ORIGINAL ARTICLE

Prevalence and impact of restless legs syndrome in pregnancy

Michal Minár [1], Hana Habánová [2], Igor Rusňák [2], Karol Planck [2], Peter Valkovič [1,3]

1 2nd Department of Neurology, Faculty of Medicine, Comenius University and University Hospital Bratislava, Bratislava, Slovak Republic
2 1st Department of Gynecology and Obstetrics, Faculty of Medicine, Slovak Medical University and University Hospital Bratislava, Bratislava, Slovak Republic
3 Institute of Normal and Pathological Physiology, Slovak Academy of Sciences, Bratislava, Slovak Republic

Correspondence to: Peter Valkovič, MD., PhD.
2nd Department of Neurology, Faculty of Medicine, Comenius University
Limbová 5, 83305 Bratislava, Slovak Republic.
TEL: +421-2-5954-2392; FAX: +421-2-5954-2698; E-MAIL: peter.valkovic@gmail.com

Abstract

BACKGROUND: Restless legs syndrome (RLS) is a frequent neurological disorder which predominantly affects women. Pregnancy is one of the most common conditions leading to secondary RLS. Severe symptoms of RLS may lead to complications of pregnancy and/or labor. The aim of this study was to determine the prevalence and characteristics of RLS in pregnant women.
METHODS: Women in the third trimester of gravidity filled out a simple questionnaire based on the official diagnostic criteria for RLS. Positive responders were interviewed in order to further characterize their symptoms. Afterwards information on changes in frequency and/or intensity of the symptoms after delivery was obtained by a telephone follow-up. All data were statistically analysed.
RESULTS: A total of 300 questionnaires were completed. All 94 RLS-positives met the four diagnostic criteria (31.33%). There was no difference in age, body mass index, or the number of previous pregnancies between RLS-positives and RLS-negatives, but weight gain during pregnancy was significantly higher in RLS-positives. More than 30% of positives had clinically significant symptoms, and 50% reported sleep disturbances. Almost 75% of the cases of RLS were secondary, i.e., symptoms occurred only during pregnancy (with a peak in the third trimester). More complications of pregnancy or labor occurred in women with RLS, but this was only marginally significant.
CONCLUSIONS: Our study confirmed the relatively high prevalence of RLS in pregnant women compared with the general population. Although almost three-fourths of the symptoms were only transient throughout pregnancy, the impact of the severe symptoms and sleep deprivation on the course of pregnancy and delivery was not negligible. Early detection and adequate treatment of severe RLS are necessary to prevent maternal discomfort and possible health risks. The questionnaire method is a simple, reliable diagnostic tool.

INTRODUCTION

The link between restless legs syndrome (RLS) and pregnancy was first described by Karl Ekbom (Ekbom 1945) in the middle of the last century. More recently one extensive French study reported that nearly three-fourths of pregnant women have some type of sleep disorder; RLS and/or periodic limb movements in sleep (PLMS) account for one fourth of these (Neau *et al.* 2010b). Sleep disturbances increase the risk of complications for both mother and child. Moreover, the presence of transient RLS during pregnancy is a significant risk factor for a new transient RLS in a subsequent pregnancy, and even for the development of a future idiopathic RLS."(Cesnik *et al.* 2010).

The appearance or worsening of pre-existing RLS occurs mainly in the third trimester of pregnancy (Manconi *et al.* 2004a; Neau *et al.* 2010a). This suggests that one or more risk factors associated with pregnancy – hormonal, metabolic (mainly iron deprivation) and psycho-behavioral changes – contribute to the development (worsening) of symptoms in predisposed women. Although RLS is a relatively frequent neurological disorder, it remains markedly under-diagnosed or misdiagnosed. Its diagnosis is simple and treatment is effective. It is necessary to detect it early in order to reduce deterioration of the quality of life. To draw more attention to this condition, we determined the prevalence and characteristics of RLS in pregnant women.

SUBJECTS AND METHODS

Subjects

The sample was comprised of 300 consecutive women in the third trimester of pregnancy, older than 18 years, who had been admitted to the 1st Department of Gynecology and Obstetrics, Medical Faculty of the Slovak Medical University and University Hospital in Bratislava for delivery. Data were collected from September 2011 to November 2012.

Tab. 1. Restless legs syndrome – essential diagnostic questions.

1.	Do you have, or have you ever had unpleasant or uncomfortable feelings in the legs or pain that occurs / occurred mainly while sitting or lying down?
2.	Do you feel, or have you ever felt the need or urge to move the legs, which occurs / occurred mainly when sitting or lying down?
3.	Does/did active movement lead to the disappearance or alleviation of these annoying feelings of pain or the urge to move?
4.	Are / were these annoying and uncomfortable feelings in the legs, or the urge to move, worse in the evening or at night, compared to the early morning?

Data collection

The questionnaire was based on the official diagnostic criteria of the International Restless Legs Study Group (IRLSSG). The Slovak version had been used earlier in an extensive study on outpatients of the Neurology Department (Valkovič *et al.* 2009). The four essential diagnostic questions are shown in Table 1.

The questionnaire was slightly modified for the examination of the pregnant population.

After signing an informed consent, patients completed the first part of questionnaire, which focused on the identification and collection of demographic data – name, age, previous pregnancy, anthropometric data, information about chronic diseases, regular medication and supplementation of iron and folic acid during pregnancy.

Responders who did not meet the diagnostic criteria were considered negative for RLS (RLS–). Women who affirmatively responded to all four questions were interviewed by a physician who confirmed the diagnosis of RLS – positive for RLS (RLS +). Disorders mimicking RLS – e.g., peripheral neuropathy, lower limb ischemic disease, peripheral vascular disease, night cramps, positional discomfort, hypnagogic myoclonus – were all excluded by skilled neurologist. The second part of the questionnaire was focused on the characteristics of RLS, e.g., description of sensory sensations, intensity, frequency and time of symptom onset, impact on sleep, occurrence before pregnancy and history of RLS in the relatives. A substantial part of the responders answered the questions of the validated International Restless Legs Syndrome Scale (IRLSS; Walters *et al.* 2003; © IRLS Study Group 2001. All rights reserved).

Telephone follow-up

Responders with RLS were asked about changes in frequency and/or intensity of their symptoms at least 4 months after delivery.

Statistical analysis

The data were analyzed with the IBM SPSS Statistics 20 software. Descriptive statistics were used to evaluate demographic and clinical ordinal data. In order to compare the two groups (RLS+ versus RLS–), individual variables were first tested with the Lilliefors test (modification of the Kolmogorov-Smirnov test). If the data distribution was normal, the variables were compared between the two groups using Student's t-test (level of significance $\alpha \leq 5\%$; $p \leq 0.05$). For correlation statistics, Pearson´s correlation coefficient was used for parametric data, ($p \leq 0.01$), and a Spearman correlation coefficient for non-parametric variables ($p \leq 0.01$).

RESULTS

A total of 300 questionnaires were collected. The demographic data of the entire study population are given in Table 2. RLS symptoms were reported to occur at a

certain frequency and intensity during pregnancy by 94 responders (31.33%). A comparison of selected parameters between the RLS+ and RLS– (Table 2) groups did not reveal a significant difference in age, number of previous pregnancies or in the body mass index. Weight gain during pregnancy, however, was significantly higher in the RLS+ group ($p \leq 0.001$).

The difference in the length of gestation was marginally significant ($p=0.06$): RLS+ women delivered almost 1 week later than RLS–. The children of the RLS+ had lower birth weight, but this was not significant ($p=0.19$).

There were more high-risk pregnancies in the RLS+ group (29.79% vs.21.84%), but this was not significant. A comparison of the different risks revealed that more serious complications – threatened spontaneous abortion, threatened spontaneous preterm labor, and intrauterine growth retardation of the fetus – occur in women with RLS.

The most prevalent, sensitive symptoms described by responders as dominant are given in Table 4. The intensity of symptoms, graded on a visual analog scale from 0 to 10 (0 – no symptoms, 10 – the most intense imaginable sensation), is shown in Figure 1. Figure 2 shows the time of symptom onset (during day). The frequency of RLS symptoms is given as the number of days with symptoms per month in Figure 3.

Symptoms of RLS started in the third trimester in 71% of responders with RLS, in 23% during the second trimester, and the remaining 6% had symptoms in early pregnancy.

Half of the responders with RLS had sleep disturbances associated with the symptoms of RLS. The deterioration of sleep quality depended only on the intensity and frequency of the symptoms.

Of all 94 RLS+ responders, 63 (n=67%) were tested on the International Restless Legs Scale (IRLS). The total symptom severity score in the last week was on the average 9.61±8.84 (out of the maximum possible score of 40). All of the categories are shown in Figure 4.

Types of RLS

Sixteen of 94 RLS-positives had symptoms before the actual pregnancy; one RLS+ reported symptoms during the previous pregnancy. Thus, almost 16% of RLS-positives had had symptoms when not pregnant and therefore were assumed to have idiopathic RLS. Almost 50% of these women had a positive family history.

In 5%, the symptoms started in pregnancy and persisted after labor (results from telephone follow-up) – they probably had idiopathic RLS, which was induced by pregnancy. Family history was positive in only one case. The proportion of different types of RLS in our sample is shown in Figure 5.

As regards postpartum changes in the severity of symptoms, 68.75% reported improvement (decrease in IRLS score), 25% the same intensity of the symptoms, and only one responder reported worsening.

Tab. 2. Basic demographic and clinical data (N=300).

Age (years)	30.81 ± 4.60
Body mass index (kg/m²)	27.30 ± 4.20
Weight gain (kg)	13.75 ± 5.25
Order of pregnancy	1.66 ± 0.91
Duration of pregnancy (weeks)	38.99 ± 3.08
Birth weight of newborn (g)	3328.75 ± 532.10

Tab. 3. Comparison of selected demographic and clinical parameters in RLS–positives and –negatives.

Parameter	group	mean	SD	SE	*p*–value
Age (years)	RLS+	30.84	4.65	0.48	0.94
	RLS–	30.80	4.59	0.32	
Body mass index (kg/m²)	RLS+	27.23	3.94	0.41	0.89
	RLS–	27.31	4.36	0.30	
Pregnancy duration (weeks)	RLS+	39.49	2.61	0.27	0.06
	RLS–	38.77	3.26	0.23	
Number of pregnancies	RLS+	1.68	1.02	0.11	0.63
	RLS–	1.82	2.74	0.19	
Birth weight of newborn (g)	RLS+	3269.35	575.49	59.68	0.19
	RLS–	3355.41	509.07	35.56	
Weight gain (kg)	RLS+	15.76	5.55	0.58	**<0.001**
	RLS–	12.86	4.86	0.34	

SD – standard deviation, SE – standard error of the mean; significant result is in bold

Tab. 4. Description and prevalence of perceived dominant sensations.

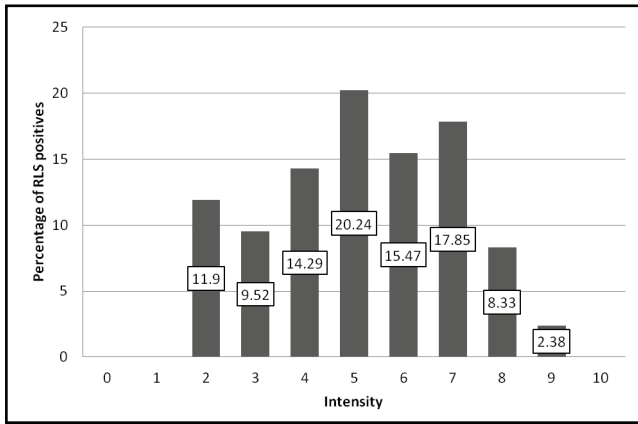| Sensation description	N	%
Nervousness	23	23.96
Pins and needles	11	11.04
Urge to move	11	11.04
Don´t know	9	9.38
Tingling	8	8.33
Restlessness	6	6.25
Cramps	6	6.25
Tearing of muscles	5	5.21
Tension	5	5.21
Numbness	3	3.2
Muscle contraction	2	2.08
Energy flow	1	1.04
Pain	1	1.04
Heavy legs	1	1.04
Pressure in veins	1	1.04
Burning	1	1.04
Bone growth	1	1.04

Fig. 1. Average intensity of RLS symptoms on visual analogue scale (0 – means no symptoms; 10 – the most intense imaginable sensation), N = 94.
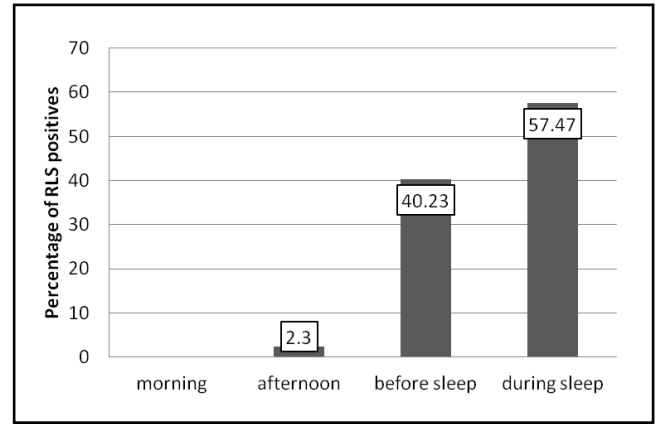

Fig. 2. Time of highest occurrence of RLS symptoms during the day (N = 94).
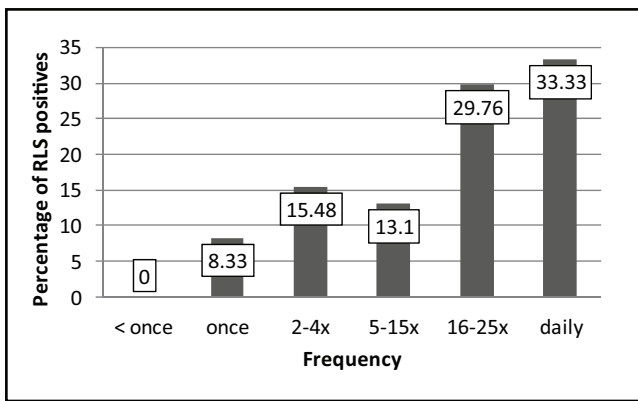

Fig. 3. Frequency of RLS symptoms given as number of days with symptoms per month (N = 94).
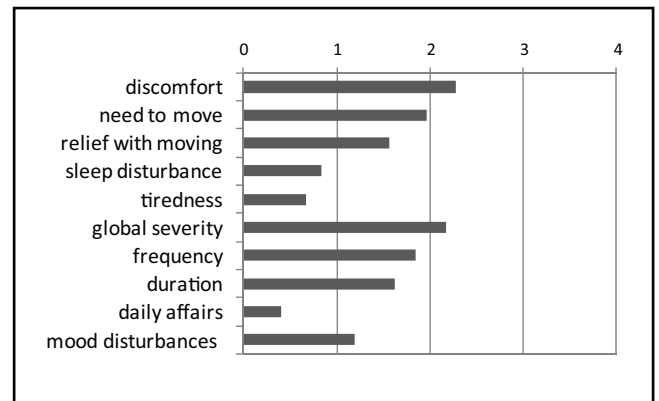

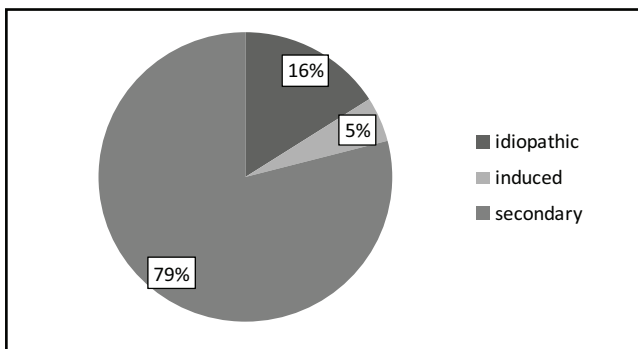**Fig. 4.** The average score of each IRLS category.

Fig. 5. The different types of RLS during pregnancy.

DISCUSSION

Our findings confirmed that the prevalence of RLS is higher in pregnant women than in the general population (7.2% according to published data) even compared with non-pregnant women in whom the prevalence of RLS is approximately twofold that in men of the same age (Allen *et al.* 2005).

The prevalence was almost 32%, which is consistent with the results of extensive epidemiological studies (e.g., 26% in Italy and 32% in France). The occurrence of RLS among the pregnant is independent of age – as in the general population (Montplaisir *et al.* 2006; Walters *et al.* 1996) – the number of previous pregnancies (Berger *et al.* 2004), or the body mass index (Gao *et al.* 2009). However, our study revealed an association between the presence of RLS and weight gain during pregnancy, a finding that stresses the role of "body mass" in the pathophysiology of RLS.

Nearly three-fourths of responders with RLS had symptoms only during pregnancy, and these culminated in the third trimester; they thus had secondary RLS. Approximately 15% had primary RLS (almost half of them had a positive family history), and the remaining had previously had "clinically silent" idiopathic RLS that was induced by pregnancy.

Most of RLS+ responders did not attribute their unpleasant sensations to neurological conditions. Some had never even heard of "Restless legs syndrome". They connected the symptoms with typical signs of a pregnancy, e.g., muscle cramps, swelling of the calves, and positional discomfort. Bizarre sensations were hardly

ever reported to their physician, who also rarely asked their patients about symptoms of RLS. This indicates that the level of awareness of RLS is quite low among patients and doctors as well.

More than 30% of RLS-positive women had clinically significant symptoms with moderate to severe intensity at least twice a week. They thus fulfilled the criteria for "RLS sufferers" according to IRLSSG (Tan & Ondo 2000). Symptoms occurred only at bedtime and during the night in almost 98%, and 50% of RLS+ responders reported having sleep disturbances, that correlated with excessive daytime fatigue, as well as with the negative impact on the activities of daily living (ADL) and mood. Moreover, in addition to its negative effects on the quality of life of pregnant women, we also observed that RLS could have an impact on the course of pregnancy and fetal development. Pregnant RLS positives had a tendency to have more serious complications during pregnancy (threatened abortion, threat of premature labor and intrauterine growth retardation). We also observed a trend for their newborns to have a lower birth weight although they had longer gestations.

The presence of RLS symptoms during pregnancy increases the risk of idiopathic forms. Severe and untreated syndromes negatively affect not only the quality of the patient's life, e.g., insomnia, excessive daytime fatigue, impaired concentration and mood, avoidance of activities that require restriction in movements, but they also have an adverse effect on the overall morbidity of the population (increased incidence of anxiety and depression, cardiovascular disease, and strokes). This is associated with negative socio-economic consequences. All these facts stress the importance of detecting RLS early in this susceptible population, and if necessary, promptly initializing adequate treatment.

Treatment of RLS during pregnancy

The therapeutic options for treating RLS symptoms are restricted in pregnant women. Since RLS associated with pregnancy is usually transient and has a mild intensity, it is not always necessary to use medication (Manconi *et al.* 2004b; Manconi & Ferini-Strambi 2004). Iron and vitamin B deficiency must first be ruled out, and sufficient supplementation provided if needed. Intravenous magnesium has also been reported to be effective (Bartell & Zallek 2006). If necessary, drugs with better safety profiles can be used at the lowest effective dose – anticonvulsants (gabapentin, carbamazepine) or some benzodiazepines (e.g., clonazepam). Although dopaminergic drugs have been approved as a first-line treatment for daily RLS symptoms, there is little information about their teratogenic potential. A prospective study based on the analysis of individual cases of severe RLS in pregnant women treated with these compounds did not observe a higher risk for major malformations or other adverse events (Dostal *et al.* 2012). Therefore, low doses of levodopa or dopamine agonist could be used in cases of very severe symptoms.

CONCLUSIONS

Our work confirmed the relatively high prevalence of RLS in pregnant women in the third trimester. Nevertheless, the awareness of the possibility of RLS in these women is extremely low, in both the general public and the medical community. Our results prove that the symptoms of RLS not only worsen the quality of life, but might increase the incidence of complications during pregnancy and labor.

Adequately chosen and timely commenced therapy (e.g., sufficient iron supplementation) may prevent discomfort, sleep disturbances, mood swings, excessive fatigue, and the above-mentioned complications.

Our findings support and stress the efficacy of using a simple questionnaire as a diagnostic tool for the early identification of patients with RLS.

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