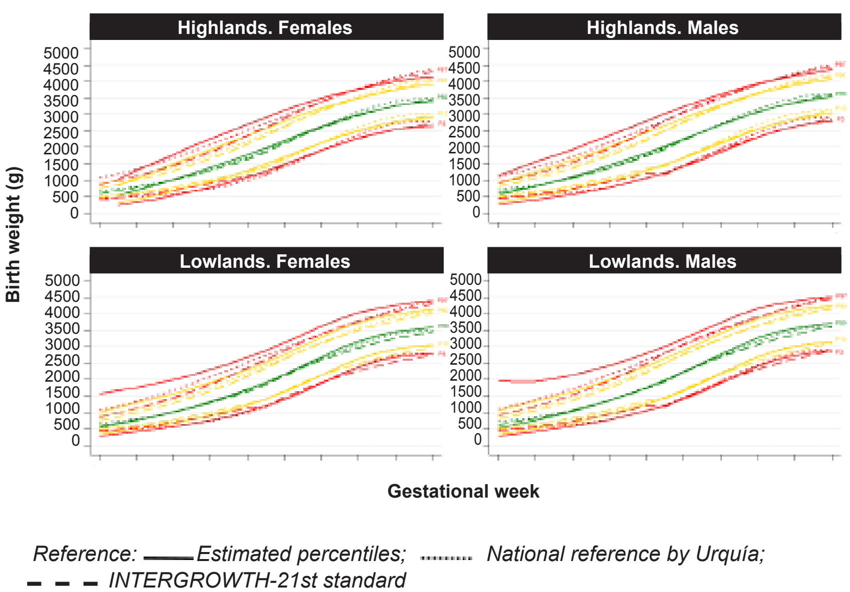
In addition, the distribution of BW in the HL, compared with the national reference, showed higher values across all percentiles for both sexes between 30 and 36 weeks of GA. The same pattern was observed at the 50th, 90th, and 97th percentiles, with a heterogeneous behavior at the 3rd and 10th percentiles (*Figure 3*). Differences were statistically significant in males across almost all percentiles, except for the 90th percentile compared with the national reference and the 50th percentile compared with both, while, in the case of females, only in the 10th percentile when compared with the national reference and at the 3rd, 90th, and 97th percentiles when compared with the international standard.

DISCUSSION

The effect of altitude on BW has been extensively studied. Several studies have proposed the existence of mechanisms of adaptation to the environment in populations living at high altitude for generations, such as a lower average birth weight that would not represent a risk, but an adaptation to the extreme environment.[6,8,22-25] The effect of altitude on BW was demonstrated even when adjusting for various maternal and socioeconomic variables.[4-8,26,27] The statistically significant differences observed in this study between the HL and the LL when analyzing the percentile distribution of BW may be explained by such adaptive mechanisms.

There are few studies comparing percentile distribution curves of BW with a reference and a standard as in this study. Our results show that, in Jujuy, the distribution of BW in both the LL and the HL differs from the growth curves selected for comparison.[14,15] The comparison with both the national reference and the international standard shows more marked differences in the LL at a GA below 32 weeks with higher

Figure 3. Percentile distribution of birth weight estimated for the highlands and the lowlands compared with the national reference by Urquía and the Intergrowth-21st standard by sex



average weights at the 3rd and 10th percentiles, but lower at the 90th and 97th percentiles. When comparing the percentile distribution of BW in the HL with the national reference, the international standard, and the LL, higher average BWs were observed across all percentiles analyzed for the GA corresponding to very preterm infants (28–32 weeks of GA) and moderate to late preterm infants (32–37 weeks of GA).[28] This pattern is reversed in term births, where the lower average BW observed as of 37 weeks of GA may be due to a decrease in oxygen saturation, hemoglobin levels, and arterial oxygen content in these environments as of the third trimester, which would lead to intrauterine growth restriction, hence a reduction in BW at high altitudes as of 36 weeks of gestation.[29–31] These results, in turn, would support the hypothesis that, in high altitude regions, due to an evolutionary mechanism of natural selection, there would be a prenatal elimination of births with extremely low birth weights.[24]

The distribution of BW was lower than that indicated in the national reference by Urquía et al.[14] up to 34 weeks of GA at the 3rd percentile and for all GA periods at the 10th percentile. This would account for what has been reported by Revollo et al.,[10] who used the same growth curves to determine the prevalence of small for gestational age (SGA) infants at a regional level in Argentina. The results indicate a higher prevalence of SGA < 3rd percentile among preterm infants compared with the international standard[15] and among term infants compared with the national reference,[14] as well as a higher prevalence of SGA < 10th percentile at all GA periods, which may be attributed to differences in the population selection criteria for the international standard and the national reference, the estimation of GA, and the method for calculating and smoothing percentiles.[10,14,15]

In general, the IG-21 standard was used by several authors mainly to determine the prevalence of deficient nutritional phenotypes. In Jujuy, Martínez et al.,[32] with the purpose of analyzing the relative usefulness of 3 proportionality indices for the assessment of nutritional status of NBs at a high altitude (≥ 2000 MASL) and in the lowlands (< 2000 MASL), used the IG-21 standard as a criterion to identify and eliminate cases with extreme length data. Revollo et al.[33] analyzed the spatial distribution of the prevalence of SGA and its secular trend between 1991 and 2014 in Jujuy and found higher values in high altitude regions (Puna and Quebrada), compared with the LL.[33]

Only one study performed an analysis similar to our study, which compared the IG-21 standard with the percentile distribution of weight, length, and head circumference of full-term NBIs above 3400 MASL in Cusco, Peru.[34] Their results did not find a statistically significant difference with the IG-21 standard at the 3rd, 10th, 50th, 90th, and 97th percentiles, unlike the results described here. According to Villamonte-Calanche et al.,[34] their results would support previous findings that hypobaric hypoxia caused by high altitude has only a marginal effect on fetal growth compared with other social determinants, such as poverty, maternal nutrition, biofuel use, and other variables commonly observed in populations living at a high altitude. However, these results are very inconsistent with several articles included in the bibliography. The study by Villamonte-Calanche et al.[34] is the only one that considers that altitude has only a marginal effect on size at birth. This discrepancy may explain the differences found with our study, which observed statistically significant differences in the distribution of BW at the 3rd, 10th, 90th, and 97th percentiles in the HL compared with the IG-21 standard. Methodological differences are also present. Villamonte-Calanche et al.[34] used a different method to estimate percentiles and to compare the distribution with the international standard; they used only term births, from mothers at an optimal age (18 to 35 years), while our study included births as of 24 weeks of GA and from mothers of all ages.

Although the effect of altitude on birth size and growth in children has been extensively studied, there are no other studies that analyze the percentile distribution of indicators of birth size at a high altitude compared with the parameters commonly used for clinical or epidemiological assessment, and this is the greatest strength of our study, which in turn included a large volume of data that represented 97.3% of births in the province of Jujuy that occurred between 2009 and 2014. However, the main limitation of this study is working with secondary data, which highlights the importance and value of data recording.

CONCLUSIONS

The percentile distribution of BW in Jujuy showed differences between the HL and the LL. Such distribution did not show the same behavior across all the estimated percentiles.

Differences were observed in the distribution of BW in both the HL and the LL with curves commonly used to assess prenatal growth at the population or individual level.

Births in the LL, regardless of gestational age, had a distribution with a higher BW at the 90th and 97th percentiles compared with both curves, although the distribution was similar to the national reference across the rest of the estimated percentiles.

Births in the HL showed a higher BW in most of the percentiles analyzed compared with the national reference and at the 90th and 97th percentiles compared with the international standard between 28 and 36 weeks of GA, but lower than the international standard at the 3rd and 10th percentiles for the same GA range.

For the assessment of prenatal growth, it is critical to consider not only anthropometric indicators (weight, length, head circumference), but also GA and the place and context where the pregnancy takes place, taking into account the differences found in this study. ■

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