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 ± 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 (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 $\geq$ 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 worldwide\(^4\). 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: SpO$_2$ $\leq$ 90% and 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 Medellin, 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 (2,520 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 MASL\(^3\). Children with unstable SpO$_2$ measurements (coefficient of variation $> 10\%$) were excluded from the analysis, as were those who did not provide authorization for 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).
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 (rₛ) of −0.67 (p < 0.001). Weight had an rₛ = −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
increases in elevation. By using a regression model, we further determined that altitude was the predictor of SpO2 (SpO2 = 98.7 – altitude [km] * 1.75, R² = 0.41, 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 = 0.06, (Fig. 3). When we classified subjects according to BMI z-scores, those with normal weight had an average SpO2 of 95.4% ± 2.4; overweight participants, 95.5% ± 2.2; and obese subjects, 95.9% ± 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 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 level\(^5\). 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 normal\(^6\). 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 MASL\(^7\). 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 $SpO_2 \leq 88\%$, or $\leq 90$ 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 develop$^{10}$.

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 elevations$^5$. 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 residents$^{11}$. 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 ($A-aO_2$) gradient at 17 mmHg. Additional studies have shown that when morbidly obese patients return to a normal BMI, the $A-aO_2$ 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 $A-aO_2$ 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 ratio$^{14}$.

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 hypoxemia$^11$, but studies of children (mostly infants with chronic pulmonary disease$^{12}$) 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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REFERENCES