CHEST

Overnight Polysomnographic Characteristics and Oxygen Saturation of Healthy Infants, 1 to 18 Months of Age, Born and Residing At High Altitude (2,640 Meters)

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BACKGROUND: Approximately 8% of the world population resides above 1,600 m, with about 10 million people living above 2,500 m in Colombia. However, reference values for polysomnography (PSG) and oxygen saturation (Spo_2) of children < 2 years old residing at high altitude are currently unavailable.

METHODS: Healthy infants aged 1 to 18 months born and residing at high altitude (Bogotá: 2,640 m) underwent overnight PSG. Four age groups were defined: group 1, < 45 days; group 2, 3 to 4 months; group 3, 6 to 7 months; and group 4, 10 to 18 months. Of 122 children enrolled, 50 had three consecutive PSG tests and were analyzed as a longitudinal subcohort.

RESULTS: A total of 281 PSG tests were performed in 122 infants (56% girls): group 1, 106 PSG tests; group 2, 89 PSG tests; group 3, 61 PSG tests; and group 4, 25 PSG tests. Active sleep diminished and quiet sleep increased with maturation. Apnea-hypopnea indexes (total, central, and obstructive) were highest in group 1 (21.4, 12.4, and 6.8/h total sleep time, respectively) and diminished with age ($P < .001$). Mean Spo_2 during waking and sleep increased with age ($P < .001$). Nadir Spo_2 values during respiratory events were lower in younger infants. Longitudinal assessments of 50 infants confirmed the temporal trends described for the cross-sectional dataset.

CONCLUSIONS: Healthy infants (≤ 18 months old) born and residing at high altitude show preserved sleep architecture but higher apnea-hypopnea indexes and more prominent desaturation with respiratory events than do those living at low altitude. The current study findings can be used as reference values for infants at high altitude. CHEST 2015; 148(1):120-127

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ABBREVIATIONS: AASM = American Academy of Sleep Medicine; AHI = apnea-hypopnea index; AS = active sleep; CA = central apnea; C-AHI = central apnea-hypopnea index; masl = meters above sea level; NREM = non-rapid eye movement; O-AHI = obstructive apnea-hypopnea index; ODI = oxygen desaturation index; PB = periodic breathing; PSG = polysomnography; QS = quiet sleep; REM = rapid eye movement; Spo_2 = oxygen saturation; TST = total sleep time

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In 1995, approximately 140 million people resided at altitudes exceeding 2,500 meters above sea level (masl), a number that most likely has increased further in the past 2 decades.[1,2] In Colombia, just > 20% of the population, approximately 10 million people, live at altitudes between 2,500 and 3,500 masl,[3] a level classified as high altitude.[4,5] As the altitude increases, the barometric pressure and inspired pressure of oxygen fall, leading to diminished P_{AO_2} and Pa_{O_2}. This causes a compensatory increase of the ventilation with Pa_{CO_2} reduction, favoring the occurrence of central apnea (CA) and periodic breathing (PB) during sleep.[6-8]

The majority of the studies examining either the polysomnography (PSG) or the respiratory and oxygen saturation (Spo_2) normative patterns during sleep in children have been conducted at sea level or at a low altitude level, and of those studies, only a few have specifically examined younger infants.[9-18] Furthermore, only a very small portion of these studies have used comprehensive PSG assessments, with most of them limiting their measurements and conclusions to oxyhemoglobin saturation trends.

In Bogotá, at 2,640 masl, the values of Spo_2 recorded in healthy infants during wakefulness range from 93% to 93.6%, corresponding to Pa_{O_2} values between 60 and 70 mm Hg (ie, very proximal to the steep component of the hemoglobin dissociation curve, $Spo_2 < 90\%$).[19] At this altitude, the relative hypoventilation that accompanies sleep onset could induce significant drops in Spo_2 and further disrupt sleep architecture. Consequently, in otherwise healthy infants, it is readily conceivable that the sleep and respiratory characteristics of infants residing at high altitude will differ from those described at sea level. We are unaware of published studies delineating the PSG characteristics of healthy children living at high altitude during their first years of life, with only one report on 3- to 5-year-old children living at 1,600 masl.[20] The main objective of this study was to perform comprehensive PSG assessments of healthy infants in Bogotá, Colombia, during their first 18 months of life to examine the effects of high altitude on sleep architecture and respiratory patterns and to delineate reference values for subsequent clinical applications.

Materials and Methods

Design, Subjects, and Groups

In this analytical cross-sectional study, we included healthy infants from 1 to 18 months of age, born and residing in Bogotá, Colombia, at a mean altitude of 2,640 masl, during the period April 2009 to August 2012. Some infants were also longitudinally evaluated. Recruitment was performed through advertisements in primary care pediatric clinics, health centers, and the community at large. The inclusion criteria were (1) normal gestational period without any reported medical problems or complications of pregnancy; (2) birth between weeks 37 to 40 postconceptional age by either vaginal delivery or cesarean section; (3) asymptomatic status without any previous or current respiratory disorder different from acute upper respiratory infections (if symptoms of acute intercurrent illness, such as nasal discharge, were present, the PSG evaluation was postponed by at least 2 weeks after complete resolution of such minor symptoms); (4) normal height and weight for age based on Colombian reference values[21]; and (5) normal physical examination done by a pulmonologist and a pediatrician (E. D.-M.). Infants with a history of an apparent life-threatening event, any genetic disorder, cardiac or respiratory illness including patent ductus arteriosus, cardiac murmur, transient tachypnea of the newborn, respiratory distress, or pneumonia were excluded.

To assess the effect of postnatal age on sleep parameters, four age groups were defined as follows: group 1, < 45 days; group 2, 3 to 4 months; group 3, 6 to7 months; and group 4, 10 to 18 months. A medical assessment was performed by one of the investigators (E. D.-M.) prior to each PSG evaluation to ascertain that the infant fulfilled the eligibility criteria, to conduct a thorough physical examination including basic anthropometric measurements, and to rule out the presence of any acute or chronic illness. Infants who completed their participation in group 1 were invited to participate in subsequent groups to enable longitudinal evaluation of a subset of the cohort. The study was approved by the ethics committee of the Fundación Neumológica Colombiana (approval act number 121 dated August 30, 2007). Informed consent was obtained from every parent or legal caretaker.

Overnight PSG and Pulse Oximetry

Standard overnight multichannel PSG was performed at the Fundación Neumológica Colombiana by PSG technologists with expertise in infants using commercially available digital acquisition equipment (Philips Respironics; Alice 5 and LE models). Children were studied for up to 10 h in a dark and quiet room with an average ambient temperature of 19°C. A parent or guardian was present throughout the study. No drugs were used to induce sleep.

Arterial Spo_2 levels and heart rate during wakefulness and sleep were recorded using a high-precision pulse oximeter (Masimo; Rad 8 model) incorporated into the PSG digital acquisition system. A period of 15 min of technically adequate and movement artifact-free signal was verified prior to initiation of the PSG.

The following parameters were measured: chest and abdominal wall movements assessed by inductance plethysmography, heart rate assessed by ECG, and airflow monitored by nasal pressure cannula and an oronasal thermistor. As mentioned, Spo_2 was assessed by pulse oximetry with simultaneous recording of the pulse waveform. Bilateral electrooculograms, three channels of EEG, chin and anterior tibial electromyograms, and analog output from a body-position sensor were also monitored. Tracheal sounds were monitored with a microphone sensor, and a digital, time-synchronized video recording was obtained.

Sleep architecture was assessed by standard techniques following the recommendations and guidelines of the American Academy of Sleep Medicine (AASM).[22-25] In infants < 6 months of age, sleep stages were scored as active sleep (AS), quiet sleep (QS), or indeterminate sleep, whereas non-rapid eye movement (NREM) stages 1 to 3 and rapid eye movement (REM) sleep scoring rules were used in older infants. The proportion of time spent in each sleep stage was expressed as a percentage of the total sleep time (TST). The apnea index was defined as the

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number of episodes of apnea per hour of TST. We used the following definitions[22-25]: obstructive apnea: the absence of airflow (>90% reduction in airflow signal) with continued chest wall and abdominal movements lasting for at least two breaths; CA: a reduction of ≥90% in airflow signal in the absence of chest or abdominal movements lasting for ≥20 s or for at least two breaths and associated with an oxygen desaturation ≥3% or with a decrease of the heart rate; mixed apnea: an event that meets the apnea criteria for at least two breaths and is associated with absent respiratory effort during one portion of the event and the presence of inspiratory effort in another portion, regardless of which portion comes first; hypopnea: a decrease in nasal flow of 50% for two breaths or more with a corresponding decrease in Spo_2 of 3%, arousal, or both; PB: the presence of three or more CAs within <20 s intervals from each other; apnea-hypopnea index (AHI): the number of episodes of apnea and hypopnea per hour of TST.

Data Analysis

Data were assessed for Gaussian distribution using the Kolmogorov-Smirnov test. If the data were normally distributed, they are presented as mean ± SD unless stated otherwise (eg, median and percentiles). For each of the four age groups, the major parameters evaluated included demographics and anthropometric measures, TST, sleep efficiency, percentage TST spent in QS or AS or REM or NREM sleep, the total AHI, the central AHI (C-AHI), the obstructive AHI (O-AHI), the percentage of TST spend in PB, the mean Spo_2 during waking and sleep states and during specific events, and the oxygen desaturation index (ODI) (ie, number of Spo_2 drops >3%/h TST). Comparisons across groups were performed using analysis of variance or Kruskal-Wallis test. Statistical analyses were conducted using SPSS 21.0 (IBM), and two-tailed *P* values <.05 were considered to reach statistical significance

Results

A total of 281 overnight PSG evaluations were performed in healthy children: 106 children were included in group 1, 89 in group 2, 61 in group 3, and 25 in group 4. Some children were evaluated longitudinally and included in more than one group: 50 children (41%) underwent three PSG evaluations, 17 (14%) underwent all four possible PSG tests, and 55 (45%) underwent two PSG tests; consequently, the 281 PSG tests were performed in only 122 subjects. Seventy-three children (60%) were born by vaginal delivery; 86% of the mothers and 80% of the fathers had been born and lived at altitudes >2,000 masl. The demographic characteristics are shown in Table 1 As planned, the mean of age for groups 1 to 4 were 1, 3½, 6½, and 13 months. respectively. Weight and length increased with age, as expected for healthy children.

Table 2 illustrates the distribution of sleep stage and its changes with age; in summary, the percentage of time spent in AS/REM sleep, the arousal index, and the respiratory arousal index were higher in group 1 than in the other groups and declined with age (*P*<.001). Conversely, QS/NREM sleep was lowest in group 1 and increased with age (*P*<.001). As shown in Table 3, the evolution of respiratory events displays a clear age group dependency: the AHI, C-AHI, and O-AHI were all higher in group 1 (21.4, 12.4, and 6.8/h TST, respectively) than in the other groups and diminished progressively with age (*P*<.001) without differences in apnea-hypopnea duration. In all groups, the AHI value was influenced mainly by central events (C-AHI).

When each age group was analyzed independently, there were no significant differences in mean Spo_2 among wakefulness and AS/REM and QS/NREM stages. However, comparing the age groups, the mean and nadir Spo_2 during respiratory events were lower, and the time spent with Spo_2 <90%, the ODI AS/REM, and the ODI QS/NREM were higher in younger subjects. As age increased, the mean and nadir Spo_2 during respiratory events increased (*P*<.001), and the time spent with Spo_2 <90% and <85%, the ODI AS/REM, and the ODI QS/NREM significantly decreased (*P*<.001) (Table 4) with some infants <4 months of age registering Spo_2 values <90%. No significant differences by sex were found.

Figure 1 shows the temporal changes in sleep architecture and respiratory and oximetry events over the first 6 months of life among the 50 infants who underwent three PSG evaluations. Longitudinal assessments of these 50 infants confirmed the temporal trends described for the cross-sectional dataset.

Discussion

For the first time to our knowledge, this study describes the sleep architecture characteristics and the respiratory and Spo_2 patterns observed in a large cohort of healthy infants aged 1 to 18 months who were born and reside at high altitude. The study also describes the

TABLE 1] Demographic and Anthropometric Characteristics

Characteristic	Group 1 (n = 106)	Group 2 (n = 89)	Group 3 (n = 61)	Group 4 (n = 25)	*P* Value
Age, mo	1.0 ± 0.3	3.6 ± 0.5	6.6 ± 0.6	13.2 ± 1.9	<.001
Weight, kg	4.1 ± 0.6	6.3 ± 0.8	7.8 ± 0.9	9.3 ± 1.1	<.001
Height, cm	53.0 ± 3.2	60.5 ± 2.9	66.6 ± 3.5	74.4 ± 4.9	<.001

Data are presented as mean ± SD. *P* values reflect analysis of variance comparisons across all groups.

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TABLE 2] Polysomnographic Findings in Healthy Infants at High Altitude: Sleep Architecture

Sleep Measure	Group 1 (n = 106)	Group 2 (n = 89)	Group 3 (n = 61)	Group 4 (n = 25)	*P* Value
Sleep efficiency, % total recording time	79.7 (67.5-90.0)	88.2 (74.2-96.0)	88.5 (72.5-95.6)	83.7 (70.8-95.7)	< .001
AS/REM, % TST	53.2 (35.5-66.1)	49.8 (32.8-61.6)	27.4 (14.8-41.7)	23.7 (14.1-30.1)	< .001
QS/NREM, % TST	45.9 (33.1-61.8)	49.6 (35.1-67.2)	72.6 (57.1-85.2)	76.3 (66.2-85.9)	< .001
Arousal index, No./h TST	19.0 (12.3-29.0)	14.9 (9.6-24.7)	10.6 (5.8-17.5)	9.5 (5.1-14.5)	< .001
Respiratory arousal index, /h TST	1.6 (0.1-7.1)	1.2 (0-5.1)	0.6 (0-1.6)	0.1 (0-1.0)	< .001

Data are presented as median (fifth-95th percentile). *P* values reflect Kruskal-Wallis comparisons across all groups. AS = active sleep; NREM = non-rapid eye movement; QS = quiet sleep; REM = rapid eye movement; TST = total sleep time.

changes and trends according to normal age-related maturational processes. These findings were obtained from infants who were scrutinized rigorously for their healthy status. All had normal weight and height at baseline (1 month old on average) and grew within the normal range according to the local reference values.[21] In children < 3 years old, these local child growth reference curves are very similar to those of the World Health Organization[26] and are considered interchangeable, suggesting that at these ages there are not significant differences in weight and height related to this high altitude (2,640 masl). (The majority of infants included in the World Health Organization Multicentre Growth Reference Study were from sea level or low altitude).

Consequently, we can reliably conclude that this population of children is healthy, and our findings can be used as normative reference values for infants living at 2,640 masl and similar altitudes (ie, high altitudes [2,500 to 3,500 masl]), particularly for clinical purposes. To date, the interpretation of sleep studies performed during the clinical evaluation of pediatric patients for sleep-disordered breathing relies exclusively on normative data summarized in the AASM guidelines or on other publications based on recordings obtained from infants and young children at sea or low altitude level.[14-16,18,22-25,27] However, the scarce normative data for very young infants[18] and, more specifically, for children living at high altitudes,[20] clearly precludes robust interpretation of clinical studies at high altitudes.

Interestingly, we did not observe gross differences in the distribution of sleep stages or their postnatal developmental patterns in the subjects when compared with infants at sea or low level.[15,16,27-29] Although head-to-head comparisons between Colombian infants residing at different altitudes were not performed in this study, the absence of major differences in sleep architecture suggests that hypobaric hypoxic conditions do not alter the homeostatic mechanisms governing sleep regulation and maturation.

On the contrary, this study illustrates the significant differences in PSG characteristics and Spo_2 during the sleep of healthy children living at high altitude in comparison with those living at sea and low altitude levels that have been published previously.[9-18,22-25] These differences could arguably be inferred as representing abnormalities rather than constituting the normative data that relate to high-altitude living conditions. Although, as mentioned, the sleep architecture was similar, in those healthy infants residing at 2,640 masl, when the low altitude level definitions were applied (also used for this study), we found a high prevalence of total, central, and

TABLE 3] Polysomnographic Findings in Infants Born and Residing at High Altitude: Respiratory Events

Respiratory Measure	Group 1 (n = 106)	Group 2 (n = 89)	Group 3 (n = 61)	Group 4 (n = 25)	*P* Value
AHI, /h TST	21.4 (3.1-74.9)	12.8 (2.7-72.4)	7.4 (1.8-21.4)	3.1 (0.8-9.2)	< .001
C-AHI, /h TST	12.4 (2.2-65.4)	8.3 (1.6-50.7)	5.5 (0.8-17.8)	2.3 (0.7-8.7)	< .001
O-AHI, /h TST	6.8 (0.6-27.6)	3.5 (0.3-15.1)	0.9 (0-4.9)	0.5 (0-1.8)	< .001
PB, % TST	2.0 (0-21.9)	0.9 (0-15.7)	0.2 (0-3.1)	0 (0-5.5)	< .001
AH duration, s	6.1 (4.8-7.2)	6.0 (5.0-7.4)	6.2 (4.8-8.8)	6.8 (5.3-8.4)	NS

Data are presented as median (fifth-95th percentile). *P* values reflect Kruskal-Wallis comparisons across all groups. AH = apnea-hypopnea; AHI = apnea-hypopnea index; C-AHI = central apnea-hypopnea index; NS = not significant; O-AHI = obstructive apnea-hypopnea index; PB = periodic breathing. See Table 2 legend for expansion of other abbreviation.

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TABLE 4] Spo_2 During Wakefulness and Sleep and During Respiratory Events in Infants Born and Residing at High Altitude

Saturation Parameter	Group 1 (n = 106)	Group 2 (n = 89)	Group 3 (n = 61)	Group 4 (n = 25)	*P* Value
Spo_2 wakefulness, %	92.5 (88.0-96.0)	93.0 (88.0-96.0)	94.0 (91.0-97.0)	95.0 (91.0-96.0)	< .001
Spo_2 AS/REM, %	92.0 (87.0-96.0)	93.0 (86.0-96.0)	94.0 (90.0-96.0)	94.0 (91.0-96.0)	< .001
Spo_2 QS/NREM, %	93.0 (88.0-96.0)	93.0 (87.0-96.0)	94.0 (90.0-96.0)	94.0 (91.0-96.0)	< .001
Mean Spo_2 during respiratory events, %	84.0 (73.0-90.0)	85.0 (77.0-91.0)	87.0 (81.0-92.0)	88.0 (83.0-93.0)	< .001
Nadir Spo_2 during respiratory events, %	70.0 (53.0-84.0)	72.0 (58.0-84.0)	76.0 (61.0-87.0)	80.0 (70.0-92.0)	< .001
T90	10.3 (0.6-56.4)	5.0 (0.2-69.6)	1.9 (0-33.3)	0.5 (0-5.3)	< .001
T85	2.1 (0-22.1)	0.7 (0-19.7)	0.1 (0-4.1)	0 (0-1.8)	< .001
ODI AS/REM, /h TST	91.7 (26.3-170.1)	76.4 (15.9-132.0)	51.6 (12.7-100.6)	31.4 (10.3-68.2)	< .001
ODI QS/NREM, /h TST	47.1 (9.0-113.6)	25.5 (2.8-124.2)	15.6 (3.0-85.6)	11.3 (2.7-41.4)	< .001

Data are presented as median (fifth-95th percentile). *P* values reflect comparisons across all groups. ODI = oxygen desaturation index (No. Spo_2 drops > 3% desaturations/h TST); Spo_2 = oxygen saturation; T85 = percentage of TST with Spo_2 < 85%; T90 = percentage of TST with Spo_2 < 90%. See Table 2 legend for expansion of other abbreviations.

obstructive apneas (high AHI, C-AHI, and O-AHI) and, particularly, a very high frequency of oxygen desaturation episodes, related or not related to respiratory events, compared with those described for the same age groups at sea level.[9-18,27-32] As described at low altitude, these events were more frequent in neonates,

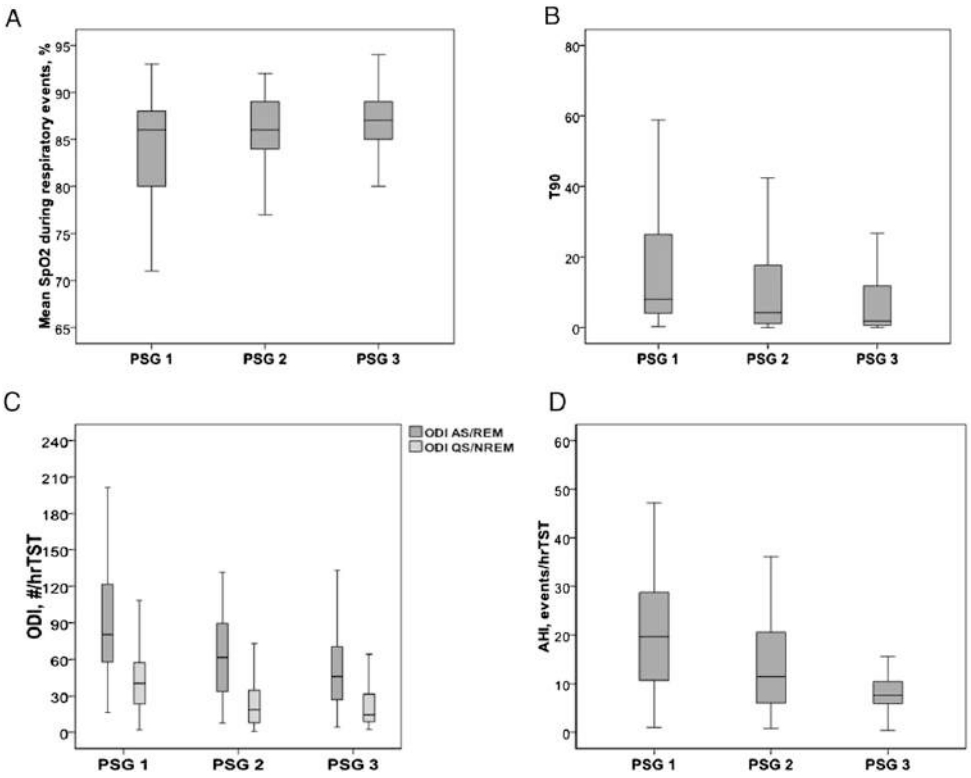

Figure 1 – *Oxygen and apnea-hypopnea index (AHI) during sleep in 50 infants followed longitudinally over time. Trends with age from PSG 1 (< 45 d) to PSG 2 (3½ mo) and PSG 3 (6½ mo) in 50 infants followed longitudinally: SpO2 increased progressively and T90, ODI, and AHI decreased progressively with age. A, SpO2. B, T90: % TST with SpO2 < 90%. C, ODI (number of SpO2 drops > 3% desaturations/h TST). D, AHI. Graphs are expressed as 25th-75th percentile. AS = active sleep; NREM = non-rapid eye movement; ODI = oxygen desaturation index; PSG = polysomnography; QS = quiet sleep; REM = rapid eye movement; SpO2 = oxygen saturation; T90 = percentage of total sleep time with oxygen saturation < 90%; TST = total sleep time.*

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and presented an age-dependent amelioration with maturation.[30,32,33]

The high frequency of the AHI and the C-AHI could be related to the values of Pao_2 and Spo_2. As described at the Bogotá altitude,[19] the baseline wakefulness Spo_2 values found in our study were lower than those found at sea level, with a significant part of the sleep time with Spo_2 near to or below 90%. At this point, the oxygen dissociation curve of hemoglobin is steep, and small reductions in Pao_2 cause significant changes in Spo_2. Because the C-AHI and hypopnea definitions involve an oxygen desaturation $\geq 3\%$, it may be expected that with minimal falls of Pao_2, these definitions may be met more easily regardless of the apnea duration. In addition, the lower Pao_2 at high altitude and the compensatory increase in ventilation with $Paco_2$ reduction can favor the occurrence of CA and PB.[6-8,33-41]

Another intriguing result was the occurrence of obstructive respiratory events, despite the absence of any evidence of craniofacial abnormalities or enlarged adenotonsillar tissues in the upper airway in the cohort or the presence of reported snoring during the preinclusion evaluation. The reasons for the high occurrence of obstructive apnea are not clear. However, it has been noted that newborns with CA and PB, particularly those with hypoxia, can develop passive pharyngeal collapse or active glottal closure, with obstructive apnea.[42,43] We posit that such obstructions may simply reflect the previously reported instability of the upper airway during hypoxia and CA that is typical in both premature infants and in very young full-term infants.[44] Alternatively, the intricate mechanisms governing upper airway function in the context of PB should also be mentioned.[42,45,46] Accordingly, with lower Spo_2 values and a higher C-AHI (including PB) at Bogotá's altitude, it would not be unexpected to see a higher prevalence of obstructive episodes. Unlike a study in young children (1-3 months of age),[18] little evidence of mixed apneas was found in our study.

Although these and probably other less apparent mechanisms could explain the high prevalence of apneas (total, central, and obstructive) and desaturation found in our study, these findings have to be viewed as normal for infants living at high altitude. Accordingly, the recurrent desaturations and markedly reduced nadir Spo_2 values recorded in the healthy subjects should be interpreted as the normal and anticipated features of infants residing at high altitude and may explain why such infants, when asleep, will manifest relatively frequent apneic events, preferentially, but not exclusively, central in nature. Supporting this assumption, as Spo_2 increased with age, the frequency of apneic events declined. The temporal trajectory of such changes, as illustrated in Figure 1, may be related to some changes occurring in the respiratory mechanics during the first 6 months of life with a more passive maintenance of functional residual capacity and reduced compliance of the chest wall, which will stabilize lung volumes and thereby provide increased resistance to desaturation during respiratory events.[47-49] In addition, postnatal developmental changes in respiratory control may further enhance the stability and robustness of the respiratory system and, thus, prevent or dampen oscillatory behaviors in respiratory patterning (eg, reduced frequency of PB).[34,50,51] We should note that although less likely, we cannot exclude the possibility that the progressive attenuation of the respiratory and hypoxemic event frequencies with age could also reflect the well-known acclimatization to high-altitude hypoxia.[52,53]

To further place our current study within the context of previously published information, we review some salient reports of Spo_2 levels in infants at high altitude. Niermeyer et al[39] reported reduced Spo_2 values in infants at 3,100 m masl from the first week until 4 months after birth that were primarily prominent during QS. In Leadville, Colorado (3,100 masl), the Spo_2 ranged from 85% to 93% during waking and during the first 24 h, from 83% to 93% during the first week, and was further reduced to 75% to 86% during QS.[38] At 4 months of age, Spo_2 levels had increased from 89% to 93% and from 81% to 91% during wakefulness and sleep, respectively, reflecting adaptive responses over time from fetal circulatory patterns to the more mature circulation in childhood.[33] These and several other studies on saturation profiles in young infants support our current findings. Of note, in the only other published PSG study in healthy 3- to 5-year-old children at 1,600 masl, both nadir and mean Spo_2 were higher than in the current study, most likely reflecting both the older age and the higher barometric pressure in that study.[20]

A limitation of our study is that we did not incorporate in the analyses end-tidal capnographic measurements taken in some of our PSG evaluations. Preliminary attempts in several very young infants resulted in substantial crowding within the nasal airway when all sensors were in place, and a substantial artifactual loss of signal throughout the night further compelled us to withhold capnography from subsequent studies. As such, we are unable to assess alveolar ventilation and its changes with normal maturation in these healthy infants residing at high altitude.

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A strength of the study is that each one of the four age groups included a significant number of healthy children (106, 89, 61, and 25), thereby empowering its validity and potential to serve as reference values, while also showing the changes and trends that occur with the increase in age. In addition, 50 of the infants (40%) recruited during their first weeks of life and included in group 1 (age 1 month on average) were also included in groups 2 (3½ months) and 3 (6½ months) and were analyzed longitudinally as a prospective cohort. The information gathered is clearly aligned with that obtained from the cross-sectional analysis findings and reinforces the conclusions of the current study.

According to the AASM[22,23] and the American Academy of Pediatrics guidelines,[54] an AHI > 1/h TST would be considered abnormal in children. If such criteria were implemented in this healthy population, then 100% of the PSG studies would be clearly abnormal, thereby stressing the importance of establishing altitude-appropriate normative reference values, such as to ultimately delineate cutoff criteria for what may constitute disease in this population. The normative data afforded by the current study should provide a better alternative guide for interpreting clinical sleep studies conducted among the relatively large sector of the worldwide pediatric population living at altitude. In summary, this study describes the overnight PSG characteristics and nocturnal Spo_2 of healthy infants aged 1 to 18 months who were born and live at high altitude.

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