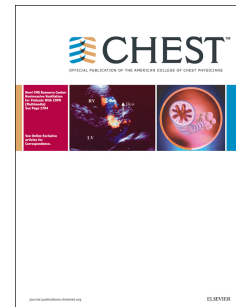


# Journal Pre-proof

## Allergic Rhinitis and Obstructive Sleep Apnea in Children Residing at High-Altitude

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Luis Fernando Giraldo-Cadavid, declares no conflict of interests related to this manuscript content

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This study was approved by the “Comité de Ética en Investigación de la Fundación Neumológica Colombiana”, approval number: 239-2018

#### **Guarantor statement**

Luis F. Giraldo-Cadavid takes responsibility for the content of the manuscript, including the data and analyses.

#### **Author contributions**

LFG, KPS and JLC had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. MIE, MS, NG, DG, and EDM contributed substantially to the study design, data analysis and interpretation, and the writing of the manuscript.

**Abbreviation list:**

AR = Allergic rhinitis  
AASM = American Academy of Sleep Medicine  
AHI = Apnea-hypopnea index  
ADHD = Attention-deficit/hyperactivity disorder  
BMI = Body Mass Index  
FNC = Fundación Neumológica Colombiana  
GE = Gastroesophageal  
IgE = Immunoglobulin E  
IL = Interleukin  
IRQ = Interquartile range  
HDL = High-density lipoprotein  
LDL = Low-density lipoprotein  
m.a.s.l. = Meters above sea level  
PSG = Polysomnography  
OSA = Obstructive sleep apnea syndrome  
OR = Odds Ratio  
ENT = Otolaryngology  
SDB = Sleep-disordered-breathing  
SD = Standard deviation  
TNF- $\alpha$  = Tumor necrosis factor  $\alpha$

## ABSTRACT

### Background

Obstructive sleep apnea (OSA) affects 2–4 % of the pediatric population; allergic rhinitis (AR) has been identified as a risk factor in sleep-disordered-breathing, but no studies evaluating such association have been conducted in high altitude environments. We aimed to assess whether the severity of AR is associated with the severity of OSA in children undergoing polysomnography (PSG) in the high-altitude city of Bogota, Colombia.

### Methods

A cross-sectional observational study of children with AR was conducted. AR severity was evaluated with ESPRINT-15 questionnaire and ARIA classification. Diagnosis and severity of OSA were established using PSG. Potential associations between AR severity and OSA severity were assessed using binary logistic regression and the Spearman correlation coefficient ( $\rho$ ).

### Results

A total of 99 children, mean age 7.9 years, 45% female, and 53% had OSA. An ESPRINT-15 score was associated with severe OSA (OR 2.0; 95%CI: 1.12-6.04;  $P=0.01$ ). Patients with moderate/severe persistent rhinitis according to ARIA exhibited a 10.1-fold greater risk of severe OSA (OR 10.15; CI 1.15 – 89.0). Furthermore, the apnea-hypopnea index was associated with the ESPRINT-15 score ( $\rho = 0.215$ ;  $P=0.03$ ) and with ARIA severity scale ( $\rho = 0.203$ ;  $P=0.04$ ).

### Conclusions

In AR symptomatic children residing at high altitude, increasing severity of AR is associated with more severe OSA.

## 1. INTRODUCTION

Obstructive sleep apnea syndrome (OSA) affects 2–4% of the pediatric population <sup>1</sup> and is an important risk factor for the presence of cardiovascular and metabolic morbidity and neurocognitive and behavioral dysfunction in children <sup>1</sup>. Sleep-disordered-breathing (SDB) are more frequent among patients with allergic diseases compared to the general population, and allergic rhinitis (AR) has been previously identified as a risk factor for SDB <sup>2,3</sup>. However, most of the studies evaluating this association have been conducted in the absence of overnight polysomnography (PSG).

AR is one of the most common chronic diseases affecting children, and is estimated to affect from 2–25% of all children and from 1–40% of all adults worldwide <sup>3,4</sup>. In Colombia, the average prevalence of AR symptoms is 32% (95% CI, 29.5-33.9) <sup>5</sup>. In the city of Bogotá, Colombia, which is located at 2,640 meters above sea level (m.a.s.l.), 17.2% (95% CI, 15.9-18.5) of children from 6 to 7 years old and 24.9% (95% CI, 23.6-26.3) of adolescents present symptom of AR <sup>6</sup>. Although AR is often viewed as a less severe condition when compared to asthma, it can dramatically alter patient quality of life, as well as adversely influence their overall performance, learning and productivity <sup>7</sup>.

Several studies have proposed the presence of an association between AR and OSA <sup>2,8-12</sup>, however, most studies have not objectively measured the presence of OSA using the gold standard diagnostic PSG. Furthermore, there are no studies at high altitude that have investigated this association, in spite of the fact that high altitude may affect the frequency and severity of both AR and OSA. We hypothesized that the severity of AR would be associated with the severity of OSA in children living in Bogotá.

## 2. METHODS

### **Design and study population.**

We performed an observational cross-sectional study of children consecutively recruited from the Sleep Laboratory of the Fundación Neumológica Colombiana (FNC) between July 2018 and January 2019. The FNC is a university affiliated institution that serves as the reference center in respiratory medicine for the city of Bogotá, which is located at high altitude (2640 m.a.s.l.). The study was approved by the institutional review board (Comite de Etica en Investigacion de la Fundacion Neumologica Colombiana, approval number 239-2018) and parents provided written informed consent, with informed assent being obtained from the children when possible.

Inclusion criteria were children ages 4 to 15 years with an established diagnosis of allergic rhinitis (AR) according to ARIA guidelines who underwent a in-laboratory overnight PSG.

All subjects with craniofacial malformations, neurological diseases, genetic syndromes and chronic lung diseases other than asthma were excluded.

The diagnosis and severity of OSA was established based on the PSG which was scored according to the American Academy of Sleep Medicine 2012 guidelines<sup>13</sup>. The Apnea-hypopnea index (AHI), which represents the number of apnea-hypopnea events per hour of sleep, was used to categorize the severity of OSA. OSA was considered abnormal if the obstructive AHI value was  $\geq 2$  events/hour, mild if AHI was 2–5 events/hour, moderate if AHI was 5–10 events/hour and severe if AHI was  $> 10$  events/hour<sup>14,15</sup>. The oxygen desaturation index 3% was reported as the number of 3% desaturations per hour (ODI3%).

According to the ARIA consensus, AR was defined clinically as a symptomatic alteration of the nose after exposure to nasal cavity allergens. Symptoms of rhinitis include rhinorrhea, nasal obstruction, nasal itching and sneezing, which revert spontaneously or under treatment<sup>7</sup>. For this study, presence of AR was classified as either intermittent or persistent, and severity was classified as either mild or moderate-severe, based on the ARIA consensus classification.<sup>7,16</sup> (Supplementary appendix e-Table 1).

From each child, the variables that could potentially alter the clinical course of allergic rhinitis or that could occur as a result of allergic rhinitis, such as history of asthma, allergic conjunctivitis, allergic dermatitis, recurrent otitis, sinusitis, gastroesophageal reflux and attention-deficit/hyperactivity disorder (ADHD) were obtained and recorded from either the medical records or directly from the parents. Recent history of tonsillitis (in the last 6 months) was also evaluated.

All included subjects underwent a physical examination, which included evaluation for the presence of turbinate or tonsil hypertrophy and evidence of nasal polyps. Turbinate hypertrophy was assessed using the Friedman scale: mild grade (turbinate with slight growth without obvious obstruction), moderate (mild to severe turbinate) and severe (turbinate completely occluding the nasal cavity)<sup>17</sup>. Tonsillar hypertrophy was classified according to the scale used by Brodsky et al.: grade 0 (non-visible tonsils), grade 1 (tonsils occupy  $< 25\%$  of the lateral dimension of the oropharynx), grade 2 (tonsils between 25% and 50% of the lateral dimension of the oropharynx), grade 3 (tonsils occupy between 50% and 75% of the lateral dimension of the oropharynx) and grade 4 (tonsils occupy  $> 75\%$  of the lateral dimension of the oropharynx)<sup>18,19</sup>. The presence of nasal polyps or a history of surgical nasal polyp resection was also evaluated<sup>20</sup>.

### Procedures and interventions

Spanish versions of the AR quality of life questionnaire for children (ESPRINT-15)<sup>21,22</sup> and the Chervin questionnaire<sup>23</sup> for symptoms of OSA were administered to the subjects before PSG. Responses to the ESPRINT-15 items were graded from 0 (no impact on

quality of life) to 6 (maximum impact on quality of life) (see ESPRINT-15 and Chervin questionnaires in the only supplementary appendix e-Tables 2 and 3).

A standard form was designed to collect the data and the resultant database was anonymized and safely stored by the investigators.

Overnight PSG studies were performed using commercial digital equipment (Philips Respironics®; Alice 5 and LE models) and scored according to the recommendations of the American Academy of Sleep Medicine (AASM)<sup>24</sup>. PSG were conducted for a minimum duration of 6 hours, and in a quiet environment with an average temperature of 19 °C. One of the parents accompanied the child during the study. The following parameters were measured during PSG: heart rate by electrocardiogram, thoraco-abdominal movements by inductance plethysmography, and airflow monitored by nasal pressure cannula and nasal thermistor. Oxygen saturation levels (SpO<sub>2</sub>) were monitored using a high precision oximeter (Massimo®, Massimo Corporation, Rad 8 model, Irvine, CA) with simultaneous recording of the pulse wave, incorporated into the digital PSG recording. Bilateral electro-oculogram, electromyogram in chin and anterior tibial region, three electroencephalogram channels and 2 sensors, one of body position and another to detect tracheal sounds were also applied. In addition, a time-synchronized video record was also obtained.

**PSG Scoring:** A single certified sleep technician performed the scoring and staging of all the studies, which were then reviewed by an expert pediatric pulmonologist, specializing in sleep medicine. A manual analysis of the PSG record was conducted according to AASM staging rules and respiratory analysis was performed according to AASM recommendations

<sup>24</sup>.

### Statistical analysis

Quantitative variables were described using measures of both central tendency (mean or median) and variability (standard deviation or interquartile range: Percentile 25 to Percentile 75) depending on their distribution. Qualitative variables were described using absolute and relative frequencies. Binary logistic regression was performed to evaluate the association between OSA severity, as a dependent dichotomous variable, and AR severity, as an independent variable, adjusting for potential confounding variables. Selection of potentially confounding variables was guided by directed acyclic graphs, built according to biological plausibility and previous knowledge. Mediator and collider variables were not treated as confounders. Variables having  $p > 0.2$  in the bivariate analysis (e-tables 4, 5 and 6) with the exposure or the outcome were not introduced in the multivariate model. Confidence intervals were calculated using the Bootstrap method to increase precision. Results were presented as OR with 95% confidence intervals (95% CI). The goodness of fit for the logistic regression model was explored using the Hosmer-Lemeshow test. A sample size of 160 patients was initially estimated for multivariate logistic regression models, including 8 covariates, based on the prevalence of OSA in children with AR. However, an interim analysis carried out after 100 subjects were collected determined that it was possible to establish statistically significant differences. Data collection was therefore concluded. Correlation between quantitative variables was analyzed using the Spearman correlation coefficient ( $\rho$ ). Correlation coefficients were interpreted according to the following rule:  $\rho < 0.3$  weak correlation;  $0.3 \leq \rho < 0.7$  moderate correlation;  $\rho \geq 0.7$  strong correlation<sup>25</sup>. A two-tailed  $P < 0.05$  was considered statistically significant. Statistical analyses were performed using IBM-SPSS Statistics software, version 22 (Armonk, NY, USA).

### 3. RESULTS

Ninety-nine of the 100 patients recruited were included in the study (Figure 1). The remaining patient was excluded due to incomplete data. In the study group, 45.5% ( $n = 45$ ) were female; subjects had an average age of 7.9 years, and with 85.9% ( $n = 85$ ) of patients born in the city of Bogotá and 94.9% ( $n = 94$ ) living in an urban area. The patients resided in Bogotá (74%) or in nearby cities of the Cundiboyacense Altiplano (26%) (2640 m.a.s.l.) (Table 1). After a nutritional assessment, 10.1% ( $n = 10$ ) were identified as overweight, and 2% ( $n = 2$ ) suffered from severe underweight. 5% used oxygen in the neonatal period due to oxyhemoglobin desaturations in the first three months of life without any subsequent repercussions, but none of the patients evaluated in this study either required or used supplemental oxygen during PSG (Table 1).

According to the ARIA classification, 30.3% ( $n = 30$ ) of patients had intermittent mild rhinitis; 7.1% ( $n = 7$ ) had intermittent moderate / severe rhinitis; 35.4% ( $n = 35$ ) had persistent mild rhinitis and 27.3% ( $n = 27$ ) had persistent moderate/severe rhinitis.

Regarding the quality of life measured by the ESPRINT-15 questionnaire, a median value of 2.27 (IQR: 1.27- 3.0) emerged (Table 1). OSA was diagnosed in 53.5% (n = 53) of the cohort, and classified as mild in 31.3% (n = 31), moderate in 8.1% (n = 8), and severe in the remaining 14.1% (n = 14) (Table 1).

In the multivariate binary logistic regression analysis, a statistically significant association emerged between the severity of AR measured by the ESPRINT-15 and the presence of severe OSA (OR 2.0; 95%CI: 1.12-6.04; P= 0.01). Other covariates associated with severe OSA included the place of residence outside of Bogotá (OR 0.16, 95%CI 0.01-0.72; P = 0.004) and a history of recent tonsillitis (OR 2.03, 95%CI 1.14-12.68, p = 0.030) (Table 2). The Hosmer-Lemeshow test found a P = 0.77, indicating that there were no significant differences between the values predicted by the model and those observed, therefore confirming adequate goodness of fit of the model.

For the purposes of the multivariate binary logistic regression analysis, assessing the association between AR severity according to ARIA and severe OSA, subjects with mild intermittent rhinitis served as the reference group. We found a 4.8-fold greater risk of severe OSA for subjects with moderate/severe intermittent rhinitis and mild persistent rhinitis, and 10.1 times greater risk of severe OSA for children with moderate/severe persistent rhinitis (95% CI 1.15-89.0; p = 0.036) (Table 3). The Hosmer-Lemeshow test found a P = 1.0, indicating an adequate goodness of fit of the model.

A positive and statistically significant weak correlation emerged between the body weight and the severity of AR based on the ARIA classification (p = 0.01,  $\rho$  = 0.245). With respect to the body mass index adjusted for age, a positive and statistically significant moderate correlation was found with the severity of AR based on both ARIA classification (p = 0.02,  $\rho$  = 0.313) and ESPRINT-15 scores (p = 0.002,  $\rho$  = 0.305). A statistically significant weak correlation was also found between ESPRINT-15 scores and tonsillar hypertrophy (p = 0.05,  $\rho$  = 0.278), as well as turbinate hypertrophy (p = 0.009,  $\rho$  = 0.263), however, these last 2 variables were not significantly associated with OSA severity (Table 4).

A significant positive weak correlation between the severity of AR, whether assessed by ARIA (p= 0.04,  $\rho$  = 0.203) or ESPRINT-15 (p = 0.03,  $\rho$  = 0.215) classifications was detected in relation to the severity of OSA, as measured by the AHI (the higher the severity of AR the higher the AHI) (Table 4). We also found a significant positive weak correlation between the severity of AR assessed by ESPRINT-15 (p = 0.008,  $\rho$  = 0.265) and the ODI3% and a trend towards a positive correlation between the ARIA scale and the ODI3% (p = 0.059,  $\rho$  = 0.190) (Table 4 and e-Table 7).

#### 4. DISCUSSION

In the present study that evaluated habitually snoring children with AR who reside at high altitude, we found that 53% of these symptomatic children had PSG-confirmed OSA. More importantly, an independent association between the severity of AR and the corresponding severity of OSA emerged. To the best of our knowledge, this is the first study that shows such relationship in children living at high altitudes. The positive correlation between the severity of AR assessed by the ESRINT-15 and ARIA scales and the AHI, the significant positive weak correlation between the ODI3% and ESRINT-15 score, (this was not found with the T90), as well as the pattern of an increasing OR for OSA when comparing the groups with mild to moderate and then to moderate/severe AR speaks to a dose-response gradient relationship between AR and OSA severities.

The place of residence outside of Bogotá, was associated with a lower risk of severe OSA (OR 0.16, 95%CI 0.01-0.72; P=0.004), such a difference could not be attribute to altitude because the other cities of residence of our patients were located at the same altitude as Bogotá. Although our study was not designed to determine which factors explain such a difference, we could hypothesize that environmental factors, including air pollution, might play a role. Therefore, future studies, specifically addressed to explore the factors (other than altitude) behind the relationship between the city of residence and OSA, are required. This association between the city of residence and OSA could be a source of bias, acting as a confounder of the association between AR and OSA. Therefore, we adjusted by city of residence in our multivariate model to control for this potential confounding factor, and the association between AR and OSA remained significant, supporting that the association between allergic rhinitis and OSA is independent of the city of residence.

We also found a significant weak correlation between the BMI/age and the severity of AR, this correlation, further reinforces the findings from previous studies suggesting a link between obesity and atopy, which could be affected by a wide dispersion of data<sup>26</sup>. Proposed mechanisms underlying the relationship between AR and obesity include inflammatory and hormonal mechanisms. For example, obesity has been linked to an increase in inflammatory mediators, such as adipokines and cytokines (interleukin-6 (IL-6) and tumor necrosis factor  $\alpha$  (TNF- $\alpha$ )), and to a decrease in anti-inflammatory mechanisms, such as lower levels of adiponectin<sup>27</sup>. The elevation of leptin released by adipocytes has also been related to an increase in the Th2 response, an accumulation of inflammatory cells and elevated IgE, promoting the development of allergic disorders<sup>27</sup>. Likewise, osteopontin, which is elevated in individuals with obesity, has been associated with increased migration and activation of eosinophils<sup>28</sup>. Obesity can also influence the production of sex hormones, such as estrogens, and these, in turn, may stimulate the secretion of proinflammatory interleukins, promoting a Th2 phenotype<sup>29</sup>. Changes in lipid

metabolism, such as increased LDL and low HDL, have also been associated with an increased risk of allergic sensitization<sup>30</sup>. Thus, even though we did not explore inflammatory pathways in the present study, our confirmatory findings are aligned with the strong association between obesity and AR.

Our current study also provides PSG-based evidence supporting previous observations that patients with AR and habitual snoring should be considered at risk for OSA, and that the more severe the AR symptoms, the higher the probability that OSA will be more severe. However, most of previous studies were limited by either small sample size of pediatric patients, and by not using the gold standard diagnosis approach for OSA. In a systematic review that included a total of 27,015 pediatric patients, two thirds of the 18 studies included reported a statistically significant association between AR and SDB. All studies included in the review, however, were either case series or case-control studies and, in 61% PSG was not used to diagnose SDB, with the assessment of OSA being predicated on questionnaires<sup>2</sup>. In addition, a recent meta-analysis established that the prevalence of AR is high in children with OSA or SDB, and that children with SDB have a higher incidence of AR than those who do not have SDB. However, for adults with OSA and AR, there was no major impact of AR on sleep parameters. Unlike our current results, and the aforementioned studies, Zheng *et al.* found no significant association between the degree of severity of AR or non-allergic rhinitis and the severity of OSA. It is possible that the differences can be explained because Zheng and colleagues study was conducted on adult patients for whom AR has a lesser impact on sleep measures<sup>11,12</sup>. We found that the central apnea index was higher than at sea level with similar values to studies carried out at intermediate heights and high altitude in healthy children by Hill *et al.*<sup>31</sup>, who performed PSG in Bolivian children native to high altitude compared to children native to low altitude; and Burg *et al.*<sup>32</sup>, who assessed the respiratory and polysomnographic values in 3- to 5-year-old healthy children in Denver, Colorado, USA (1,600 m.a.s.l.)<sup>32</sup>. So this finding is likely related to living at high altitude and not with rhinitis.

Interestingly, the current study suggests that compared to published reports of patients with OSA and AR who live at sea level, the children at high altitude with OSA and AR are more likely to exhibit lower average SpO<sub>2</sub> ( $90.9 \pm 1.6$  versus  $94.1 \pm 2.7$ ;  $90.9 \pm 1.6$  vs  $95.68 \pm 2.93$ )<sup>33,34</sup>. The percentage of the time during which SaO<sub>2</sub><90% (median 45.7; IQR: 10-159) and desaturation index (12.30; IQR: 8.4 18.3) were higher than the cut-off points found in healthy children, children with OSA with and without AR at sea level<sup>34-37</sup>. A possible explanation for these differences is that with the natural decreases in barometric pressure as altitude increases, the inspired pressure of oxygen will proportionately fall, leading to diminished P<sub>A</sub>O<sub>2</sub> and P<sub>a</sub>O<sub>2</sub>. In addition, at the altitude in which our study was carried out (2640 m.a.s.l.), the relative alveolar hypoventilation that naturally accompanies sleep onset could induce significant drops in SaO<sub>2</sub> and a greater desaturation during apneas-hypopneas. Consequently, it is readily conceivable that the sleep and respiratory

characteristics of children with AR and OSA residing at high altitude will differ from those described at sea level.

In recent years, a possible association between allergic pathologies and respiratory sleep disorders has been described, including AR. Explanations raised for this relationship include a mechanical obstruction to airflow which worsens during sleep, to the physiological fall of cortisol levels during sleep<sup>38</sup>, thus leading to an increase in apnea episodes during sleep. On the other hand, inflammatory mediators released during allergic reactions, such as histamine and pro-inflammatory cytokines, such as TNF $\alpha$ , IL-1, and IL-6, could have a direct effect on the central nervous system, contributing to alterations of sleep structure and architecture and daytime drowsiness; of note, histamine has also been centrally involved in the regulation of the sleep-wake cycle<sup>39</sup>.

Strengths of the present study include the large sample size of exclusively pediatric subjects with AR who were also symptomatic snorers. Similar studies were previously conducted using much smaller cohorts. In addition, evaluation of the presence of OSA was performed by blind scoring of in-laboratory overnight PSG using standardized stringent criteria, as set by the American Sleep Academy<sup>24</sup>. In addition, implementation of two standard and validated instruments for AR, namely the ESPRINT-15 questionnaire and ARIA classification, enabled consistent and unbiased evaluation of AR-related symptoms and impact on quality of life. Of course, the study was limited by its cross-sectional design, such that it was not possible to establish temporally-derived inferences regarding the time of appearance of AR and the onset of OSA, which limits our ability to establish causality. In addition, the AR cohort was a clinical referral cohort, such that no controls or asymptomatic children with AR were included as comparators, and therefore the prevalence of OSA in AR children cannot be determined.

## 5. CONCLUSION

In summary, we report on a strong and significant and independent association between the severity of AR and the severity of OSA in children living at high altitude. Further studies are needed to explore potential mechanisms underlying these findings.

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LFG takes responsibility for the content of the manuscript, including the data and analyses. LFG, KPS and JLC had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. MIE, MS, NG, DG, and EDM contributed substantially to the study design, data analysis and interpretation, and the writing of the manuscript. Authors declare no conflict of interests related to this manuscript content.

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**Table 1. General Characteristics of the cohort (n:99)**

|                                                        |                                          |                      |
|--------------------------------------------------------|------------------------------------------|----------------------|
| Sex                                                    | Male: No. (%)                            | 54 (54.5%)           |
|                                                        | Female: No. (%)                          | 45 (45.5%)           |
| Age (years)                                            | Mean (SD)                                | 7.96 (3.07)          |
| Born in Bogotá                                         | Yes: n. (%)                              | 85 (85.9%)           |
| Reside in Bogotá                                       | Yes: n. (%)                              | 73 (73.7%)           |
| Urban housing                                          | Yes: n. (%)                              | 94 (94.9%)           |
| Weight (kg)                                            | Mean (SD)                                | 31.74 (14.67)        |
| Height (cm)                                            | Mean (SD)                                | 128.45 (18.77)       |
| Body Mass Index (Kg/m <sup>2</sup> )                   | Mean (SD)                                | 18.31 (4.11)         |
| Interpretation Height for Age                          | ≥ -1 = Normal stature: n (%)             | 81 (81.8%)           |
|                                                        | ≥-2 Y <-1 = Risk of short stature. n (%) | 17 (17.2%)           |
|                                                        | < -2 = Short stature: n (%)              | 1 (1.0%)             |
| Interpretation BMI/Age                                 | Severe thinness n. (%)                   | 2 (2.0%)             |
|                                                        | Moderate thinness: n. (%)                | 6 (6.1%)             |
|                                                        | Normal range n. (%)                      | 49 (49.5%)           |
|                                                        | Overweight risk: n. (%)                  | 32 (32.3%)           |
|                                                        | Overweight: n. (%)                       | 10 (10.1%)           |
|                                                        | Obesity: n. (%)                          | 0 (0.0%)             |
| Apnea–hypopnea index                                   | Median (IQR)                             | 4.00 (2–8)           |
| Central apnea index                                    | Median (IQR)                             | 1.20 (0.4–3)         |
| OSA Mild                                               | Yes: n. (%)                              | 31 (31.3%)           |
| OSA Moderate                                           | Yes: n. (%)                              | 8 (8.1%)             |
| OSA Severe                                             | Yes: n. (%)                              | 14 (14.1%)           |
| T90                                                    | Median (IQR)                             | 45.70 (10–159)       |
| ODI3%                                                  | Median (IQR)                             | 12.30 (8.4–18.3)     |
| Sleep efficiency                                       | Median (IQR)                             | 90.00 (81.00– 95.00) |
| Sleep latency                                          | Median (IQR)                             | 16.00 (7.00–35.00)   |
| Arousal index                                          | Median (IQR)                             | 7.90 (5.90–11.00)    |
| REM sleep percentage                                   | Mean (SD)                                | 18.68 (6.84)         |
| Deep sleep percentage                                  | Mean (SD)                                | 28.07 (6.76)         |
| Average saturation of O2 at night                      | Mean (SD)                                | 90.90 (1.66)         |
| Allergic rhinitis                                      | Yes: n. (%)                              | 99 (100.0%)          |
| Severity of allergic rhinitis (by ARIA classification) | Mild Intermittent: n. (%)                | 30 (30.3%)           |
|                                                        | Moderate/Severe Intermittent: n. (%)     | 7 (7.1%)             |
|                                                        | Mild Persistent: n. (%)                  | 35 (35.4%)           |
|                                                        | Moderate/Severe Persistent: n. (%)       | 27 (27.3%)           |
| ESPRINT15                                              | Median (IQR)                             | 2.27 (1.27–3)        |

|                                                           |                               |                  |
|-----------------------------------------------------------|-------------------------------|------------------|
| Turbinate hypertrophy                                     | Mild n. (%)                   | 41 (41.4%)       |
|                                                           | Moderate n. (%)               | 55 (55.6%)       |
|                                                           | Severe n. (%)                 | 3 (3.0%)         |
| Tonsil hypertrophy                                        | Grade 0 (Non visible): n. (%) | 11 (11.1%)       |
|                                                           | Grade 1 (< 25%): n. (%)       | 16 (16.2%)       |
|                                                           | Grade 2 (25 - 49%): n. (%)    | 34 (34.3%)       |
|                                                           | Grade 3 (50 - 74%): n. (%)    | 30 (30.3%)       |
|                                                           | Grade 4 (>75%): n. (%)        | 8 (8.1%)         |
| Asthma                                                    | Yes: n. (%)                   | 50 (50.5%)       |
| Allergic conjunctivitis                                   | Yes: n. (%)                   | 29 (29.3%)       |
| Allergic dermatitis                                       | Yes: n. (%)                   | 51 (51.5%)       |
| Recent tonsillitis                                        | Yes: n. (%)                   | 20 (20.2%)       |
| Nasal polyps                                              | Yes: n. (%)                   | 3 (3.0%)         |
| Recurrent otitis                                          | Yes: n. (%)                   | 12 (12.1%)       |
| Sinusitis                                                 | Yes: n. (%)                   | 12 (12.1%)       |
| Current treatment for rhinitis with antihistaminic        | Yes: n. (%)                   | 18 (18.2%)       |
| Current treatment for rhinitis with nasal corticosteroid  | Yes: n. (%)                   | 72 (72.7%)       |
| Current treatment for rhinitis with hypertonic saline     | Yes: n. (%)                   | 5 (5.1%)         |
| Current treatment for rhinitis with leukotriene modifiers | Yes: n. (%)                   | 2 (2.0%)         |
| Current treatment for rhinitis with anticholinergics      | Yes: n. (%)                   | 1 (1.0%)         |
| No treatment                                              | Yes: n. (%)                   | 18 (18.2%)       |
| Nasal congestion                                          | Yes: n. (%)                   | 80 (80.8%)       |
| GE reflux                                                 | Yes: n. (%)                   | 18 (18.2%)       |
| Bruxism                                                   | Yes: n. (%)                   | 54 (54.5%)       |
| Daytime sleepiness                                        | Yes: n. (%)                   | 32 (32.3%)       |
| Morning headache                                          | Yes: n. (%)                   | 31 (31.3%)       |
| Attention-deficit hyperactivity disorder                  | Yes: n. (%)                   | 35 (35.4%)       |
| ENT surgeries                                             | Yes: n. (%)                   | 13 (13.1%)       |
| Oxygen during sleep                                       | Yes: n. (%)                   | 5 (5.1%)         |
| Sum replies Chervin questionnaire                         | Median (IQR)                  | 14 (10–16)       |
| Positive responses ratio Chervin questionnaire            | Median (IQR)                  | 0.67 (0.48–0.76) |
| SDB Positive                                              | Yes: n. (%)                   | 88 (88.9%)       |

Notes: SD: Standard deviation; IRQ: interquartile range (percentile 25 to percentile 75); OSA: Obstructive Sleep Apnea Hypopnea Syndrome; GE: Gastroesophageal; ENT= Otolaryngology; SDB: Sleep-disordered-breathing

**Table 2. Multivariate analysis using binary logistic regression**

| <b>Dependent variable</b> | <b>Covariable</b>         | <b>OR</b> | <b>CI 95%</b> | <b>P (two-tailed)</b> |
|---------------------------|---------------------------|-----------|---------------|-----------------------|
| Severe Apnea/hypopnea     | ESPRINT-15                | 2.00      | 1.12 - 6.04   | 0.01                  |
|                           | Resides outside of Bogotá | 0.17      | 0.01 - 0.72   | 0.004                 |
|                           | Recent tonsillitis        | 2.03      | 1.14 - 12.68  | 0.030                 |
|                           | BMI adjusted for age      | 1.56      | 0.52 - 5.45   | 0.42                  |

**Table 3. Association between the severity of Allergic Rhinitis by ARIA vs Severe OSA**

| <b>Rhinitis severity classification ARIA</b> | <b>OR</b> | <b>CI 95%</b> | <b>P</b> |
|----------------------------------------------|-----------|---------------|----------|
| Mild, intermittent rhinitis                  |           |               |          |
| Moderate/severe, intermittent rhinitis       | 4.83      | 0.2 – 88.5    | 0.288    |
| Mild, persistent rhinitis                    | 4.83      | 0.5 – 43.9    | 0.162    |
| Moderate/severe, persistent rhinitis         | 10.15     | 1.15 – 89.0   | 0.036    |

Notes: multivariate binary logistic regression analysis; statistical significance at  $P < 0.05$  (two-tailed)

**Table 4. Correlation with rhinitis severity**

| Variable 1            | Variable 2                      | Spearman correlation coefficient ( $\rho$ ) | P      |
|-----------------------|---------------------------------|---------------------------------------------|--------|
| Weight                | Rhinitis severity by ARIA scale | 0.245                                       | 0.015* |
|                       | ESPRINT-15 scale                | 0.190                                       | 0.059  |
| BMI/Age               | ESPRINT-15 scale                | 0.305                                       | 0.002* |
|                       | Rhinitis severity by ARIA scale | 0.313                                       | 0.002* |
| Tonsillar hypertrophy | ESPRINT-15 scale                | 0.278                                       | 0.005* |
|                       | Rhinitis severity by ARIA scale | -0.004                                      | 0.965  |
| Turbinate hypertrophy | ESPRINT-15 scale                | 0.263                                       | 0.009* |
|                       | Rhinitis severity by ARIA scale | 0.101                                       | 0.322  |
| AHI                   | ESPRINT-15 scale                | 0.215                                       | 0.033* |
|                       | Rhinitis severity by ARIA scale | 0.203                                       | 0.044* |
| ODI3%                 | ESPRINT-15 scale                | 0.265                                       | 0.008* |
|                       | Rhinitis severity by ARIA scale | 0.190                                       | 0.059  |
| T90                   | ESPRINT-15 scale                | -0.058                                      | 0.567  |
|                       | Rhinitis severity by ARIA scale | -0.118                                      | 0.246  |

Notes: \* statistical significance at  $P < 0.05$  (two-tailed)

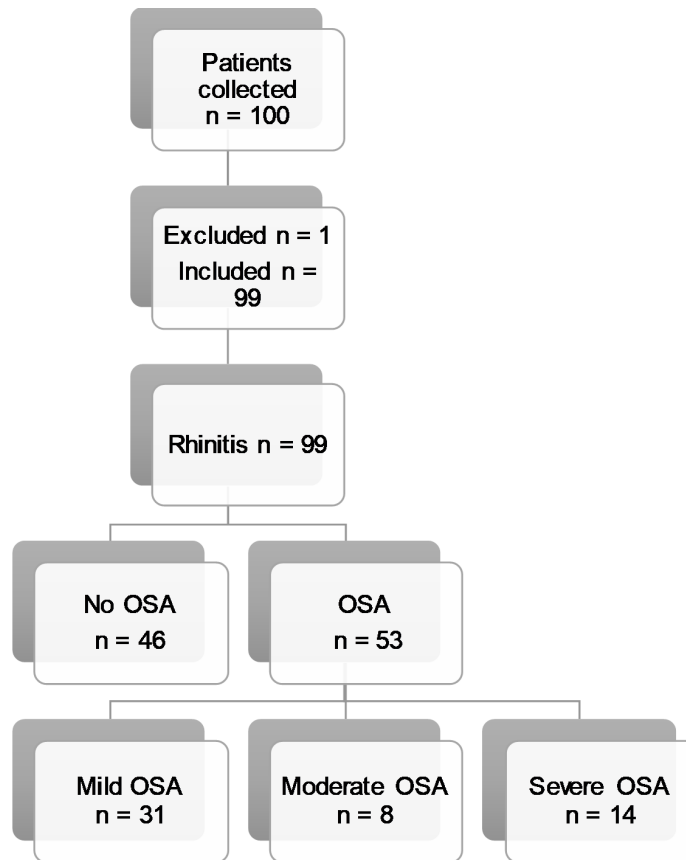
**Figure 1. Subject Recruitment**

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**e-TABLE 1. AR CLASSIFICATION ACCORDING TO ARIA(1)**

- 1. "Intermittent" means that the symptoms are present:**
  - Less than 4 days a week,
  - Or for less than 4 weeks.
- 2. "Persistent" means that the symptoms are present:**
  - More than 4 days a week,
  - And for more than 4 weeks.
- 3. "Mild" means that none of the following items are present:**
  - Sleep disturbance,
  - Impairment of daily activities, leisure and/or sport,
  - Impairment of school or work,
  - Troublesome symptoms.
- 4. "Moderate-severe" means that one or more of the following items are present:**
  - Sleep disturbance,
  - Impairment of daily activities, leisure and/or sport,
  - Impairment of school or work,
  - Troublesome symptoms.

**e-TABLE 2. CHERVIN QUESTIONNAIRE(2)**

| <b>P.S.Q. Pediatric Sleep Questionnaire.</b><br><b>Cuestionario de Sueño Pediátrico de Chervin</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |        |                      |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|----------------------|----------------|--------------------------------------------|----|----|----|-----------------------------|--|--|--|----------------------|--|--|--|-----------------------------------------|--|--|--|-------------------|--|--|--|----------------------|--|--|--|----------------------------------------|--|--|--|-----------------------------------------------------------------------|--|--|--|----------------------------------------------------------------------------|--|--|--|--------------------------------------------------------------------------------------------------|--|--|--|-------------------------------------|--|--|--|----------------------------------------------------------|--|--|--|
| <p><b>Instrucciones:</b> Por favor responda las preguntas siguientes relacionadas con el comportamiento del niño o niña, tanto durante el sueño como cuando esta despierto. Las preguntas hacen referencia al comportamiento habitual, no necesariamente al observado en los últimos días porque puede que no sea representativo si no se ha encontrado bien. Si no esta seguro de cómo responder a alguna pregunta consulte con nosotros. Cuando se usa la palabra habitualmente significa que ocurre la mayor parte del tiempo o más de la mitad de las noches. Usamos el término niño para referirnos tanto a niñas como a niños.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |        |                      |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
| Nombre del niño:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |        | Fecha de Nacimiento: |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
| Edad:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Curso: | Fecha de la Encuesta |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
| Encuesta hecha por:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Madre  |                      | Observaciones: |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Padre  |                      |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Ambos  |                      |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
| <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <th style="width: 70%;">Comportamiento nocturno y durante el sueño</th> <th style="width: 10%;">SI</th> <th style="width: 10%;">NO</th> <th style="width: 10%;">NS</th> </tr> <tr> <td>Mientras duerme su hijo....</td> <td></td> <td></td> <td></td> </tr> <tr> <td>1. Ronca alguna vez?</td> <td></td> <td></td> <td></td> </tr> <tr> <td>2. Ronca más de la mitad de las noches?</td> <td></td> <td></td> <td></td> </tr> <tr> <td>3. Siempre ronca?</td> <td></td> <td></td> <td></td> </tr> <tr> <td>4. Ronca con fuerza?</td> <td></td> <td></td> <td></td> </tr> <tr> <td>5. Tiene respiración fuerte o ruidosa?</td> <td></td> <td></td> <td></td> </tr> <tr> <td>6. Alguna vez ha visto que su hijo deje de respirar durante la noche?</td> <td></td> <td></td> <td></td> </tr> <tr> <td>7. Alguna vez le ha preocupado la respiración de su hijo durante el sueño?</td> <td></td> <td></td> <td></td> </tr> <tr> <td>8. En alguna ocasión ha tenido que sacudir o zarandear a su hijo o despertarle para que respire?</td> <td></td> <td></td> <td></td> </tr> <tr> <td>9. Tiene su hijo un sueño inquieto?</td> <td></td> <td></td> <td></td> </tr> <tr> <td>10. Tiene movimientos bruscos de las piernas en la cama?</td> <td></td> <td></td> <td></td> </tr> </table> |        |                      |                | Comportamiento nocturno y durante el sueño | SI | NO | NS | Mientras duerme su hijo.... |  |  |  | 1. Ronca alguna vez? |  |  |  | 2. Ronca más de la mitad de las noches? |  |  |  | 3. Siempre ronca? |  |  |  | 4. Ronca con fuerza? |  |  |  | 5. Tiene respiración fuerte o ruidosa? |  |  |  | 6. Alguna vez ha visto que su hijo deje de respirar durante la noche? |  |  |  | 7. Alguna vez le ha preocupado la respiración de su hijo durante el sueño? |  |  |  | 8. En alguna ocasión ha tenido que sacudir o zarandear a su hijo o despertarle para que respire? |  |  |  | 9. Tiene su hijo un sueño inquieto? |  |  |  | 10. Tiene movimientos bruscos de las piernas en la cama? |  |  |  |
| Comportamiento nocturno y durante el sueño                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | SI     | NO                   | NS             |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
| Mientras duerme su hijo....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |        |                      |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
| 1. Ronca alguna vez?                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |        |                      |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
| 2. Ronca más de la mitad de las noches?                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |        |                      |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
| 3. Siempre ronca?                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |        |                      |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
| 4. Ronca con fuerza?                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |        |                      |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
| 5. Tiene respiración fuerte o ruidosa?                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |        |                      |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
| 6. Alguna vez ha visto que su hijo deje de respirar durante la noche?                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |        |                      |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
| 7. Alguna vez le ha preocupado la respiración de su hijo durante el sueño?                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |        |                      |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
| 8. En alguna ocasión ha tenido que sacudir o zarandear a su hijo o despertarle para que respire?                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |        |                      |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
| 9. Tiene su hijo un sueño inquieto?                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |        |                      |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |
| 10. Tiene movimientos bruscos de las piernas en la cama?                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |        |                      |                |                                            |    |    |    |                             |  |  |  |                      |  |  |  |                                         |  |  |  |                   |  |  |  |                      |  |  |  |                                        |  |  |  |                                                                       |  |  |  |                                                                            |  |  |  |                                                                                                  |  |  |  |                                     |  |  |  |                                                          |  |  |  |


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|                                                                                            |  |  |  |
|--------------------------------------------------------------------------------------------|--|--|--|
| 11. Tiene "dolores de crecimiento" (dolor que no conoce la causa) que empeoran en la cama? |  |  |  |
| 12. Mientras su hijo duerme ha observado si da pataditas con una o ambas piernas?          |  |  |  |
| 13. Da patadas o tiene movimientos regulares, rítmicos, por ejemplo cada 20-40 segundos?   |  |  |  |
| 14. Durante la noche suda mucho, mojando los pijamas?                                      |  |  |  |
| 15. Durante la noche se levanta de la cama por alguna causa?                               |  |  |  |
| 16. Durante la noche se levanta a orinar?                                                  |  |  |  |
| 17. En caso afirmativo cuantas veces de media se levanta por la noche?                     |  |  |  |
| 18. Normalmente su hijo duerme con la boca abierta?                                        |  |  |  |
| 19. Suele tener su hijo la nariz obstruida o congestionada?                                |  |  |  |
| 20. Tiene su hijo alguna alergia que le dificulte respirar por la nariz?                   |  |  |  |
| 21. Durante el día su hijo suele respirar con la boca abierta?                             |  |  |  |
| 22. Se levanta con la boca seca?                                                           |  |  |  |
|                                                                                            |  |  |  |

**e-TABLE 3. ESPRINT-15 QUESTIONNAIRE(3)**

| <b>Spanish Version of the ESPRINT-15 Questionnaire (Validated Version)</b>                         |                                                                                   |             |                  |             |                 |             |              |                  |
|----------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|-------------|------------------|-------------|-----------------|-------------|--------------|------------------|
| <b>Durante las últimas 2 semanas, ¿cuánto le ha molestado cada uno de los siguientes síntomas?</b> |                                                                                   |             |                  |             |                 |             |              |                  |
|                                                                                                    | <b>Síntomas</b>                                                                   | <b>Nada</b> | <b>Casi nada</b> | <b>Poco</b> | <b>Moderado</b> | <b>Poco</b> | <b>Mucho</b> | <b>Muchísimo</b> |
| 1                                                                                                  | Sensación de nariz tapada o de obstrucción                                        | 0           | 1                | 2           | 3               | 4           | 5            | 6                |
| 2                                                                                                  | Mucosidad nasal líquida o como agua                                               | 0           | 1                | 2           | 3               | 4           | 5            | 6                |
| 3                                                                                                  | Picor en la nariz o estornudos repetidos                                          | 0           | 1                | 2           | 3               | 4           | 5            | 6                |
| 4                                                                                                  | Picor de ojos o tener que rascarse los ojos                                       | 0           | 1                | 2           | 3               | 4           | 5            | 6                |
| 5                                                                                                  | Dificultad para respirar, sensación de asfixia o ahogo                            | 0           | 1                | 2           | 3               | 4           | 5            | 6                |
| <b>Durante las últimas 2 semanas, ¿cuánto le ha molestado cada uno de los siguientes síntomas?</b> |                                                                                   |             |                  |             |                 |             |              |                  |
|                                                                                                    | <b>Actividades de la vida diaria</b>                                              | <b>Nada</b> | <b>Casi nada</b> | <b>Poco</b> | <b>Moderado</b> | <b>Poco</b> | <b>Mucho</b> | <b>Muchísimo</b> |
| 6                                                                                                  | Incomodidad o dificultad para trabajar, a causa de la rinitis                     | 0           | 1                | 2           | 3               | 4           | 5            | 6                |
| 7                                                                                                  | Síntomas de rinitis cenando o tomando algo fuera de casa                          | 0           | 1                | 2           | 3               | 4           | 5            | 6                |
| 8                                                                                                  | Interrumpir constantemente lo que está haciendo, a causa de la rinitis            | 0           | 1                | 2           | 3               | 4           | 5            | 6                |
| <b>Durante las últimas 2 semanas, ¿cuánto le ha molestado cada uno de los siguientes síntomas?</b> |                                                                                   |             |                  |             |                 |             |              |                  |
|                                                                                                    | <b>Sueño</b>                                                                      | <b>Nada</b> | <b>Casi nada</b> | <b>Poco</b> | <b>Moderado</b> | <b>Poco</b> | <b>Mucho</b> | <b>Muchísimo</b> |
| 9                                                                                                  | Problemas para dormir o dificultad para conciliar el sueño, a causa de la rinitis | 0           | 1                | 2           | 3               | 4           | 5            | 6                |
| 10                                                                                                 | Levantarse con sequedad de boca o despertarse por esto, a causa de la rinitis     | 0           | 1                | 2           | 3               | 4           | 5            | 6                |

|                                                                                                    |                                                                                                 |             |                  |             |                 |             |              |                  |
|----------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|-------------|------------------|-------------|-----------------|-------------|--------------|------------------|
| 11                                                                                                 | Dormir mal, a causa de la rinitis                                                               | 0           | 1                | 2           | 3               | 4           | 5            | 6                |
| <b>Durante las últimas 2 semanas, ¿cuánto le ha molestado cada uno de los siguientes síntomas?</b> |                                                                                                 |             |                  |             |                 |             |              |                  |
|                                                                                                    | <b>Afectación psicológica</b>                                                                   | <b>Nada</b> | <b>Casi nada</b> | <b>Poco</b> | <b>Moderado</b> | <b>Poco</b> | <b>Mucho</b> | <b>Muchísimo</b> |
| 12                                                                                                 | Tener que estar pendiente de la rinitis                                                         | 0           | 1                | 2           | 3               |             | 5            | 6                |
| 13                                                                                                 | Estar más irritable o de mal humor, a causa de la rinitis                                       | 0           | 1                | 2           | 3               | 4           | 5            | 6                |
| 14                                                                                                 | Pasarlo o sentirse mal, a causa de la rinitis                                                   | 0           | 1                | 2           | 3               | 4           | 5            | 6                |
| 15                                                                                                 | En general, teniendo en cuenta su rinitis y ningún otro trastorno, ¿cómo diría que es su salud? |             |                  |             |                 |             |              |                  |
|                                                                                                    |                                                                                                 | Excelente   | Muy Buena        | Buena       | Regular         |             |              | Mala             |

**e-TABLE 4. BIVARIATE ANALYSIS WITH SEVERE OSA**

| Dependent variable | Covariable               | OR    | CI 95%         | P (two-tailed) |
|--------------------|--------------------------|-------|----------------|----------------|
| Severe OSA         | Age in years             | 1.032 | 0.859 - 1.239  | 0.737          |
|                    | Female Sex               | 1.130 | 0.361 - 3.539  | 0.833          |
|                    | Born in Bogotá           | 1.835 | 0.441 - 7.629  | 0.404          |
|                    | Reside outside of Bogotá | 0.288 | 0.09 - 0.923   | 0.036*         |
|                    | Urban Housing            | 4.556 | 0.689 - 30.124 | 0.116          |
|                    | Weight                   | 1.035 | 1.000 - 1.071  | 0.047*         |
|                    | Height                   | 1.018 | 0.988 - 1.048  | 0.244          |
|                    | BMI adjusted for Age     | 1.560 | 1.012 - 4.212  | 0.046*         |
|                    | Tonsillar Hypertrophy    | 1.541 | 0.877 - 2.705  | 0.132          |
|                    | Asthma                   | 2.025 | 0.626 - 6.546  | 0.239          |
|                    | Recent tonsillitis       | 2.030 | 1.14 - 12.68   | 0.030*         |
|                    | No rhinitis treatment    | 0.786 | 0.195 - 3.164  | 0.734          |
|                    | GE reflux                | 0.597 | 0.137 - 2.608  | 0.493          |
|                    | ENT surgery              | 0.892 | 0.176 - 4.531  | 0.890          |

\*Significant  $p < 0.05$ 

BMI= Body mass index, ENT= Otolaryngology

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**e-TABLE 5. BIVARIATE ANALYSIS WITH ESPRINT – 15 SCORE USING BINARY LOGISTIC REGRESSION**

| Dependent variable        | Independent variable                        | OR    | CI 95%        | P     |
|---------------------------|---------------------------------------------|-------|---------------|-------|
| Female Sex                | Severity rhinitis Classification ESPRINT 15 | 1.136 | 0.807 - 1.601 | 0.465 |
| Born in Bogotá            |                                             | 0.939 | 0.579 - 1.523 | 0.799 |
| Reside in Bogotá          |                                             | 1.279 | 0.854 - 1.915 | 0.233 |
| Urban Housing             |                                             | 0.966 | 0.447 - 2.088 | 0.930 |
| Asthma                    |                                             | 1.285 | 0.907 - 1.822 | 0.158 |
| Recent tonsillitis        |                                             | 1.263 | 0.831 - 1.921 | 0.274 |
| Antihistamine treatment   |                                             | 0.980 | 0.630 - 1.524 | 0.928 |
| Nasal corticoid treatment |                                             | 1.073 | 0.731 - 1.577 | 0.718 |
| No treatment              |                                             | 0.736 | 0.459 - 1.179 | 0.202 |
| Turbinate hypertrophy     |                                             | 0.584 | 0.234 - 1.458 | 0.249 |
| ENT surgery               |                                             | 0.968 | 0.584 - 1.605 | 0.900 |

ENT= Otolaryngology

**e-TABLE 6. BIVARIATE ANALYSIS WITH SEVERITY OF RHINITIS BY ARIA CLASSIFICATION USING BINARY LOGISTIC REGRESSION**

| Dependent variable        | Independent variable                        | OR    | CI 95%        | P     |
|---------------------------|---------------------------------------------|-------|---------------|-------|
| Female Sex                | Severity of rhinitis by ARIA classification | 1.005 | 0.719 - 1.406 | 0.975 |
| Born in Bogotá            |                                             | 0.961 | 0.594 - 1.556 | 0.873 |
| Reside in Bogotá          |                                             | 1.057 | 0.725 - 1.543 | 0.772 |
| Urban Housing             |                                             | 1.157 | 0.545 - 2.458 | 0.704 |
| Asthma                    |                                             | 1.164 | 0.832 - 1.628 | 0.376 |
| Recent tonsillitis        |                                             | 1.050 | 0.691 - 1.595 | 0.819 |
| Antihistamine treatment   |                                             | 1.178 | 0.755 - 1.837 | 0.471 |
| Nasal corticoid treatment |                                             | 0.932 | 0.639 - 1.360 | 0.715 |
| No treatment              |                                             | 0.920 | 0.598 - 1.414 | 0.703 |
| Turbinate hypertrophy     |                                             | 0.638 | 0.291 - 1.400 | 0.262 |
| ENT surgery               |                                             | 1.016 | 0.619 - 1.668 | 0.949 |

ENT= Otolaryngology

**e-TABLE 7. CORRELATIONS**

| Variable 1            | Variable 2                                  | Spearman correlation coefficient ( $\rho$ ) | P      |
|-----------------------|---------------------------------------------|---------------------------------------------|--------|
| Age in years          | AHI                                         | 0.026                                       | 0.799  |
|                       | Severity rhinitis Classification ESPRINT 15 | 0.092                                       | 0.365  |
|                       | Severity rhinitis Classification ARIA       | 0.081                                       | 0.427  |
| Weight                | AHI                                         | 0.296                                       | 0.106  |
|                       | Severity rhinitis Classification ESPRINT 15 | 0.190                                       | 0.059  |
|                       | Severity rhinitis Classification ARIA       | 0.245                                       | 0.015* |
| Height                | AHI                                         | 0.044                                       | 0.667  |
|                       | Severity rhinitis Classification ESPRINT 15 | 0.129                                       | 0.202  |
|                       | Severity rhinitis Classification ARIA       | 0.151                                       | 0.136  |
| BMI/Age               | AHI                                         | 0.109                                       | 0.283  |
|                       | Severity rhinitis Classification ESPRINT 15 | 0.305                                       | 0.002* |
|                       | Severity rhinitis Classification ARIA       | 0.313                                       | 0.002* |
| Tonsillar Hypertrophy | AHI                                         | 0.113                                       | 0.267  |
|                       | Severity rhinitis Classification ESPRINT 15 | 0.278                                       | 0.005* |
|                       | Severity rhinitis Classification ARIA       | -0.004                                      | 0.965  |
| Turbinate hypertrophy | AHI                                         | 0.129                                       | 0.204  |
|                       | Severity rhinitis Classification ESPRINT 15 | 0.263                                       | 0.009* |
|                       | Severity rhinitis Classification ARIA       | 0.101                                       | 0.322  |

AHI = Apnea / hypopnea index

\*Significant  $p < 0.05$

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