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Prevalence and Clinical Characteristics of the Restless Legs Syndrome (RLS) in Patients Diagnosed with Attention-Deficit Hyperactivity Disorder (ADHD) in Antioquia

Prevalencia y características clínicas del síndrome de piernas inquietas (SPI) en pacientes diagnosticados con trastorno por déficit de atención con hiperactividad (TDAH) en Antioquia

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Abstract

Introduction: Attention Deficit Hyperactivity Disorder (ADHD) is the most common behavioral issue for children. One of the sleeping disorders most frequently related to ADHD is the Restless Legs Syndrome (RLS), characterized by an irresistible urge to move the legs, something that is generally associated with paresthesias and motor restlessness. The prevalence rate of RLS in children diagnosed with ADHD is close to 18%, but in Colombia, these cases have been hardly studied. *Objective:* To determine the frequency of RLS, in children with ADHD. *Methods:* A cross-sectional study, filled out by parents of children diagnosed with ADHD, were analyzed. This questionnaire contained clinical criteria for classifying ADHD according to the DSM-IV, as well as diagnostic criteria for RLS by the National Institutes of Health (2003). *Results:* A predominance rate of 65.6% in combined ADHD was observed in children with RLS criteria. Upon carrying out an exploratory data analysis, it was found that having a family history of RLS and belonging to the middle or low socioeconomic strata are conditions associated with the presence of RLS in children with ADHD, with a significant p ($p < 0.000$) and a PR of 4.47 (3.16-6.32). *Conclusions:* The prevalence of RLS was similar to the findings of other clinical investigations. However, it highlights new prevalence values in relation to the comorbidity between ADHD and RLS, suggesting the need for new clinical and therapeutic alternatives amidst the presence of both syndromes.

Resumen

Introducción: El trastorno de hiperactividad con déficit de atención (TDAH) es el problema de comportamiento más común en la infancia. Uno de los trastornos de sueño que más se ha relacionado el TDAH es el síndrome de piernas inquietas (SPI) el cual conlleva un deseo irresistible de mover las piernas que, en general, se asocia con parestesias e inquietud motora. La prevalencia del SPI en la población infantil diagnosticada con TDAH es de cerca del 18 %. Sin embargo, en Colombia han sido escasamente estudiados. *Objetivo:* Determinar la frecuencia de SPI en niños con TDAH. *Método:* se realizó un estudio de corte transversal, con el uso de cuestionarios diligenciados por los padres de niños con diagnóstico de TDAH. Dicho cuestionario contenía criterios clínicos para la clasificación del TDAH según el DSM-IV, y criterios diagnósticos para SPI del National Institutes of Health pediatric restless legs syndrome (2003). *Resultados:* Los niños con criterios de SPI tuvieron predominio del TDAH combinado en un 65.6%. Al realizar el análisis exploratorio se encontró que tener historia familiar de SPI y estrato medio o bajo se asocian con la presencia del SPI en niños con TDAH, con una p significativa ($p < 0.000$) y una RP de 4.47 (3.16-6.32). *Conclusiones:* La prevalencia de SPI fue similar a los hallazgos de otras investigaciones clínicas, sin embargo, resalta nuevos valores de prevalencia en relación a la comorbilidad entre el TDAH y el SPI, sugiriendo la necesidad de habilitar nuevas alternativas clínicas y terapéuticas en la presencia de ambos síndromes.

Keywords:
Restless Legs Syndrome, RLS, Attention Deficit Hyperactivity Disorder, ADHD, sleeping disorders, comorbidities, disorder prevalence.

Palabras Clave:
Síndrome de piernas inquietas, Trastorno de déficit de atención e hiperactividad, Trastornos del sueño, comorbilidad, prevalencia del trastorno

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Introduction

The Restless Legs Syndrome (RLS) is a chronic sensory and motor disorder characterized by the presence of pain or discomfort in the legs, generally when the sufferer is at rest, causing a strong urge to move or stretch one's limbs. This symptomatology produces great anxiety and may interfere with the initiation and maintenance of sleep (Benes, Walters, Allen, Hening, & Kohnen,2007). Currently, RLS is considered to be a circadian disorder, since the symptoms progress and worsen at night and disappear in the morning. They generally affect both legs, although they may alternate between legs and are rarely unilateral. Additionally, the frequency of the symptoms may vary from occurring daily to being occasional (Wijemanne & Ondo, 2017). In untreated patients, a gradual but irregular progression of the symptoms has been observed over time (Yeh et al., 2016). The symptoms usually affect both legs and the movements are not necessarily symmetrical or synchronous: they vary from day to day, may alternate between legs, and are rarely purely unilateral (Montplaisir et al., 1997; Rinaldi et al., 2016).

RLS prevalence data have, so far, been controversial (Salas, Gamaldo, & Allen, 2010), but with the use of the International Restless Legs Study Group (IRLSSG) criteria, RLS prevalence rate in Europe and in the United States has been estimated to be between 2.4% and 10.8% (García-Borreguero & Williams, 2014). The data for Latin American countries, however, are still confusing. It is known that, although RLS has a higher prevalence rate in advanced ages, the symptoms began during childhood and adolescence in 25% of the cases. Nevertheless, it remains an underdiagnosed disease and its clinical and pathophysiological comorbidity with ADHD prompts the need for improved differential diagnosis schemes that can provide better treatment and early intervention alternatives for both syndromes (Manconi et al., 2012).

For its part, ADHD is one of the most prevalent neurodevelopmental disorders that occur during childhood (Rubió Badía, Mena Pujol, & Murillo Abril, 2006); its appearance at an early age affects school performance, decreases children's quality of life, and alters their relationship with their social and family environment (Rubió Badía et al., 2006). Moreover, ADHD is very likely to persist for a lifetime (Cornejo et al., 2005; Elliott, 2002).

Studies on the prevalence of RLS in children with ADHD have obtained discordant results until now. Table 1 shows the main studies on the prevalence of RLS in patients with ADHD. However, there exist underreporting and deficiencies in the diagnosis of sleeping disorders in patients with ADHD (Goodyear-Smith & Arroll, 2006; Sadeh, Pergamin, & Bar-Haim, 2006).

The relationship between ADHD and sleeping disturbances is currently a fundamental area of research in the etiopathogenesis of both clinical conditions for which neurological involvement of similar functional areas has been identified, namely: attention (Pearson et al., 2006; Sadeh, Gruber, & Raviv, 2003), inhibition (Lecendreux & Konofal, 2002), and working memory (Pagel, Forister, & Kwiatkowki, 2007; Picchietti & Picchietti, 2008; Sadeh et al., 2003). In this regard, existing theories suggest that sleeping disorders may increase ADHD symptoms or, in some cases, manifest ADHD-like symptoms (Chervin, Dillon, Archbold, & Ruzicka, 2003; Archbold, 2006; Hurtig et al., 2007; Sadeh et al., 2006; Walters, Silvestri, Zucconi, Chandrashekariah, & Konofal, 2008).

In particular, different studies have shown that children with ADHD have an increased motor restlessness during sleep (Chervin, Dillon, Bassetti, Ganoczy, & Pituch, 1997; Golan, Shahar, Ravid, & Pillar, 2004; Lecendreux & Konofal, 2002). These findings were confirmed through the use of actigraphy (Van der Heijden, Smits, & Gunning, 2006; Wiggs, Montgomery, & Stores, 2005) and were based on records obtained from infrared cameras (Goldman, Genel, Bezman, & Slanetz, 1998; Sadeh et al., 2003). In these works, the polysomnography showed a higher frequency of periodic short movements in children with ADHD, although the total time of movements was not superior in comparison with healthy controls (Kushida, 2007;

Sobanski, Schredl, Kettler, & Alm, 2008). However, one of the sleeping disorders most commonly associated with ADHD is RLS (Cortese et al., 2005; Cortese et al., 2008; Chervin et al., 1997; Picchietti et al., 2007; Picchietti, England, Walters, Willis, & Verrico, 1998; Walters et al., 2000; Walters, Picchietti, Ehrenberg, & Wagner, 1994; Walters et al., 2008).

Children with ADHD and who were also diagnosed with RLS frequently presented diurnal alterations, such as higher degree of inattention, mood instability, and paroxysms of hyperactivity, resulting to poor school performance (Crowell et al., 2002; Kotagal & Silber, 2004).

Current studies suggest that attention deficits in these patients are secondary to the sleeping disorder caused by RLS or that there is a molecular mechanism involved in both clinical conditions. It can also be the expression of a dopaminergic deficit in the pathogenesis of both disorders (Walters et al., 2000). Unfortunately, there are only but a few studies on the close etiopathogenic relationship between both clinical manifestations in children; some of them indicated that 18% to 44% of the patients with ADHD had RLS symptoms (Chervin et al., 2003) and that 26% of the patients with RLS also had ADHD (Cortese et al., 2005; Picchietti & Picchietti, 2008; Wagner, Walters, & Fisher, 2004). However, the use of stimulant medications with dopaminergic action can reduce or mask RLS symptoms, resulting to the undervaluation of its prevalence in children with ADHD (Sobanski et al., 2008; Zak, Couvadelli, Fischer, Moss, & Walters, 2009).

Additionally, the cognitive and emotional deficits associated with RLS have not been thoroughly evaluated (Angriman, Cortese, & Bruni, 2017). Pearson and colleagues had previously suggested that the cognitive tasks that depend on the activity of the prefrontal cortex are especially sensitive to sleeping disorders. In particular, patients with RLS have manifested low performance in cognitive flexibility and verbal fluency tasks, similar to what has been observed in those with ADHD (Bahcivan Saydam, Ayvasik, & Alyanak, 2015). However, cognitive deficits are probably a consequence of chronic sleeping disturbances rather than a direct effect of RLS (Pearson et al., 2006). In summary, characterizing the neurocognitive effects associated with the different types of sleep deprivation in RLS, with or without ADHD, still poses a challenge to research for the promotion of more successful therapeutic interventions.

Table 1. *Prevalence reported in studies on RLS and ADHD*

AUTHOR	# PATIENTS	RESULTS
Kwon et al., 2014	56 patients	42.9% of ADHD patients with RLS symptoms and 7.1% of them, diagnosed with RLS
Pullen et al., 2011	374 patients with child-onset RLS	Prevalence rate of ADHD: 25%
Zak et al., 2009	30 adult patients diagnosed with ADHD	20% (6) of the patients with ADHD had RLS symptoms vs. 7.2% of control patients
Oner et al., 2007	87 children diagnosed with ADHD, aged 6 to 16 years	33.3% of the patients had definite RLS criteria
Picchietti et al., 2007	206 children diagnosed with definite RLS, aged 8 to 17 years	14.8% of the patients between 8 and 11 years old, and 17.6% of the patients between 12 and 17 years of age had ADHD.
Picchietti et al., 2007	10,523 households with children aged 8 to 17 years	ADHD among children with definite RLS: 8 to 11 years old age group, 14.8%; 12 to 17 years old age group
Cortese et al., 2005	5 studies on ADHD and RLS symptoms (average age: 2 to 18 years), 3 studies with patients diagnosed with RLS (average age: 2 and > 17 years)	The prevalence rate of RLS symptoms in patients with ADHD ranged from 10.5% to 24%. The prevalence rate of ADHD in patients diagnosed with RLS ranged from 18% to 25%
Kotagal & Silber, 2004	32 patients diagnosed with RLS	Inattention was observed in 25% (8) of the patients with RLS
Konofal, 2003	52 children diagnosed with ADHD	44% of children with ADHD had RLS symptoms
Chervin et al., 2002	866 children diagnosed with ADHD, aged 2 to 14 years	17% of children with ADHD had RLS symptoms
Picchietti et al., 1998	69 diagnosed with ADHD	8 (44.4%) are in RLS criteria

Physiopathological Hypothesis

Iron deficiency is one of the causes that may explain the shared physiopathology between ADHD and RLS: The greater the deficiency in iron, the greater the severity of the clinical manifestations (Cortese et al., 2008; Walther, 2002). Some reports claim that iron in the dopaminergic system as cofactor of the tyrosine hydroxylase enzyme plays a crucial role in dopaminergic synthesis; this condition was described by Walters and colleagues in patients with ADHD and RLS who had 41 ng/ml as levels of ferritin (Walters et al., 2000). However, whether changes in the optimum levels of ferritin determine a relevant etiopathogenic finding that explains the presence of both syndromes is still under discussion (Cortese et al., 2008; Konofal, 2003). Although the physiopathology of RLS is not yet fully determined, the neuropathological clues it shares with ADHD suggest dopaminergic dysfunction; problems in iron metabolism; changes in the central opioid system; (García-Borreguero & Williams, 2014); genetic factors mainly associated with the expression of neurotensin, a neuropeptide that probably modulates dopaminergic transmission (Desautels et al, 2001); and some polymorphisms in the MAP2K5-LBXCOR1 and PTPRD genes that may be participating in the regulation, metabolism, and transport of iron (Winkelmann et al, 2007).

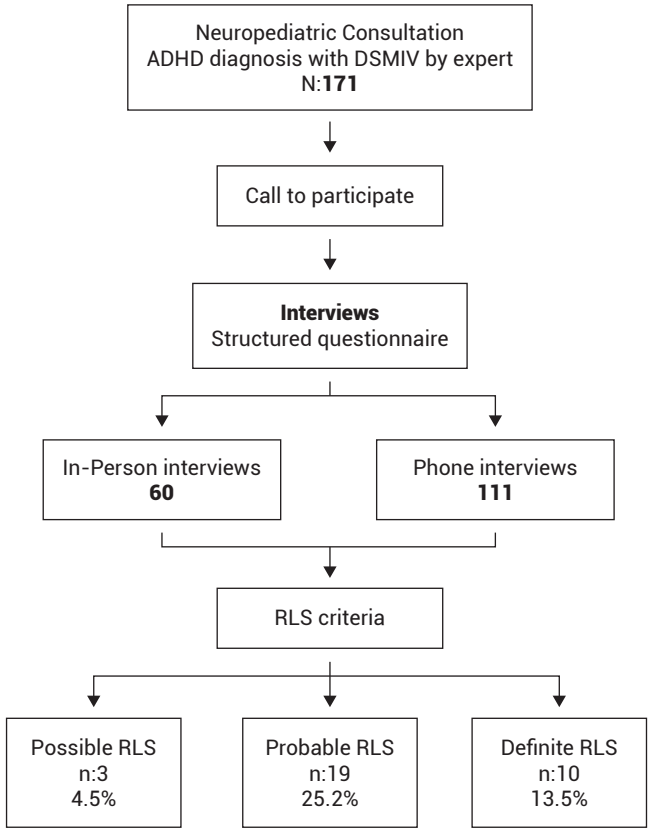
Although the bidirectional relationship existing between ADHD and RLS has been determined, there are so far no clinical studies with significant-size samples that can outline shared neurologic and cognitive involvements that may turn out to be differentiators of probable clinical subtypes or can establish the evolution and prognosis of both disorders when they occur simultaneously.

The main purpose of this research is to determine the clinical characteristics and the prevalence of RLS and ADHD in children and adolescents, defining the correlated clinical manifestations in both syndromes.

Patients and Methods

A descriptive, cross-sectional, non-random, consecutive, convenience study was conducted in the child neurology and neuropediatrics section of *San Vicente Fundación University Hospital* (HUSVP) of Medellín and the metropolitan area of Valle de Aburrá, Colombia. Both patients and their parent´s were recruited and evaluated from investigator´s clinical practice, all 171 participating children provided assent. The consent and assent forms, study protocol, and advertisements for recruitment were reviewed and approved by the Institutional Review Board of Universidad de Antioquia. Two experts—a child neurologist and a neuropediatrician—assessed each child and adolescent using a structured interview to establish current ADHD diagnosis according to DSM-IV, for a period of 18 months or more. The study excluded children under 6 and over 15 years old, children with ADHD diagnosis defined as any nosological entity sharing phenomenology of inattention and hyperactivity, but secondary to other pathologies, and children diagnosed with mental retardation (figure 1).

Figure 1. *Algorithm of RLS Assessment and Diagnosis in Children with ADHD.*



Instruments

The DSM-IV clinical criteria were applied for ADHD, and the RLS diagnosis criteria for pediatric age according to the 2003 RLS international classification by the National Institutes of Health (Allen et al., 2003) (table 2). The Chervin questionnaire was chosen for its validity, reliability, and sensitivity measures, which are higher than 0.80. One of its characteristics is that it compares inattention and hyperactivity symptoms and correlates them with the findings of pediatric polysomnography of sleeping disorders (Albin et al., 2000), as well as with other sociodemographic and clinical variables, including the risk factors previously related to RLS.

Moreover, the parents were also invited to take part in the study. Those who accepted the invitation underwent an in-person or phone interview (according to the validation of the phone interview for RLS) (Allen et al., 2003). One of the pediatric neurologists of the

neuropediatrics and puericulture section of HUSVP was put in charge of this interview.

Afterwards, a descriptive analysis of the sample was conducted using averages, standard deviations for the quantitative variables, and frequencies and proportions for qualitative variables. RLS prevalence in children with ADHD was estimated using the following formula:

Number of RLS cases determined in the clinical assessment / Total number of children and adolescents participating during the period of the study. Data were analyzed using the Statistical Package for Social Sciences (SPSS), version 22.

Table 2.
RLS diagnosis criteria for pediatric age.

Definite RLS +	Probable RLS *	Possible RLS
Urgency to move the legs, generally with unpleasant sensations in the legs.	Urgency to move the legs, generally with unpleasant sensations in the legs.	Child has recurring movements of extremities and has a biological relative with definite RLS diagnosis.
Motor restlessness manifested by incessant turning over in bed, leg rubbing, and sleepwalking.	Motor restlessness manifested by incessant turning over in bed, leg rubbing, and sleepwalking.	
Symptoms start to worsen during rest or periods of inactivity.	Symptoms are aggravated or present only during rest and partially or temporarily alleviated by physical activity.	
Discomforts are reduced totally or partially through movements such as walking, bending over, stretching, etc. and while such activities last.		

+ Aside from meeting the four minimum criteria, the following also need to be met: The child describes discomfort in the legs using his/her own words—tickling, tingling, bedbugs, spiders, ants—or the urge to run. Alternatively, besides meeting the four minimum criteria, the child should manifest two of the following conditions: Sleeping disorders according to his/her age, a biological relative diagnosed with definite RLS, or a study showing recurring movements of extremities for five or more hours during sleep.
* The three criteria must be met, in addition to the following: The child feels discomfort in his lower extremities upon sitting or lying down, motor activity or movement of extremities are affected, and having a biological relative diagnosed with definite RLS.
Note: The definite RLS criteria for adolescents (13 to 18 years old) are the same as those for adults (the four minimum criteria).

Subsequently, an exploratory analysis was conducted to compare some qualitative and quantitative variables existing between the ADHD group without RLS symptoms and the ADHD group with RLS symptoms. The Student's t-test was used to compare the normal distribution quantitative variables with the dichotomy qualitative variables using the chi-squared test. The analysis used a 95% trust level, which corresponds to a p of 0.05.

Results

171 children diagnosed with ADHD, all of whom took part in the pediatric neurology and neuropediatrics consultation service of the HUSVP, were clinically evaluated. The average age of the patients was 10.25 years (SD: 2.867), with a ratio of boys to girls of 3:1, and most of whom belonging to the middle socioeconomic stratum (53.8%) (table 3). The ADHD distribution according to the subtypes was predominantly combined in 122 patients (71.3%) (table 3).

Table 3.
Sociodemographic characteristics of 171 children with ADHD in Medellín and Valle de Aburrá.

	Category	Number of children with ADHD	%
Gender	Male	129	75.4%
	Female	42	24.5%
Stratum	Low (1.2)	34	19.9%
	Middle (3.4)	92	53.8%
	High (5.6)	45	26.3%
Age (years)	4-8	54	31.6 %
	9-13	88	51.4%
	>13	29	17%
ADHD Type	Inattentive type	34	19.9%
	Hyperactive-impulsive type	15	8.8%
	Combined type	122	71.3%

A total of 73 children and adolescents manifested RLS symptoms (42.7%) and 10 of them met the criteria for the diagnosis of definite RLS. This corresponds to a prevalence rate of 13.5%. Algorithm 1 (figure 1) shows the evaluation sequence and summarizes the prevalence of children and adolescents with possible, probable, and definite RLS. None of the patients underwent a previous polysomnographic study.

The ADHD subtype most frequently observed in children with some RLS symptoms was the combined type, found in 65.6% of the patients: 25% of which with definite RLS, 37.5% with probable RLS, and 3.1% with possible RLS. From the analysis of the established age range, socioeconomic stratum, and gender, it was determined that patients diagnosed with RLS were in the 10 to 13 years of age range (56.2%), mainly from the middle economic stratum (59.3%), and with predominance in male patients (75%). The predominant symptoms of RLS described by these children were unpleasant sensations in the legs (39.2%) and discomfort (14.6%).

One of the more relevant aspects of this study was determining that 93.2% of the evaluated sample received stimulant medications (in some cases, combined with antipsychotics, tricyclics, alpha agonists, and antidepressants), 1.3% only received risperidone, and 2% only used clonidine.

Sleeping disorders

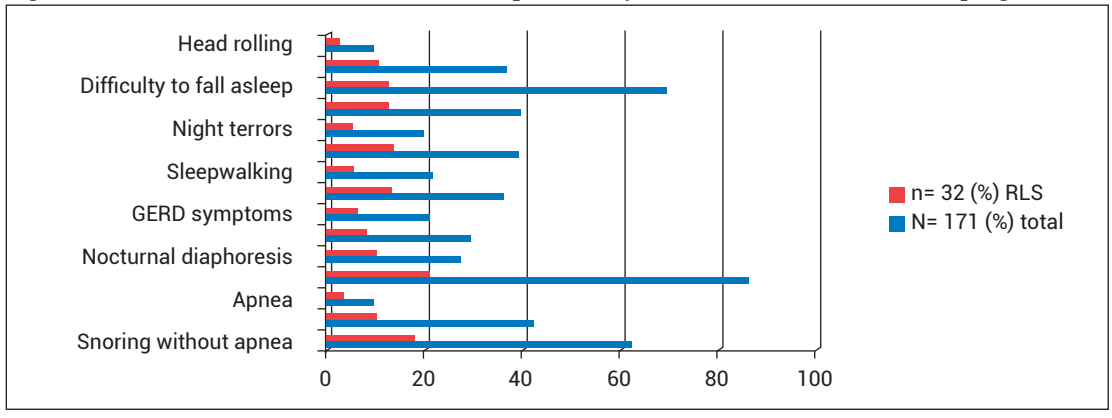
The sleeping disorders most commonly identified in both the total number of patients and those who met the criteria for RLS are referenced in table 4 and figure 2.

Table 4.
Sleeping disorders and sleep characteristics in patients with RLS.

			No RLS symptoms or criteria			
	N =171	(%) total	n =98	(%)	n =32	(%) RLS
Snoring without apnea	62	36.2%	38	27.1%	18	56.2%
Rhinitis AP	42	24.6%	23	12.6%	10	31.2%
Apnea	9	5.3%	2	2.04%	3	9.3%
Restless sleep	86	50.3%	36	36.7%	21	65.3%
Nocturnal diaphoresis	27	15.8%	14	14.2%	10	31.2%
Nocturnal enuresis	29	17%	13	13.2%	8	25%
GERD symptoms	21	12.3%	11	11.2%	6	18.7%
Bruxism	36	21%	19	19.3%	13	40.6%
Sleepwalking	21	12.3%			5	15.6%
Nightmares	39	22.8%	15	15.2%	13	40.6%
Night terrors	19	11%	10	10.2%	5	15.6%
Somniloquy	39	22.9%	15	15.2%	12	37.5%
Insomnia (Resistance to falling asleep)	69	40.5%	29	29.5%	12	37.5%
Insomnia in the middle of the night	36	21%	9	9.2%	10	31.2%

*Patients may have more than one sleeping disorder
GERD: Gastroesophageal Reflux Disease

Figure 2. *Characteristics associated with the presence of RLS, comorbidities, and sleeping disorders.*



By exploring the relationship of each RLS criteria (probable, possible, and definite) to the clinical conditions associated with ADHD, some characteristics were determined and are listed in table 5.

Table 5.
Comparison of patients with ADHD with and without RLS diagnosis.

	Patients with ADHD but without RLS symptoms or criteria		Patients with ADHD and with RLS criteria			
	n=139	%	n=32	%	Prevalence ratio	p
Age					1.19 (0.5-2.5)	0.37
4-8	47	33.8%	7	21.8%		
9-13	67	48.2%	17	51.3%		
>13	25	17.9%	8	25%		
Gender					0.97 (0.4-2.0)	0.86699
Boys-adolescents	105	75.5%	24	75%		
Girls- adolescents	34	24.4%	8	25%		
Stratum					7.22 (3.1-16.3)	0.0
Low	25	17.9%	26	81.25%		
Middle	79	56.8%	6	18.75%		
High	35	25.1%	0			
ADHD Type					1.16 (0.39-3.4)	0.39
Inattentive	26	18.7%	8	25%		
Hyperactive/Impulsive	12	8.63%	3	9.35%		
Combined	101	72.6%	21	65.6%		
Hereditary RLS	4	2.87%	24	75%	4.47 (3.16-6.32)	0.000
Preterm birth	15	10.7%	2	6.25%	0.64 (0.16-2.4)	0.7356
No breastfeeding	26	18.7%	6	18.7%	1.00 (0.45-2.23)	0.8061
Iron supply	15	10.7%	3	9.37%	0.87(0.29-2.5)	0.9330
Family history of ADHD	56	40.2%	14	43.75%	1.12(0.59-2.1)	0.8731

Additionally, most of the patients diagnosed with RLS reported growing pains, compared to patients without RLS (a proportion of 40% and 10% respectively, with p = 0.0000029, X^2= 21.85, prevalence ratio of 7.21, and CI of 2.82-18.62).

Discussion

Existing data on the prevalence of RLS in children with ADHD reveal deep discrepancies that can be explained, in part, by the different methodologies implemented in the investigations and the samples under study, given that some of these investigations included broader age groups (Castano-De la Mota et al., 2017). In the sample analyzed in this study, the prevalence rate of RLS symptoms in children diagnosed with ADHD was 42.7% (73 children). This rate was very similar to those in previous studies such as that of Konofal, with 44%, and those of Pinchiett, with a prevalence rate of 32% to 44% (Cortese et al., 2008; Chervin et al., 2002; Picchietti et al., 2007).

The differences that may exist in this broader spectrum, as compared to Chervin's study that showed a RLS symptoms prevalence rate of 17%, can be explained by the fact that the said research did not use the international criteria for RLS (Cortese et al., 2008; Chervin et al., 2002; Picchietti et al., 2007), but only made use of the sleep questionnaire to address RLS symptoms, where only two questions are used for screening. By narrowing the phenotype, taking into account the criteria of possible, probable, and definite RLS, the results obtained became more accurate, showing a prevalence rate of 4.5%, 25.2%, and 13.5% respectively, in comparison to the total sample. These data coincided with those of Rappley's study, where 14% to 17% of the patients with definite RLS criteria had ADHD (Rappley, 2005). However, making a comparison is a complicated matter because that was a population-based study conducted with RLS patients. In contrast, Oner described 33.3% of definite RLS in patients with ADHD; a value superior to that found in the present work, perhaps due to the usage of scales to diagnose ADHD: Oner used the Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version (K-SADS-PL), which somehow varies from the DMS-IV criteria (Oner et al., 2007).

In addition, different studies have reported a higher prevalence of RLS in women of all age groups. Although our work sought to relate the clinical aspects of RLS to ADHD, it can be inferred from table 5 that RLS has a relatively similar prevalence rate in female and male population. This finding is consistent with the reports of previous studies (Per, Gunay, Ismailogullari, Oztop, & Gunay, 2017) that have also pointed out an increase of this disorder in men (Cortese et al., 2008; Chervin et al., 2002; Picchietti et al., 2007). However, it is the frequency of ADHD in women that contributes to mask the prevalence of RLS in the female population. Although a higher prevalence of sleeping disorders has been reported in patients with ADHD as compared to the general population, it is still uncertain whether the diagnosis of ADHD actually contributes to the presence of these sleeping disturbances, outlining a particular clinical subtype.

As regards the socioeconomic stratum, a higher prevalence rate of RLS was found in the lower strata, but determining the impact of the socioeconomic variables on sleeping disorders in children and adolescents is still complicated. In this regard, the results of the study developed by El-Sheikh and colleagues indicated that economic difficulties in the family could contribute to a greater variability in the initiation of sleep and to a shorter sleeping duration for children. Moreover, the low level of educational attainment of parents were likewise associated with lower efficiency of sleep for their offsprings (El-Sheikh et al., 2013). In addition to these findings, there are also claims that ADHD is a more frequent disorder in families with low income and low level of educational attainment (Senol, Unalan, Akca, & Basturk, 2018). For its part, the reported physiopathological findings for RLS and ADHD involving the bioavailability of iron as an essential trace element in diet raise the probability of the occurrence of nutritional deficiencies in the low-income population. Iron, as a cofactor, plays a relevant role in the synthesis and catabolism of monoaminergic neurotransmitters. Its deficiency, therefore, decreases the transport of dopamine and the density of the D2 and D4 receptors. This condition leads to a dysfunction of the basal ganglia, which is a pathophysiological finding shared between ADHD and RSL (Demirci et al., 2017).

Similarly, the evident prevalence rate of family history highlights the need to review the hypothesis of a hereditary and hormonal component as a risk factor, and confirms the relevance of implementing a genetic segregation analysis and performing a selection and evaluation of molecular targets that can contribute to explaining the etiopathogenesis of the disease (Schimmelmann et al., 2009; Silvestri et al., 2009).

This investigation determined that the majority of RLS cases also had ADHD combined type, which points out the need to evaluate the average score in the International Restless Legs Syndrome Rating Scale (IRLSRS); in the RLS +group, it was 18.6 (SD 8.6). However, the classification of the ADHD subtype in the sample does not specify its prevalence in RLS. Up to now, there are not enough studies to determine which of the ADHD subtypes is more closely related to RLS.

As shown in several studies (Cortese et al., 2005; Walters et al., 2000), the prevalence ADHD might have been undervalued in their studied sample since most of the patients were on medication during the evaluation phase (Cortese et al., 2005; Walters et al., 2000). 93.2% of the sample evaluated in this investigation received stimulants (in some cases, combined with antipsychotics, tricyclics, alpha agonists, and antidepressants), 1.3% received only risperidone, and 2% took only clonidine. However, it has been suggested that stimulants drugs have no direct effect on RLS symptoms (Buchfuhrer, Hening, & Kushida, 2006).

In relation to the presence of the sleeping disorders evaluated through the Pediatric Sleep Questionnaire (PSQ) by R. Chervin, no significant differences were found in RSL. This result might be related to methodological restrictions of the study rather than to a particular physiopathological element of the syndrome itself. So far, different studies have shown the coexistence of different sleeping disorders associated with ADHD and RLS in children (Albin et al., 2000; Blunden & Beebe, 2006; Cortese et al., 2008; Chervin et al., 1997; Van Der Heijden, Smits, & Gunning, 2005). This study found high prevalence of sleeping disorders, especially in the form of nightmares, snoring, and restless sleep.

Conclusions

Although the evidence of RLS in children with ADHD is still limited, our study showed a behavior similar to the other clinical investigations on RLS prevalence. This work helps to delineate the clinical and pharmacological intervention for both syndromes and highlights the need to take a closer look at the pathophysiological bases of ADHD and RLS, as a distinctive clinical entity that promotes the urgency of enabling new clinical, pharmacological, and therapeutic approaches.

Limitations

Although this study contributes to reaffirm the high prevalence of RLS in pediatric ADHD, several methodological limitations must be considered for the interpretation of results. First, due to its eminently clinical nature, the questionnaire might reflect parental perceptions rather than real RLS symptoms. Second, we only used parental reports and not objective measures such as polysomnography. However, we believe that parental perception can constitute an alert mechanism for the detection of specific problems, making this investigation a necessary first step to future studies

in which the reports of teachers and children can also be analyzed. Furthermore, the international RLS criteria are undeniably clinical. Third, the information related to family history and the disorders themselves may be subject to memory biases that undervalue real prevalences. Fourth, the selected sample was not made random and is not representative of the entire ADHD population in Antioquia.

For the development of subsequent studies, we suggest introducing the evaluation of executive functioning for both syndromes, which could delineate clinical subtypes in RLS, with and without ADHD, creating new clinical and therapeutic approaches that favor the recognition of shared pathophysiological pathways and the characterization of putative neurocognitive domains.

In this investigation, the current criteria on restless legs syndrome were not used during the period in which the study was conducted.

Recommendations

The current findings establish an evident prevalence between RLS and ADHD strong enough to generate a considerable attributable risk calculated at 13.5%, which could reach 44% if the presence of symptoms is taken into account. These results might suggest that, if restless legs contribute to hyperactivity, then dopaminergic therapy—which controls and reduces the symptoms of restless legs—should be considered in the clinical and therapeutic management of ADHD and RLS in children.

These data underline the importance of a continuous investigation of the common physiopathology, the methods in identifying patients with RLS, and its treatment.

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