

ALTITUDE ABOVE SEA LEVEL AND BODY MASS INDEX AS DETERMINANTS OF OXYGEN SATURATION IN CHILDREN: THE SON@ STUDY

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ABSTRACT

Background: Altitude above sea level and body mass index are well-recognized determinants of oxygen saturation in adult populations; however, the contribution of these factors to oxygen saturation in children is less clear. **Objective:** To explore the contribution of altitude above sea level and body mass index to oxygen saturation in children. **Methods:** A multi-center, cross-sectional study conducted in nine cities in Mexico. Parents signed informed consent forms and completed a health status questionnaire. Height, weight, and pulse oximetry were recorded. **Results:** We studied 2,200 subjects (52% girls) aged 8.7 ± 3.0 years. Mean body mass index, z-body mass index, and oxygen saturation were 18.1 ± 3.6 kg·m⁻², 0.58 ± 1.3 , and $95.5 \pm 2.4\%$, respectively. By multiple regression analysis, altitude proved to be the main predictor of oxygen saturation, with non-significant contributions of age, gender, and body mass index. According to quantile regression, the median estimate of oxygen saturation was 98.7 minus 1.7% per km of altitude above sea level, and the oxygen saturation fifth percentile 97.4 minus 2.7% per km of altitude. **Conclusions:** Altitude was the main determinant of oxygen saturation, which on average decreased 1.7% per km of elevation from a percentage of 98.7 at sea level. In contrast with adults, this study in children found no association between oxygen saturation and obesity or age. (REV INVES CLIN. 2015;67:366-71)

Key words: Oxygen. Altitude. SpO₂. Body mass index. Children

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INTRODUCTION

Altitude above sea level is the main determinant of the percentage of oxygen saturation (SpO_2)¹. Data from the PLATINO study, a population-based survey conducted among adults in Latin America, concluded that additional predictive factors for hypoxemia include age, body mass index (BMI), and a low forced expiratory volume at one second (FEV_1). The prevalence of hypoxemia ($\text{SpO}_2 \leq 88\%$) reported in that study was 6% (95% CI: 4.6–7.7) for Mexico City, which is located at an altitude of 2,240 meters above sea level (MASL). The PLATINO Study included only adult subjects ≥ 40 years of age^{2,3}. Although, intuitively, the determinants of oxygen saturation in children could be similar to those reported in adults, the relative contribution of altitude and BMI to oxygen saturation in this population has not been explored in detail. This issue is especially relevant in Mexico as it is the country with the highest prevalence of childhood obesity worldwide⁴. In addition, 20% of Mexico's population lives in the metropolitan area of Mexico City at an altitude of 2,240 MASL. Therefore, both altitude and obesity could simultaneously and synergistically affect oxygen saturation levels and produce a high prevalence of hypoxemia in Mexican children. Thus, the objectives of the SON@ Study (Study of Oxygen Saturation in Children; in Spanish, Estudio de Saturación de Oxígeno en Niños y Niñas) are to: (i) investigate the potential effect of altitude and BMI on oxygen saturation levels in children aged 2–16 years; (ii) formulate an SpO_2 reference equation for this population; (iii) explore potential independent variables associated with SpO_2 (e.g., age, sex, weight, height, ambient exposures, respiratory comorbidities); and (iv) determine the prevalence of hypoxemia in those children using two cutoff points: $\text{SpO}_2 \leq 90\%$ and $\text{SpO}_2 \leq 88\%$. Preliminary results of the SON@ Study were presented as an abstract at the 2014 Latin American Thoracic Association Meeting (Congreso de la Asociación Latinoamericana del Tórax) in Medellín, Colombia.

MATERIAL AND METHODS

The study was approved by the Science and Bioethics Committee of the National Institute of Respiratory Diseases of Mexico (code number C60-11), and authorized by the Mexican Department of Education (SEP). All children and parents signed an informed consent form.

The SON@ Study is a cross-sectional, school-based survey designed to analyze the effect of altitude and BMI on oxygen saturation in children. It included schools in the following cities in Mexico: Mérida (sea level), Monterrey (530 MASL), Tepic (915 MASL), Guadalajara (1,450 MASL), Mexico City (2,240 MASL), Texcoco de Mora (2,250 MASL), and Toluca (2,680 MASL). Schools were selected through a non-probabilistic sampling of private and public educational institutions. Participants' age range was 2–16 years. All children were invited to participate.

Children and their parents first completed a standardized respiratory questionnaire that explores environmental exposures (tobacco, charcoal, wood smoke, outdoor pollution), premature birth, chronic diseases, sleep-disordered breathing, and chronic or acute respiratory symptoms. Once the questionnaires were received, a pediatric pulmonologist and three respiratory therapists visited each school, where they measured the participants' height twice (in centimeters) with a SECA portable stadiometer (Seca GMBH & Co., Hamburg, Germany; model 206), and weight (in kilograms) with a Tanita scale (Tanita UK Ltd. Middlesex, United Kingdom; model UM-061). They used a Nonin oximeter (Nonin Medical Inc.; model Onyx 9500) to take six readings of pulse oximetry (percentage), and the average of those measures was used for analysis. During these procedures, subjects were seated and at rest with the oximeter placed on their right index finger. The device had previously been validated at 2,240 MASL³. Children with unstable SpO_2 measurements (coefficient of variation $> 10\%$) were excluded from the analysis, as were those who did not provide authorization for the anthropometric measurements or SpO_2 test.

Statistical analysis

Data are presented as means and standard deviations, or as percentages and 95% confidence intervals (95% CI). We used the Kolmogorov-Smirnov test to analyze the distribution of the variables. After graphically verifying that a straight line described the relation among variables, we generated multiple linear regression models using SpO_2 as the dependent variable. We also obtained the relative contribution of the co-variables in the final model. Random distributions of residuals were verified. The accepted level of significance was two-tailed $p < 0.05$. All statistical analyses were performed with commercially available STATA v.13 software, (Stata Corp. College Station, TX).

Table 1. General characteristics according to altitude above sea level; unless otherwise specified, results are presented as means and standard deviation

	Mérida (9 m)	Monterrey (530 m)	Tepic (915 m)	Guadalajara (1,540 m)	Mexico City (2,240 m)	Toluca (2,680 m)	All
Participants	247	80	230	157	1,068	418	2,200
Girls, n (%)	130 (52.6)	38 (47.5)	130 (56.5)	76 (48.4)	552 (51.6)	217 (51.9)	1,143 (52)
Age, years	7.41 (2.3)	8.2 (2.2)	8.9 (2.2)	6.2 (3.1)	9.8 (3.02)	7.4 (2.4)	8.7 (3.0)
Weight, kg	29.2 (10.9)	30.4 (9.1)	36.6 (15.1)	25.2 (12.7)	36 (15.6)	24.9 (8.9)	32.2 (14.4)
Weight, Z-score	0.88 (1.34)	0.82 (0.9)	0.87 (1.20)	0.87 (2.0)	0.02 (1.2)	-0.07 (1.29)	0.32 (1.37)
Height, cm	124.4 (14.7)	130.8 (14.5)	136.2 (15.6)	118 (18.8)	134.9 (20.0)	121.3 (14.1)	129.9 (18.9)
Height, Z-score	0.23 (1.17)	0.56 (1.61)	0.69 (1.12)	0.77 (1.75)	-0.42 (1.19)	-0.34 (1.17)	-0.11 (1.31)
BMI, kg/m ²	18.2 (3.5)	17.5 (3.0)	18.9 (4.2)	17.0 (3.3)	18.7 (3.6)	16.4 (2.7)	18.1 (3.6)
BMI, z-score	1.0 (1.4)	0.54 (1.3)	0.8 (1.4)	0.4 (1.5)	0.6 (1.1)	0.1 (1.2)	0.58 (1.3)
Overweight or obesity*, n (%)	110 (44.5)	35 (43.7)	106 (46)	37 (23.5)	387 (36.2)	93 (22.2)	768 (34.9)
SpO ₂ , %	98.7 (0.6)	97.5 (0.8)	96.8 (1.8)	96.8 (1.2)	94.7 (1.7)	93.8 (2.7)	95.5 (2.4)
SpO ₂ [†] , (LLN) %	98.8 (98)	97.5 (95)	97.5 (90.6)	97.2 (93.8)	95.3 (92)	94.8 (90.3)	96 (92.5)

*Defined as BMI > 1 z-score.

†Numbers are median SpO₂ and, in parenthesis, the lower limit of normality.BMI: body mass index; SpO₂: oxygen saturation; LLN: lower limit of normal.

RESULTS

A total of 2,524 children answered the general questionnaire. Of these, 324 were excluded from analysis because they failed to provide either anthropometric or SpO₂ measurements (n = 318), or had unstable SpO₂ signals (n = 6). The study population thus consisted of 2,200 children (1,143 girls, 52%) with a mean age of 8.7 ± 3.0 years. Table 1 shows the general characteristics of the study population according to city altitude. We found that children living at low altitudes have more overweightness and obesity than those living at moderate elevations (Fig. 1).

The only significant variable in the univariate analysis associated with SpO₂ proved to be altitude, which had a Spearman correlation coefficient (r_{sp}) of -0.67 ($p < 0.001$). Weight had an $r_{sp} = -0.09$ ($p < 0.001$), but once adjusted for altitude it showed no differences in SpO₂. Altitude adjusted for previous exposure to smoke from wood or charcoal combustion decreased oxygen saturation (SpO₂ coefficient -1.66 %/km; $p < 0.001$) as did a history of acute respiratory disease 15 days prior to testing (coefficient = -0.2 ; $p < 0.008$). Other variables, such as prematurity, presence of chronic respiratory diseases, and snoring or wheezing, did not prove to be risk factors for low oxygen saturation. Figure 2 presents SpO₂ by altitude, showing that oxygen saturation decreased with

Figure 1. Percentage of overweightness and obesity, according to altitude; the error bars show the 95% confidence interval.

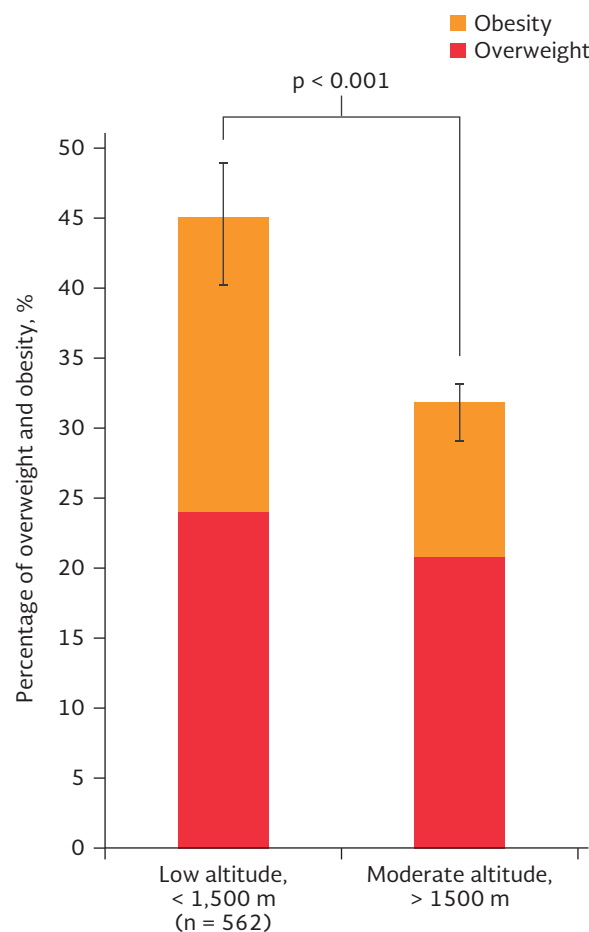
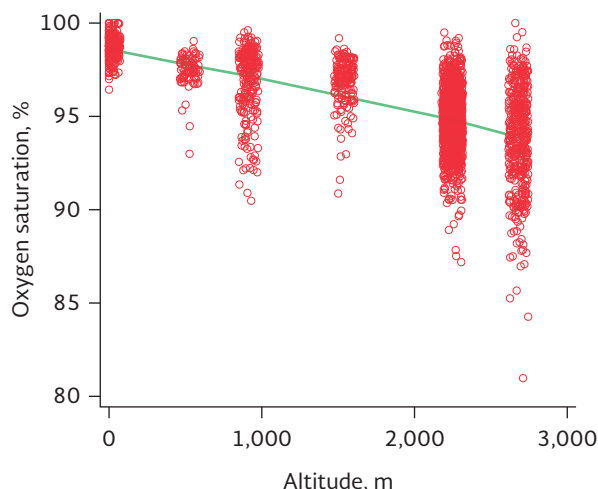


Figure 2. Oxygen saturation (SpO₂) in the cities studied.

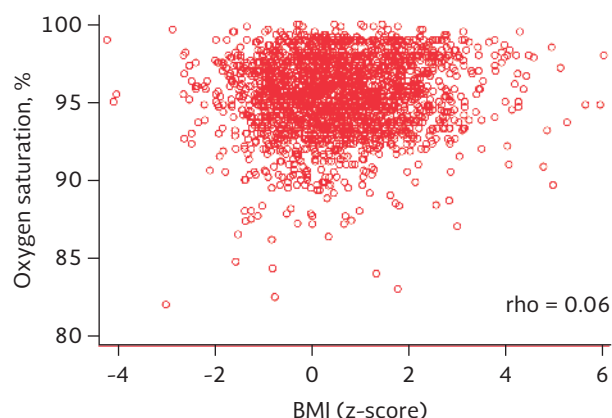
increases in elevation. By using a regression model, we further determined that altitude was the predictor of SpO₂ ($\text{SpO}_2 = 98.7 - \text{altitude [km]} \times 1.75$, $R^2 = 0.41$, $\text{MSE} = 1.83$). In a quantile regression, the estimated median of SpO₂ was 98.8 minus 1.7% per km above sea level, whereas at the fifth percentile SpO₂ was 97.4 – (altitude [km] × 2.7).

The BMI was found to be only minimally associated with SpO₂, $r_s = 0.06$, (Fig. 3). When we classified subjects according to BMI z-scores, those with normal weight had an average SpO₂ of $95.4\% \pm 2.4$; overweight participants, $95.5\% \pm 2.2$; and obese subjects, $95.9\% \pm 2.3$. The latter showed the highest SpO₂, but in no case were between-group differences statistically significant ($p = 0.07$).

Prevalence of SpO₂ ≤ 88% was 0.86% ($n = 19$) with a 95% CI of 0.47–1.2, while for SpO₂ ≤ 90% prevalence was 2.4% ($n = 53$) with a 95% CI of 1.8–3.0. Of the 19 participants with hypoxemia, one was obese; 11 had been exposed to cigarette, charcoal, or wood smoke; nine had shown symptoms of respiratory problems in the two weeks prior to testing; three had previously been diagnosed with a respiratory disease by a physician; and one reported wheezing in the past year.

DISCUSSION

Our results confirm that altitude above sea level is the main determinant of SpO₂ in children and young

Figure 3. Scatterplot showing body mass index z-scores and oxygen saturation (SpO₂) results for the complete group. BMI: body mass index.

people aged 2–16 years. Contrary to results obtained in adults, BMI, at least in the range detected in the sample, was not seen to have a biologically relevant effect on SpO₂. Also, this study identified a relatively small group of subjects (0.86%) with hypoxemia, most of whom also manifested respiratory symptoms; however, neither altitude nor BMI was the cause of this condition.

As in adults, some previous reports show that the SpO₂ in young people living at high altitudes is lower than in those who live at sea level⁵. Schult, et al. reported a mean SpO₂ of 85.7% in young people 5–16 years of age living at an altitude of 4,340 m, and considered an SpO₂ of 75.8% to be the lower limit of normal⁶. Subhi, et al. published a systematic literature review in an attempt to define altitude-specific hypoxemia. They reported reference equations to predict mean SpO₂ in children (aged 0–60 months) and an equation to predict hypoxemia thresholds at given altitudes, concluding that SpO₂ < 90% was the cutoff point to define hypoxemia in regions located at altitudes above 2,500 MASL, and < 85% for people living at 3,200 MASL⁷. This lower statistical limit of normality for SpO₂ does not define whether or not any particular individual will benefit from oxygen therapy as this information could only be obtained through a cohort study that compares hypoxemic patients treated with oxygen against a control group. But this would indeed be a complicated task due to the ethical implications involved. Currently, the most common clinical recommendation is to use an absolute or arbitrary cutoff

point to prescribe oxygen (based on criteria identified in adults with chronic obstructive pulmonary disease living at sea level): i.e., when partial pressure of arterial oxygen (PaO_2) < 55 mmHg or < 60 mmHg with *cor pulmonale*^{8,9}, which is equivalent to $\text{SpO}_2 \leq 88\%$, or ≤ 90 with *cor pulmonale*, polycythemia, or a history of edema. The rationale for this recommendation is that any point below these levels will create adverse health consequences regardless of the altitude at which an individual lives, or any adaptive mechanism to altitude that she/he might develop¹⁰.

Although some authors have suggested a possible effect of ancestry and ethnic background on SpO_2 , others do not confirm this hypothesis. In 2001, Huicho, et al. found an association between ethnicity and SpO_2 , but this is probably explained to a greater degree by acclimatization to altitude in people with a longer history of exposure to high elevations⁵. Weitz, et al. found no substantial difference in arterial oxygen saturation during growth or among young adults in a comparative study of 818 Tibetans and 668 Han individuals born and raised at altitudes between 3,200 and 4,300 m in Qinghai Province, western China. They had hypothesized that variations in resting SpO_2 values appeared to be inheritable since Tibetans have been described as being better adapted to high-altitude hypoxia than acclimatized newcomers or other lifelong, high-altitude residents¹¹. In our study, most subjects were still living in the city where they were born, and in all cases their parents were Mexican, so we believe it is safe to say that no ethnic background condition affected oxygen saturation in our study group.

There is scientific evidence to support the notion that, at least in adults, morbid obesity induces significant abnormalities in lung function. Obesity decreases lung volume due to the restrictive effect exerted by abdominal fat on the diaphragm and lungs. The most significant mechanical finding in this regard is a decrease of the expiratory reserve volume with a secondary reduction of functional residual capacity (FRC)¹².

Zavorsky, et al. demonstrated that obese patients living at sea level have a PaO_2 17 mmHg lower than that predicted by Crapo, et al.¹³, with a broader alveolar-arterial oxygen (A-a O_2) gradient at 17 mmHg. Additional studies have shown that when morbidly obese patients return to a normal BMI, the A-a O_2

gradient decreases. One recent proposal is that the waist-hip ratio is more closely related to SpO_2 than BMI. Research has also found differences in PaO_2 and gradient A-a O_2 between men and women, even with the same BMI, due to differences in fat accumulation between the sexes. Our study found no significant differences in oxygenation status between males and females; however, one limitation of our work is that we did not measure the waist-hip ratio¹⁴.

D'Ávila-Melo, et al. studied patients within a broad range spectrum of BMI and concluded that SpO_2 , specifically, is influenced by progressive increases in BMI. However, our study found no such association with BMI. One potential explanation for this finding is that oxygenation could be influenced by the chest size of young people; i.e., the larger the chest, the larger the gas exchange surface, leading to increased oxygenation. However, this hypothesis still needs to be demonstrated.

We know that the main goal of oxygen therapy is to prevent, reduce, or revert the effects of chronic hypoxemia¹¹, but studies of children (mostly infants with chronic pulmonary disease¹²) have focused more on quality of life and the costs associated with the adverse effects of this condition. Despite the considerable ethical challenges involved, we recommend a prospective study designed to evaluate the survival rates, growth, development, and lung function of children living at high altitudes in order to obtain evidence-based criteria for hypoxemia and oxygen prescription recommendations since oxygen availability in developing countries is generally poor. While pulse oximetry is widely used by health workers, there is an urgent need to reach a consensus as to the level of SpO_2 that requires oxygen supplementation.

One limitation of the present study is that spirometry and oximetry during sleep were not measured to rule out the presence of obstructive disease or deoxygenation during sleep. However, we believe that the items included in the questionnaire to evaluate obstructive diseases and sleep-disordered breathing permitted us to adjust for this variable in the final results.

In summary, as in adults, altitude was the main determinant of oxygen saturation in school-aged children. At least for the range observed in this study, BMI seems to have contributed only minimally to SpO_2 .

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