

Original article

Overlapping features of restless legs syndrome and growing pains in Turkish children and adolescents

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Abstract

Background: Restless legs syndrome (RLS) and growing pains (GPs) share many common features and are sometimes overlapping diagnoses. The present study aims to investigate the shared features of patients with RLS, classified based on the 2013 diagnostic criteria of International Restless Legs Syndrome Study group and of patients with GPs, diagnosed based on the combined criteria proposed in 2013.

Methods: A cross-sectional population study was conducted in 7 Istanbul schools, which were selected randomly. A total of 4565 (56.1% female) children aged 9 to 18 years were included. In the first stage, candidates of RLS and GPs were identified based on 2 separate questionnaires, whose diagnoses were confirmed by a second survey applied to them under parental supervision.

Results: Out of 192 children (65.6% female) diagnosed as definite RLS (yearly prevalence: 4.2%), 30 (15.6%) reported bilateral leg muscle pain localized typical regions for GPs, which started <13 years of age in 17 children. An urge to move the legs to relieve unpleasant sensations or pain was present in 39.3% of 140 children (64.3% female) classified as GPs (yearly prevalence: 3.1%). Occurrence of symptoms at rest or when lying down was present in 36.4% of GPs children and relief by gross movements was in 21.4% children. Only 12 patients (9 with definite RLS and 3 with GPs) (0.03% of total cohort) were eligible for overlapping diagnosis of GPs and RLS.

Conclusion: Although a considerable number of patients with RLS and GPs share some clinical features, a combined phenotype is very rare.

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Keywords: Restless legs syndrome; Growing pains; Prevalence; Combined diagnostic criteria; Overlapping features; Combined phenotype

1. Introduction

Restless legs syndrome (RLS) and growing pains (GPs) are common childhood disorders. The prevalence of RLS is approximately 2% in school children and 3.2% in adolescents [1,2], which continues throughout adult-

hood, along with comorbid disorders [3]. Contrary to the chronic nature of RLS, GPs are more prevalent in childhood (ranged 3–14 years), particularly in preschool children [4], and decrease in adolescents without long-term consequences [5,6].

Regarding clinical findings and genetic background, RLS and GPs share many common features and are occasionally overlapping diagnoses [7,8]. Co-occurrence of GPs and RLS in the same patient or within the family has been reported in some clinical

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and epidemiological studies [1,2,9,10]. Genetic association between RLS and GPs has also been delineated by a twin family survey [11]. On the contrary, various epidemiological and clinical data have reported lack of association between RLS and GPs or misdiagnosis of GPs for RLS [12–14].

Lack of standardized and universally accepted diagnostic criteria and criterion-based diagnostic questionnaires for GPs pose limits on the estimation of precise prevalence and the discovery of overlapping features with RLS. To establish unified criteria for the diagnosis of GPs and its differentiation from RLS, Walters et al. [8] combined the criteria previously proposed by Evans and Scutter [4,15] and Champion et al. [11].

This epidemiological survey was conducted to investigate overlapping clinical features of RLS and GPs and the rate of coexistence of the two phenotypes among Turkish children and adolescents.

2. Material and methods

2.1. Study design

This cross-sectional study was carried out in three districts of Istanbul province. The study was conducted in three primary and four high schools, which were randomly selected (approx. 0.2% of the public primary and high schools in the municipality) and included a total of 5000 students. The survey aimed to include all students from 3rd through 12th grade in each school.

A formal consent was obtained from the Education Bureau and Governorship of Istanbul (09.05.2017/590 90411-44-E.6592397). The Ethics Committee of Marmara University Medical Faculty approved the study (09.2017.265).

Before the administration of questionnaires, the aim of the study and the procedure were clearly explained in each classroom. Two structured screening questionnaires (1A and 1B) were given to children aged >11 years in the classrooms, or were sent home to be filled out with parents' guidance for children ≤11 years, excluding students absent on the day of the survey. Accordingly, the coverage rate was above 98%. Additionally, documents including information on RLS and GPs and consent forms were given to parents.

The 7-item structured questionnaire 1A, validated in Turkish language with the clinical expert's interview in our previous epidemiological survey [2], aimed to investigate the first 4 diagnostic criteria of RLS for children and adolescents, which were proposed by the 2003 diagnostic criteria of the International Restless Legs Syndrome Study Group (IRLSSG) [16] and kept by the 2013 revised classification [17].

Six questions assessing the 4 primary diagnostic criteria of RLS were designed to avoid false-negative or false positive diagnoses of RLS, as detailed in our previous

study [2]. Questions #1 and #2 assessed criterion #1 of the recent IRLSSG revised classifications [17]. Additionally, children were requested to describe sensations or feelings consistent with leg discomfort in their own words (item #3), which was considered as an essential criterion by the 2013 criteria of IRLSSG [17]. Questions #4, #5, and #6 assessed revised criteria #2, #3, and #4, respectively. Item #7 was used as a proxy measure of severity [2].

The aim of the first 8 questions, enclosed in the 10-item questionnaire 1B, was to investigate the clinical "combined diagnostic criteria" of GPs, proposed by Walter et al. [8] who combined previously proposed GPs criteria, except for criteria #2, #7, #8, #9, and #10 [4,11,15] (Table 1). Considering recall bias of children, criteria #2, #9, and #10 were inquired under the supervision of parents in the second stage of the survey. We considered that more reliable data would be obtained in relation to these criteria if children were accompanied by parents, based on the first author's clinical experience. Similarly, criteria #7 and #8 assessing the results of physical and laboratory examinations, respectively, were not included in the first stage. Questions #1 and #2 assessed criterion #1 of the combined criteria of GPs [17]. Patients who suffered from bilateral leg pain were surveyed on the other diagnostic features of GPs (Table 1). Questions #3 and #4 assessed combined criterion #5 and questions #6 and #7 assessed combined criterion #4. Combined criteria #3 and #6 were inquired by questions #5 and #8, respectively. Questions #9 and #10 assessed the temporal relationship of leg pain with the position of the patient and the methods for relieving leg pain, respectively.

In the second stage, both questionnaires from 4585 cases were returned. Subjects who responded affirmatively to questions #1 (or #2), #4, and #5 of questionnaire 1A were selected as candidates for probable RLS. Subjects who gave affirmative responses to questions #1 (or #2), #4, #5, and #6 and who also described feelings consistent with leg discomfort in their own words were selected as candidates for definite RLS. Subjects with bilateral leg pains were selected as candidates for GPs based on their responses to items #3–8 in questionnaire 1B.

Candidates for RLS or GPs were administered a confirming 22-item questionnaire, to be filled out by children under parental supervision. This survey aimed to find out about the following: 1) common conditions with symptoms similar to the diagnostic criteria or behavioral conditions of RLS (possible "RLS mimics" including rheumatologic disorders, diabetes, dermatitis, myalgia, neuropathy, spinal trauma or disc problems, back, hip or leg pains, positional discomfort, daily or nocturnal leg cramps, habitual foot tapping, involuntary movements of the lower extremities, epilepsy, tic disorders or psychiatric disorders) [1] to assess criterion #5

Table 1

The questionnaire (1B) for the selection of candidates of growing pain cases at the first stage of the survey.

During the last 12 months:

- (1) Do you feel pain in your legs?
Yes, or No
 - (2) Do you feel pain in both legs on the same occasion?
Yes, or No
- If you responded “yes” to both questions, answer the following:
- (3) Where in your legs do you experience pain?
a) muscles b) joints
 - (4) In which part of your legs do you feel most pain? (You can choose more than one)
a) front of the thighs b) calves c) back of knees d) hips e) back of thighs f) feet
 - (5) When do you most experience leg pain?
a) Morning b) Noon c) Evening d) Night
 - (6) Do you limp when you experience leg pain?
a) Yes b) No
 - (7) Are you able to move when you experience leg pain?
a) Yes b) No
 - (8) How often do your leg pains occur?
a) one time per year
b) less than one time per month but more than 1 time per year
c) 1–3 times per month
d) 1–2 times per week
e) 3–5 times per week
f) once or more per day
 - (9) Do you experience leg pain when you are... (you can choose more than one)
a) sitting b) lying down c) moving around
 - (10) How do you relieve leg pains? (You can choose more than one)
a) standing up b) walking around, hopping and/or kicking c) rubbing legs against each other d) stretching legs e) nothing

of 2013 consensus criteria [17]; 2) criteria #2, #9, and #10 of “combined diagnostic criteria” of GPs [8]; 3) differentiation of “secondary causes” of leg pains by questioning previous history of infections or systemic disorders associated with bony pain, arthralgia, local trauma or symptoms of inflammation (pain, edema, reduced range of motion, erythema or tenderness), the presence of orthopedic deformities/disorders or overuse, and results of physical (criterion #7) and laboratory and radiological examinations (criterion #8), if present; 4) family history of GPs and RLS, which has been considered as a supportive criterion for diagnosis of RLS by IRLSSG [18]; 5) parents’ medicine-seeking behaviors.

At the beginning of the survey, a pilot study was conducted for all questionnaires. Questionnaires 1A and 1B were administered to 20 children at the same age and the 22-item questionnaire was administered to 15 children under supervision of parents to test the feasibility of the questionnaire.

2.2. Diagnosis of RLS and GP

Children with probable RLS were determined by the exclusion of those with “RLS mimics” among candi-

dates for probable RLS. After exclusion of children with “RLS mimics” among candidates for definite RLS, children with definite RLS were classified [17].

Diagnosis of GPs was verified among GPs candidates associated with the following features: 1) onset of age of symptoms between 3 and 12 years of age (criterion #2 of combined diagnostic criteria), lasting 3 and more months (criterion #9 of combined diagnostic criteria); 2) well-being (criterion #10 of combined diagnostic criteria); 3) lack of “secondary causes” of leg pain [8].

2.3. Selection of overlapping symptoms

The essential clinical features of RLS, not necessary for the diagnosis of GPs are: 1) an urge to move the legs, usually but not always accompanied by or felt to be caused by uncomfortable and unpleasant sensations in the legs; 2) the urge to move or unpleasant sensations partially or totally relieved by movement of legs; 3) the urge to move the legs and any accompanying unpleasant sensations worsened during periods of rest or inactivity [17]. The diagnostic criteria of GPs which are not a prerequisite for RLS diagnosis are: 1) bilateral leg pain, 2) involvement of specific parts of legs, 3) onset of symptoms between 3 and 12 years of age, and 4) intermittent nature of leg pain [8]. Based on the above criteria, we selected the patients with definite RLS who had one or more diagnostic clinical features of GPs, which are not a prerequisite for diagnosis of RLS and the patients with GPs who had also one or more diagnostic features of RLS, which are not a prerequisite for diagnosis of GPs. The shared symptoms were named “overlapping features.”

2.4. Statistical analysis

The statistical package SPSS (version 22.0) was used for the statistical analyses. Categorical data comparisons were done using Pearson’s chi-squared test and Fisher’s Exact test. The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request

3. Results

The total number of our sample including valid answers was 4565 (2564, 56.1% female) subjects and the participation rate was 99.6%. The number of children in elementary school (9–12 years of age) and high school (13–18 years of age) were 1140 (25%) and 3425 ($p < 0.05$), respectively. The mean age was 14.1 ± 2.2 (ranged 9–18) years and there was no significant mean age difference between males (14.0 ± 2.2 , ranged 9 to 18 years) and females (14.0 ± 2.3 , ranged 9–18 years) ($p > 0.05$).

3.1. Diagnosis of RLS

Of 1702 (37.3%) positive responders to the question #1 or #2 of the first questionnaire, 503 (11% of total population) (9.1% in male, 12.5% in female; $p < 0.001$) were diagnosed as probable RLS (Fig. 1). Definite RLS was diagnosed in 192 (38.2%) (aged 14.6 ± 2.2 ;

ranged 9–18) of children with probable RLS. The yearly prevalence rate of definite RLS was 4.2% in total, 0.68% (34 patients, 67.6% female) in 9–12-year-old children, and 3.2% (158 patients, 65.2% female) in 13–18-year-old adolescents. Definite RLS is significantly more prevalent in females (4.9%) than in males (3.3%) ($p = 0.007$) (female: male ratio = 1.9:1). The dominance

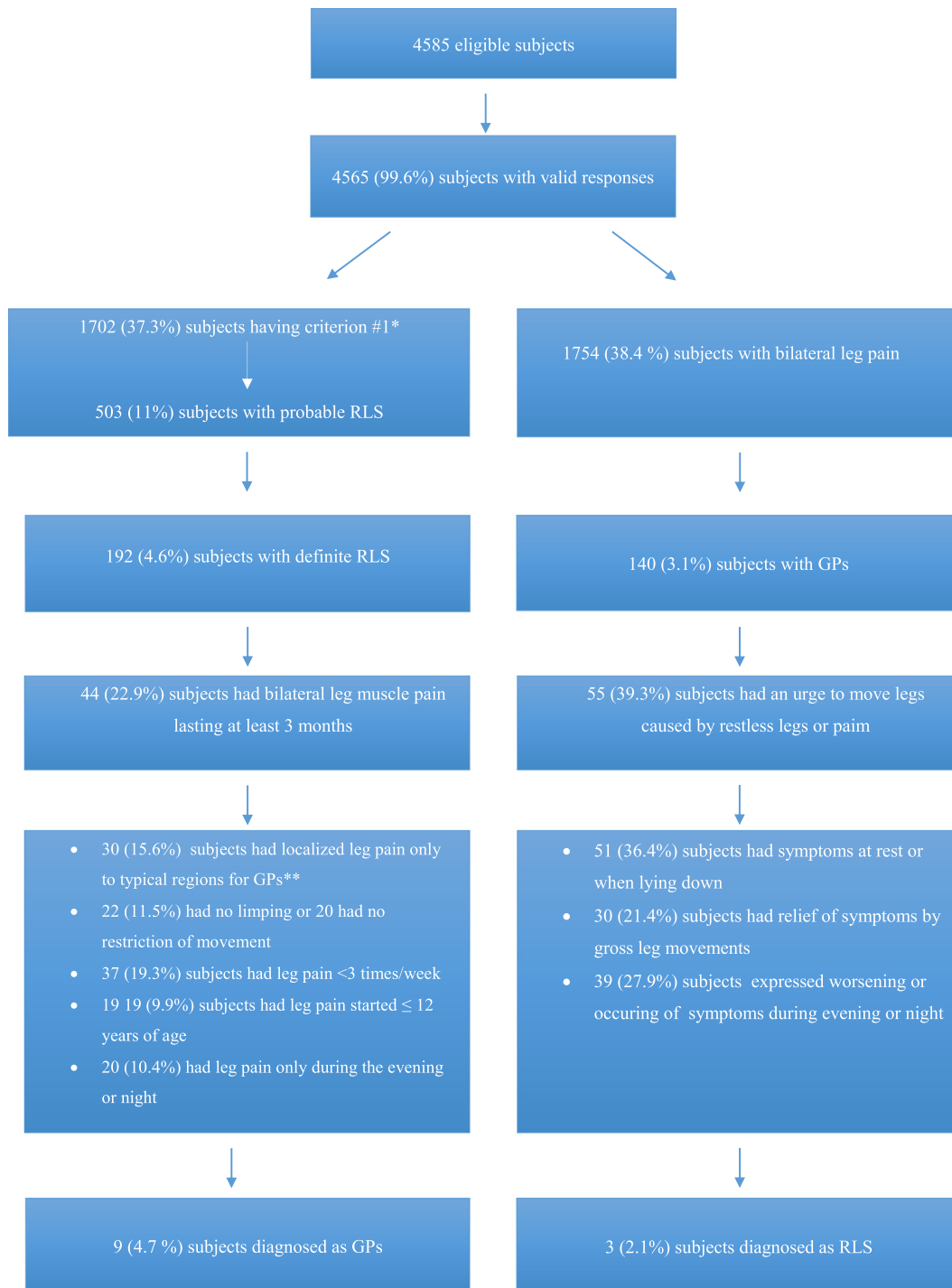


Fig. 1. Flowchart of diagnostic procedures of restless legs syndrome, growing pains, and overlapping symptoms. *Pediatric restless legs syndrome diagnostic criteria of International Restless Leg Study group (2013) [17]. **anterior thigh, popliteal fossa or calf.

Table 2
Distribution of rate of prevalence (in parenthesis) of restless legs syndrome based on age and gender.

Age	Male (%)	Female (%)	Total (%)
9	1 (0.02)	4 (0.08)	5(0.10)
10	5 (0.10)	7 (0.14)	12(0.24)
11	4 (0.08)	5 (0.10)	9(0.18)
12	1(0.02)	7(0.14)	8(0.16)
13	6(0.12)	11(0.22)	17(0.34)
14	11(0.22)	5(0.10)	16(0.32)
15	11(0.22)	31(0.62)	42 (0.84)
16	19(0.38)	35(0.70)	54 (1.08)
17	7(0.14)	19(0.38)	26 (0.52)
18	1(0.02)	2(0.04)	3 (0.06)
Total	66 (1.4)	126 (2.8)	192 (4.2)

of the prevalence rate in females did not change by age (Table 2).

The frequency of symptoms in children with RLS was reported as 1 or more times per year, but less than 1 per month (12.2%), 1–3 times per months (27.1%), 1–2 times per week (25.3%), 3–5 times per week (14.1%), and at least 1 per day (21.3%) ($p > 0.05$). Duration of RLS symptoms were longer than 3 months in 155 (80.7%) of patients. Sixty-five patients (34.2%) have been treated for iron deficiency anemia.

Family history for RLS was positive in 14.5% children. Only one member of each family had positive history for RLS. Medical reference rate was 21.1%.

3.2. Diagnosis of GPs

GPs were diagnosed in 140 (mean age: 12.6 ± 2.2 ; ranged 9–18, 64.3% female) of 1754 (%38,4) patients with bilateral leg pains (Fig. 1). The yearly prevalence of GPs was 3.1% (3.5% in females, 2.5% in males; $p = 0.049$). The female: male ratio was 1.8:1. The yearly prevalence rate of GPs in 1140 children aged 9–12 years was 5.9% (6.9% in females and 4.1% in males, $p > 0.05$) (Table 3). The yearly prevalence rate of GPs in 3425 adolescents aged 13–18 years was 2.1% (2.4% in females and 1.8% in males, $p > 0.05$).

Table 3
Distribution of prevalence (in parenthesis) of growing pains based on age and gender.

Age	Male (%)	Female (%)	Total (%)
9	4 (0.08)	7 (0.14)	11(0.22)
10	6 (0.12)	12 (0.24)	18(0.36)
11	6 (0.12)	11 (0.22)	17(0.34)
12	7 (0.14)	14 (0.28)	21(0.42)
13	10 (0.20)	15 (0.30)	25(0.50)
14	8 (0.16)	11 (0.22)	19(0.38)
15	5 (0.10)	7(0.14)	12(0.24)
16	1 (0.02)	8(0.16)	9(0.18)
17	3 (0.06)	4(0.08)	7(0.14)
18	–	1(0.02)	1(0.02)
Total	50 (1.1)	90 (1.97)	140 (3.1)

Localization of leg pain was popliteal fossa in 39.6% children, anterior thigh in 15.1%, and shine or calf in 41.7%. Leg pains occurred during movement (63.6%), while sitting (57.9%) or lying down (52.1%). Eighty-five (60.7%) of GPs patients stated occurrence or worsening of leg pains or discomforts only in the evening or at night. In addition, 10% of children experienced leg pain in the morning and 25.7% at noon. Prolonged leg pains from night to the following morning were reported in %0.7 of children.

Resolution of pain in %61.4 children was attained by applying pressure to the legs or rubbing the legs as counter-stimuli. Medications relieved leg pain in 38.6% children, whereas 11.4% children never used medications. Medical assistance was sought in only 25% children and diagnosis of GPs was confirmed in all of them, based on clinical and laboratory examinations.

Family history of GPs was positive in 44.2% children. Only one member of each family had a history for GPs.

3.3. Classification of overlapping features

Overlapping features of GPs and RLS in children with RLS and GPs, respectively were given in Fig. 1. Only 12 patients (9 with definite RLS and 3 with GPs) (0.03% of total cohort) were eligible for overlapping diagnosis of GPs and RLS.

4. Discussion

RLS and GPs are not uncommon clinical phenotypes in childhood and adolescence. IRLSSG defined essential criteria for diagnosis of pediatric RLS in 2003 [16] and revised them in 2013 [17]. However, standardized and unified diagnostic criteria for GPs are yet to be determined. Walters et al [8] combined two sets of the criteria, including similar and different features, proposed by Evans and Scutter [4,15,16] and by Champion et al. [11]. They assumed that these combined criteria would be more useful for classifying GPs and differentiating GPs from RLS, in comparison to previous classification systems. To our knowledge, our study is the first epidemiological survey of school children and adolescents aiming to find prevalence of both RLS diagnosis based on revised IRLSSG 2013 criteria and GPs diagnosis based on combined diagnostic criteria, as well as the first epidemiological survey to search for overlapping symptoms of these two conditions.

RLS and GPs seem to be different clinical entities based on age distribution, natural history and etiopathogenesis. While prevalence of RLS demonstrates a significant increase with age during childhood and adolescence [1,2] and slowly progresses throughout adulthood [18], GPs are mainly seen in preschool children (37% of all cases) [4] and progressively decreases throughout childhood and adolescence [5,6,19,20]. The

present study confirmed this epidemiological data, as the yearly prevalence rate of GPs in 8–12-year-old children declined prominently compared to that in 13–18-year-old adolescents (5.9% versus 2.1%). Previous pediatric clinical and epidemiological studies estimated the prevalence of GPs in a wide range of 2.6–49.4% [1,4,6,19–21]. Various methodological issues, such as retrospective design causing recall bias, disparity of sample size or age ranges, and lack of standardized criteria for diagnosis of GPs were considered to be responsible for this variance [7,8]. The low prevalence rate (3.1%) of GPs in our population may be related to the age distribution of our sample, which mainly included adolescents (mean age = 14 years) and excluded preschool children who were expected to be in the most prevalent age period of GPs [4].

Possible pathogenesis underlying RLS and GPs is distinct. Several hypotheses proposed for the mechanisms of GPs as local overuse, low pain threshold, changes in vascular perfusion in painful regions or decreased local bone strength have been suggested so far [22,23], but no study has clearly delineated significant effects in the pathogenesis.

Iron and dopaminergic therapy alleviate symptoms of RLS. Reduction of brain iron levels especially in the most severe RLS patients has been actually implicated in the pathophysiology of RLS. Lack of iron regulatory protein activity in the microvasculature has been suggested as the cause of dysregulation of iron transport across the blood–brain barrier and thus leads to insufficient iron storage in endothelial cells and distribution of iron to brain structures [24]. Dopaminergic abnormalities seen in RLS has also been causally linked to low levels of iron in brain [25].

The yearly prevalence of definite RLS in our 9–12-year-old children (0.68%) is less than that reported (1.7%) for 10–12-year-old children in our previous study [2], whereas the prevalence in adolescence (3.2% for 13–19-year-old adolescents) and distribution of prevalence based on age was similar. Epidemiological studies from different continents reported 1.9–3.6% prevalence rate of RLS in similar age groups [1,2,26]. The presence of female predominance for the prevalence of RLS in children and adolescents is compatible with our previous epidemiological data [2], although lack of gender difference was also reported [1]. We also found a slight female preponderance of GPs, as reported in some previous studies [20,21].

The present study demonstrated that overlapping features of RLS or GPs are prevalent, mainly in patients with GPs. On the other hand, only a small number of patients with overlapping features fulfilled all the diagnostic criteria of both RLS and GPs. A previous epidemiological study with a large pediatric cohort demonstrated that GPs had a very low positive predictive value for diagnosis of RLS [1,27]. Retrospective

studies showed that childhood GPs were not significantly related to RLS [13] or misdiagnosis of RLS, which was reported in adults with RLS [14]. All these issues cast doubt on the presence of a combined phenotype of RLS and GPs.

Contradictory data are also present. Our previous epidemiological study comprising of similar age and number of Turkish children, demonstrated GPs in 54.5% of RLS cases [2] in accordance with a clinical study (55.5%) [28]. Similarly, GPs were significantly more frequent in children with RLS (80.6%), compared to control children (63.2%) [1]. Numerous factors, such as whether the design of the study assesses current or retrospective data, variations in selected diagnostic criteria, number of participants in study group or methods for collection of data may be related to this discrepancy [8,29,30].

As the most common overlapping clinical feature, muscle pain of bilateral legs- as stated by 23% of our RLS patients- is commonly reported in previous studies. Almost half of the total population with RLS experienced unilateral or bilateral leg pain [1,2,9,31]. RLS sensations localized to lower extremity and mainly to thighs (73%) or knees (68%) [32]. In a similar ratio (68.2%) of our RLS patients with bilateral leg pain, symptoms were restricted only to typical regions defined for diagnosis of GPs.

The occurrence or worsening of leg discomfort at night is a primary criterion for diagnosis of RLS [17] and has been included in both previous sets of diagnostic criteria of GPs [4,11] and proposed combined criteria [8]. However, it is uncertain if symptoms of GPs are worse at night as the patients are lying down [8]. Previous studies reported nocturnal occurrence or worsening of GPs in a wide range of children (25–89%) [5,19–21,33]. In addition to nocturnal occurrence or worsening of leg pain, one-third of our patients with GPs expressed day time symptoms or pain from night to the following morning. Bilateral GPs have been reported in some children with leg pain solely in the daytime [20,21]. On the other hand, all diagnostic criteria of GPs suggested that pain is “not a problem in the morning“ [8] or “gone in the morning“ [4,15]. The schedule of leg pain should be re-assessed in further clinical studies with larger study groups.

The age of onset before 13 years of age, an essential feature of GPs, was reported in only one-third of RLS patients with bilateral leg muscle pain localized to typical body regions for GPs. Recall bias could have negative affect for precise estimation.

The most prevalent overlapping symptom in patients with GPs was an urge to move legs to relieve unpleasant sensations or pain which frequently occurred at rest or when lying down. Relief of symptoms by gross movements such as stretching or walking around was the other common overlapping symptom. Typically, chil-

dren with GPs relieved pain by applying pressure to legs or by rubbing legs rather than standing up or walking around [19,20,33]. RLS patients also expressed rubbing their legs [31], although relief of restless symptoms by walking or stretching is a diagnostic criterion for RLS. Our study supports that relief by gross activity of legs is an overlapping feature of RLS and GPs and seems to be a questionable differential diagnostic feature of GPs.

RLS and GPs are chronic conditions. Over 80% of our patients, including a wide age range of pediatric RLS population, had a disease history of minimum three months. Although a minimal duration of three months of disease is a prerequisite for the diagnosis of GPs, it has seldomly been studied in pediatric RLS population.

Intermittent nature of symptoms was included as an essential diagnostic criterion of GPs [8]. However, the definition of “intermittent” was not clearly given, but rather described as “. . . some pain-free days and nights”. “Chronic-persistent RLS”, described for adults as the presence of symptoms occurring on average at least twice weekly for the past year, has not been accepted as the best determinant for pediatric population due to insufficient data [17]. About 60% of our RLS population described frequency of symptoms at least once per week and two-thirds reported frequency of symptoms as less than 3 per week which are compatible findings with previous epidemiological studies [1,2] and were often reported during early periods of RLS [14].

The diagnosis of GPs and RLS is based on clinical criteria and mainly exclusion, rather than inclusion. Laboratory evaluations are generally not necessary for diagnosis [7,34], except low levels of ferritin or vitamin D which have been associated with increased severity of RLS and GPs, respectively [25,35]. It is challenging to detect secondary causes in relation to restless leg or recurrent limb pain in epidemiological surveys, especially in pediatric populations [17]. In an adult epidemiological survey, inclusion of a few questions to identify “RLS mimics” reduced false positive responses [36]. The present study aimed to examine secondary causes of leg pain or restless leg through a parental survey inquiring a history of associated clinical findings and also laboratory assessments, if present. We considered that the standardized questionnaires for epidemiological surveys would provide more precise data on prevalence of GPs and RLS and on clinical phenotypes.

A wide range of positive family history of GPs and RLS has been reported in several studies [1,2,4,10,11]. The rate of family history of GPs in our children with GPs and the RLS family history in our RLS children, was similar to the findings of previous epidemiological [2,21] and clinical data [5,10]. A twin family study of GPs confirmed the role of heredity for GPs and reported

GPs in 47% of their parents, close to the ratio found in our study [11].

Medical assistance was sought in a limited number of GPs patients and particularly in RLS patients. Low-ratio awareness or lack of interest of parents in their children’s restless leg or pain may be related to limited symptoms of RLS in pediatric age or difficulties in expression of symptoms, mainly in young children.

Despite the increasing number of epidemiological studies coming from different continents, lack of the gold standard for case definition of RLS and GPs remains an important issue for researchers and contributes to the wide variations in the reported prevalence of RLS and GPs. In the large-scale population-based studies, case classification based on standardized questions, culturally adapted to native language has been suggested as critical, since a physician-based interview and examination is usually impossible to obtain due to high resource needs [4,37]. Our RLS cases were diagnosed based on the previously validated questionnaire for Turkish children, confirmed by expert interview and the results of two studies were comparable. Likewise, using a standardized and identical assessment method within the same country, different population studies elicited quiet similar results [36]. The other unclear/obscure methodological problems in the field of RLS or GPs epidemiology is if assessments based on self-report questionnaires versus face-to-face interviews versus telephone interviews yield different prevalences [4,37]. In our study, which has a large sample and a high response rate, the selection of RLS or GPs cases was based on not only self-reported data, but also on confirmative self and parental statements to exclude “RLS mimics” or secondary causes of leg pain. Parental reports were used to verify RLS and GPs diagnosis in children aged ≤ 11 years considering possible difficulties in expression of cardinal symptoms.

We concluded that a combined phenotype is very rare, although a considerable number of patients with RLS and GPs share some clinical features.

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Disclosure Statement

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