

# Arterial oxygen saturation in healthy Mexican full-term newborns at different altitudes above sea level

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## Abstract

**Background:** Arterial oxygen saturation ( $S_aO_2$ ) values are used to make clinical decisions that might change a patient's prognosis, and it has been proposed as the fifth vital sign. This study aimed to determine the variation of  $S_aO_2$  at different altitudes above sea level (ASL) in healthy Mexican full-term newborns. **Methods:** From July 2018 to June 2019, a cross-over study was conducted in six hospitals at different altitudes ASL in Mexico.  $S_aO_2$  was measured in 4015 newborns after the first 24 h of birth and before leaving the hospital using pulse oximetry. We analyzed three groups: < 250 m ASL (group 1), 1500 m ASL (group 2), and 2250 m ASL (group 3). **Results:** The mean  $S_aO_2$  was  $97.6 \pm 1.8\%$ . For group 1, mean oxygen saturation was  $98.2 \pm 1.9\%$ ; for group 2,  $96.7 \pm 1.9\%$ , and for group 3,  $96.0 \pm 2.1\%$ . A statistically significant difference was observed among the groups ( $p < 0.001$ ), and this difference was higher between groups 1 and 2 (1.5%,  $p < 0.001$ ). Linear regression analysis showed a decrease in oxygen saturation of 1.01% for every 1000 m ASL. **Conclusions:** We demonstrated a statistically significant reduction in  $S_aO_2$  levels at higher altitudes. This observation can be relevant for clinical decision-making based on pulse oximetry such as critical congenital heart disease screening in Mexico, where more than half of the population lives above 1500 m ASL.

**Keywords:** Altitude. Newborn. Oxygen saturation. Pulse oximetry.

## Saturación arterial de oxígeno en recién nacidos mexicanos a término sanos a diferentes altitudes sobre el nivel del mar

## Resumen

**Introducción:** Los valores de  $S_aO_2$  (saturación de oxígeno) se utilizan para la toma de decisiones clínicas que podrían cambiar el pronóstico del paciente. El objetivo de este estudio fue determinar la variación de la  $S_aO_2$  en recién nacidos mexicanos a término sanos a diferentes altitudes en México. **Métodos:** Se llevó a cabo un estudio transversal en seis hospitales situados a diferentes altitudes en México. Se determinó la  $S_aO_2$  usando oximetría de pulso en 4015 recién nacidos después de las primeras 24 horas de vida, pero antes del egreso del hospital de nacimiento. Se formaron tres grupos para el análisis: grupo 1 con altitud < 250 m sobre el nivel del mar (SNM); grupo 2, altitud de 1500 m SNM y grupo 3, altitud de 2250 m SNM. **Resultados:** El promedio de la  $S_aO_2$  fue de  $97.6 \pm 1.8\%$ . Para el grupo 1, la media fue  $98.2 \pm 1.9\%$ , para el 2,  $96.7 \pm 1.9\%$  y para el 3,  $96.0 \pm 2.1\%$ . Se observó una diferencia estadísticamente significativa entre los grupos ( $p < 0.001$ ), que fue mayor entre los grupos 1 y 2 (1.5%,  $p < 0.001$ ). El análisis de regresión lineal mostró una reducción

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Date of reception: 24-02-2023

Date of acceptance: 30-05-2023

DOI: 10.24875/BMHIM.23000032

Available online: 01-09-2023

Bol Med Hosp Infant Mex. 2023;80(4):242-246

www.bmhim.com

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de 1.01% en la  $S_aO_2$  por cada 1000 m SNM. **Conclusiones:** Se demostró una disminución estadísticamente significativa de los valores de  $S_aO_2$  conforme aumenta la altitud. Esto puede ser de particular relevancia en la toma de decisiones clínicas basadas en la oximetría de pulso, como el tamiz neonatal cardiaco, sobre todo en México donde mas de la mitad de la población vive a una altitud superior a 1500 m SNM.

**Palabras clave:** Altitud. Recién nacidos. Saturación de oxígeno. Oximetría de pulso.

## Introduction

Noninvasive arterial oxygen saturation ( $S_aO_2$ ) is routinely used in neonatal intensive care units and other clinical settings. The measurement of  $S_aO_2$  is used to make clinical decisions that might change a patient's prognosis, and it has been proposed as the fifth vital sign<sup>1-3</sup>.

Pulse oximetry determinations are based on spectrophotometry principles<sup>4</sup>; this technology has contributed to great advances in the management of patients, offering an easy, quick, noninvasive, and reproducible estimation of  $S_aO_2$ <sup>5</sup>. Until now, pulse oximetry has been one of the main tools for noninvasive monitoring of in-hospital patients, especially for those with critical conditions.

The first hour of life is an adaptive period from fetal to extrauterine life, and factors such as altitude above sea level (ASL) might significantly affect  $S_aO_2$  of the newborn<sup>6</sup>.

Although the inspired oxygen fraction in the air is constant (21% regardless of altitude), partial oxygen pressure is a function of the barometric pressure. For this reason,  $S_aO_2$  is expected to be lower at high altitude locations, considering a lower atmospheric pressure<sup>7</sup>.

The relationship between  $S_aO_2$  and altitude ASL varies among ages<sup>8</sup>. Therefore, it is important to have precise reference values in healthy full-term newborns.

This study aimed to analyze  $S_aO_2$  levels in healthy full-term newborn patients at different altitudes ASL.

## Methods

### Study design

We conducted a multicenter cross-over study including six hospitals in Mexico located at different altitudes. Three hospitals were located < 250 m ASL, one at 1500 m ASL and two at 2250 m ASL. The study was approved by the research and ethics committees of each institution, and informed consent was obtained from parents or legal tutors before patients were included.

### $S_aO_2$ measurement

We obtained  $S_aO_2$  values in healthy full-term newborns, after the first 24 hours of life.

Besides  $S_aO_2$ , the following variables were obtained: age in hours, gender, gestational age determined by Capurro's score, weight and length at birth, type of birth, Apgar's score, and maternal disease if present.

Healthy full-term newborns were defined as those newborns who needed no supplementary oxygen and showed no respiratory distress, cyanosis, cardiac murmur, or any other evident clinical perturbation.

The device used for  $S_aO_2$  determinations was the Masimo pulse oximeter Radical-7 model (Masimo, Irvine, CA, USA) with neonatal sensors (factory code 2514).

Before the study, the participating physicians were trained for the proper use of the oximeter to standardize the technique.

All measurements were performed when the newborn was awake with no agitation or irritability. The sensor was placed in the newborn's right hand, with a stabilization period of at least 1 min or until the plethysmographic curve was steady.

### Statistical analysis

All data were collected in Excel format (Microsoft Office 2016) and exported to STATA 17.0 (Stata Corp LLC 4905 Lakeway Drive College Station, Texas. USA).

General patterns of healthy full-term newborns are expressed as frequencies or proportions considering qualitative variables, while quantitative variables were expressed as mean and standard deviations.

Analysis of variance (ANOVA) and  $\chi^2$  were used to identify significant differences between the three groups, the first test for quantitative variables and the second for qualitative variables. For both tests, a p-value < 0.05 was considered significant.

Simple linear regression and multiple linear regression analysis were used to evaluate altitude ASL and  $S_aO_2$ , and other related variables. Regression analysis results are shown as correlation coefficients with 95% confidence intervals.

## Results

A total of 4015 healthy Mexican full-term newborns from six centers were included (Table 1). Mean weight and height were 3252 g and 49.6 cm, respectively. Eutocic delivery was present in 66.5% of cases, and only 1.6% of newborns were born from multiple pregnancy.

The mean gestational age was 39 weeks, and the Apgar's score at the first minute of life was 8.2 and at 5 minutes, 8.9 (Table 2). The mean  $S_aO_2$  of all healthy Mexican full-term newborns was  $97.6 \pm 1.8\%$ . For group 1, the mean  $S_aO_2$  was  $98.2 \pm 1.4\%$ , for group 2,  $96.7 \pm 1.9\%$  and for group 3,  $96.0 \pm 2.1\%$ .

A significant difference was observed among the three groups ( $p < 0.001$ ), and higher between groups 1 and 2 (1.5%,  $p < 0.001$ ) as compared with groups 2 and 3 (0.7%,  $p < 0.001$ ) (Table 3).

Other variables, such as weight, age (postpartum hours), cesarean section, maternal disease, and gestational age, showed a significant difference among the three groups (Table 4). The analysis showed a negative correlation between  $S_aO_2$  and altitude ASL (coefficient =  $-0.00101$ ), meaning that for every 1000 m ASL,  $S_aO_2$  reduces by 1.01% (Figure. 1).

## Discussion

$S_aO_2$  values at different altitudes ASL have not been clearly established, which is why a "normal range", rather than a specific number has been used.

Rojas-Camayo et al.<sup>8</sup> reported  $S_aO_2$  decrease as altitude increases in all age groups, which is evident above 2500 m ASL.

Other authors suggest that  $S_aO_2$  in newborns only decreases in altitudes  $> 1500$  m ASL<sup>9</sup>; however, Samuel et al.<sup>7</sup> described a small but statistically significant difference between  $S_aO_2$  values in healthy full-term newborns close to sea level (25 m ASL) compared with locations with a moderate high altitude (780 m ASL) (98.9 vs. 98.5%,  $p = 0.03$ ).

Our findings are consistent with other studies (Poets et al.<sup>4</sup>, Levesque et al.<sup>10</sup>, Guo et al.<sup>11</sup>, and O'Brien et al.<sup>12</sup>) reporting  $S_aO_2$  values in healthy full-term newborns between 97% and 98.3% at an altitude close to sea level.

In our study,  $S_aO_2$  fluctuates between 96 and 96.7% at altitudes  $> 1500$  m ASL, similar to those reported by Guo et al.<sup>11</sup> (96.4-95.5%) and Bakr and Habib<sup>13</sup> (95.4%) but different from those reported by Thilo et al.<sup>6</sup> (92.7%)

**Table 1.** Study population

Center	Location	Altitude in meters above the sea level	Number of newborns
Group 1	Mérida, Yucatán Tampico, Tamaulipas Hermosillo, Sonora	8-210	2437
Group 2	Zapopan, Jalisco	1571	1300
Group 3	Mexico City	2240-2265	278
Total			4015

**Table 2.** General features of healthy Mexican full-term newborns

Characteristics	Number/mean	Percentage/SD*
Male	2020	50.3%
Female	1995	49.7%
Weight (g)	3253	$\pm 435$
Length (cm)	49.6	$\pm 2.4$
Gestational age (weeks)	39	$\pm 1.2$
APGAR'S score At the 1 <sup>st</sup> min At 5 min	8.2 8.9	$\pm 0.6 \pm 0.3$
Type of birth Regular delivery Cesarean section Multiple pregnancy Maternal disease	2671 1344 64 193	66.5% 33.5% 1.6% 5.2%
Groups considering altitude Group 1 Group 2 Group 3	2437 1300 278	60.7% 32.4% 6.9%

SD: standard deviation.

and Morgan et al.<sup>14</sup> (93%). This difference could be attributed to the type of oximeter sensor used in our study (similar to the one used by Guo et al. and Bakr and Habib)<sup>11,13</sup> which uses signal extraction technology to provide precise lectures with slightly higher values.

As predicted, we demonstrated a statistically significant decrease of  $S_aO_2$  as altitude ASL increases ( $< 250$  m =  $98.2 \pm 1.4\%$ , 1500 m =  $96.7 \pm 1.9\%$ , and 2250 m =  $96.0 \pm 2.1\%$ ). Our results are supported by other studies reporting  $S_aO_2$  values 0.4% lower than those observed at sea level in newborns at moderate-high altitudes (780 m ASL).

**Table 3.** Group analysis

Characteristics	Group 1 (< 250 m ASL)	Group 2 (1 500 m ASL)	Group 3 (2 250 m ASL)	p-value
S <sub>a</sub> O <sub>2</sub> (mean ± SD)	98.2 ± 1.4	96.7 ± 1.9	96.0 ± 2.1	< 0.001
Males (%)	50.2	50.1	52.1	0.819
Weight in kilograms (mean ± SD)	3.3 ± 0.4	3.2 ± 0.4	3.1 ± 0.3	< 0.001
Gestation weeks (mean ± SD)	39.1 ± 1.3	38.9 ± 1.1	38.9 ± 1.2	< 0.001
Cesarian section (%)	28.7	34	72.6	< 0.001
Maternal disease (%)	6.4	2.7	7.9	< 0.001
Age in hours at the time of measurement (mean ± SD)	39.3 ± 15	47.1 ± 8.9	36.6 ± 11	< 0.001

ASL: above sea level; SD: standard deviation; S<sub>a</sub>O<sub>2</sub>: arterial oxygen saturation.

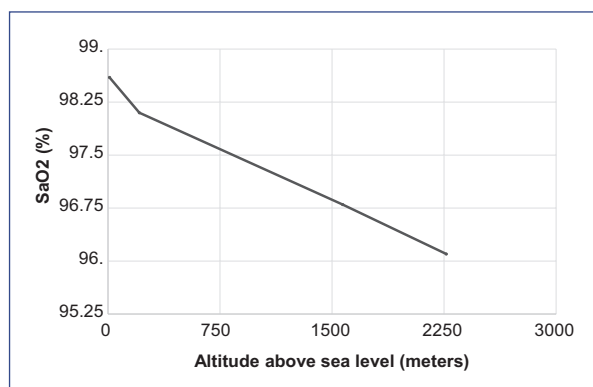
**Table 4.** Linear regressions between S<sub>a</sub>O<sub>2</sub> and other variables

Variables	Simple linear regression		Multiple linear regression	
	S <sub>a</sub> O <sub>2</sub> (raw)		S <sub>a</sub> O <sub>2</sub> (adjusted)	
	Coefficient (CI 95%)	p-value	Coefficient (CI 95%)	p-value
Altitude ASL (1000 m)	-1.01 (-1.08/-0.94)	< 0.001	-1.01 (-1.08/-0.94)	< 0.001*
Weight (Kg)	-0.04 (-0.17/0.08)	0.525	-	
Gestation weeks	-0.0014 (-0.0441/46.9)	0.952	-	
Cesarian section	-0.35 (-0.47/-0.23)	< 0.001	-0.07 (-0.18/-0.03)	0.188**
Maternal disease	-0.01 (-0.28/0.26)	0.923	-	
Age in hours (10 <sup>3</sup> )	-10 (-14/-6)	< 0.001	-0.3 (-3.5/4.2)	0.848**

\*Adjusted for weight, age by hours and cesarian section.

\*\*Adjusted for ASL.

ASL: above sea level; CI: confidence interval; S<sub>a</sub>O<sub>2</sub>: arterial oxygen saturation.

**Figure 1.** Altitude and S<sub>a</sub>O<sub>2</sub> above sea level (m). S<sub>a</sub>O<sub>2</sub>: arterial oxygen saturation.

Guo et al.<sup>11</sup> reported a mean S<sub>a</sub>O<sub>2</sub> of 97.9% close to sea level (0-500 m ASL), with 1.5% of decrease for

higher altitudes (500-1500 m ASL) and 2.4% at moderate-high altitudes (1500-2500 m ASL). That study concluded that S<sub>a</sub>O<sub>2</sub> decreased by 1.54% for every 1000 m ASL, while our results showed a 1.01% decrease for every 1000 m ASL. This difference might be attributable to the altitude of the centers located at the extremes of the samples: in Guo's report, the center with the lowest altitude was located at 267 m ASL. Conversely, half of the centers in our study were located < 250 m ASL and in these places the mean S<sub>a</sub>O<sub>2</sub> was 98.5%.

Here, we report an association between altitude and other variables such as weight, gestational age, type of birth, and preexistent maternal comorbidity (Table 3). The linear regression analysis showed that only two variables (besides altitude) were inversely related to S<sub>a</sub>O<sub>2</sub>: age in hours and type of birth. Multiple

regression analysis was adjusted for altitude to exclude the possibility of confounding variables. Age in hours and type of birth had a stronger relationship with the health center than  $S_aO_2$  (Table 4). As more specialized centers are expected to have more cesarean sections, a lower gestational age and weight or other related variables might be conditioned. To manage a possible effect of these factors on  $S_aO_2$ , we used multiple regression analysis showing a persistent reduction of 1.01% for every 1000 m ASL, meaning that the variation of  $S_aO_2$  is mainly due to altitude instead of other factors.

In the present study, we demonstrated a statistically significant reduction in  $S_aO_2$  level at higher altitudes ASL (1.01% for every 1000 m ASL).

This observation can be particularly relevant for clinical decision-making based on pulse oximetry as critical congenital heart disease screening in countries such as Mexico where more than half of the population lives above 1500 m ASL.

One limitation of this study was that the  $S_aO_2$  values described were obtained only from the right hand and not the average of the right hand and foot.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author has this document.

## Conflicts of interest

The authors declare no conflicts of interest.

## Funding

No funding.

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