



Restless leg syndrome in pregnancy

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Abstract

Objective: Pregnancy is considered as a risk factor of onset and progression of restless leg syndrome. The purpose of this study was to evaluate the etiology of restless leg syndrome (RLS) in pregnant women.

Methods: Five hundred pregnant women who applied to a university hospital obstetrics clinic were received to this study. A questionnaire evaluating demographic and pregnancy characteristics, and RLS symptoms was conducted. Pregnant women were divided into two groups, as with and without RLS. Age, gravidity, parity, body mass index, gestational age, hemoglobin value, biochemical parameters such as thyroid stimulating hormone (TSH), creatinine and aspartate aminotransferase / alanine aminotransferase (AST/ALT) values were compared between pregnant women with and without RLS.

Results: The incidence of RLS in pregnancy was found 15.4%. The mean age of pregnant women with and without RLS was 27.5±6.6 and 26.9±5.7, respectively, and there was no significance difference between two groups (p>0.05). There was no significant difference in number of number of pregnancy, delivery and abortion between two groups (p>0.05). Gestational age, weight and body mass index were significantly higher in pregnant with RLS (p=0.005). The rate of iron supplementation was higher in pregnant with RLS (p=0.009), but hemoglobin and hematocrit values were not different between two groups (p>0.05). TSH, thyroxine, creatinine and AST/ALT values were found to be similar in both groups. The incidence rate of RLS were found as 9.7%, 14.5% and 19.5%, respectively according to the trimesters.

Conclusion: The rate of restless leg syndrome was found higher in pregnant women with advanced gestational weeks and high body mass index. Pregnant with high body mass index, and advanced gestational weeks should be evaluated for RLS symptoms.

Key words: Pregnancy, restless leg syndrome, etiology.

Gebelikte huzursuz bacak sendromu

Amaç: Gebelik, huzursuz bacak sendromunun oluşumu ve gelişimi açısından bir risk faktörü olarak bilinmektedir. Bu çalışmanın amacı gebelikte huzursuz bacak sendromu (HBS) sıklığının ve ilişkili olabilecek demografik parametrelerin araştırılmasıdır.

Yöntem: Üniversite hastanesi Kadın Hastalıkları ve Doğum polikliniğine başvuran gebelerden çalışmaya katılmayı kabul eden 500 olgu araştırmamıza dâhil edildi. Tüm gebelere demografik ve gebelik özelliklerini, HBS semptomlarını değerlendiren anket formu dolduruldu. Gebeler HBS olan ve olmayan olmak üzere iki gruba ayrıldı. Yaş, gebelik ve doğum sayısı, vücut kitle indeksi, gebelik haftası, hemoglobin değeri, tiroid stimulan hormon (TSH), kreatinin, aspartat aminotransferaz / alanin aminotransferaz (AST/ALT) gibi biyokimyasal parametreler HBS olan ve olmayan gebelerde karşılaştırıldı.

Bulgular: Gebelikte HBS sıklığı %15.4 olarak bulundu. Huzursuz bacak sendromu olan ve olmayan gebelerin yaş ortalaması sırasıyla 27.5±6.6 ve 26.9±5.7 olup aralarında istatistiksel olarak anlamlı fark saptanmadı (p>0.05). İki grup arasında gebelik, doğum ve düşük sayıları açısından anlamlı fark saptanmazken gebelik haftası, kilo ve vücut kitle indeksi HBS olan gebelerde anlamlı olarak daha yüksek tespit edildi (p<0.05). Huzursuz bacak sendromu olan gebelerde demir replasmanı alma oranı anlamlı olarak daha yüksek saptandı (p=0.009). Fakat hemoglobin ve hematokrit değerlerinde iki grup arasında fark saptanmadı (p>0.05). TSH, tiroksin, kreatinin ve AST/ALT değerleri her iki grupta da benzerdi. Huzursuz bacak sendromu sıklığı trimesterlere göre sırasıyla %9.7, %14.5 ve %19.5 olarak bulundu.

Sonuç: Huzursuz bacak sendromu sıklığı ileri gebelik haftası ve yüksek vücut kitle indeksi olan gebelerde daha fazla bulunmuştur. Yüksek vücut kitle indeksi ve ileri gebelik haftası olan gebeler HBS semptomları açısından değerlendirilmelidir.

Anahtar sözcükler: Gebelik, huzursuz bacak sendromu, etiyojoloji.

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Introduction

Restless leg syndrome (RLS) is a chronic progressive disorder characterized by sensory and motor symptoms and appears as an irresistible urge to move one's legs to stop uncomfortable or odd sensations.^[1] It was first described by Thomas Willis in 1685 in patients with sleeplessness and restlessness in the legs. Afterwards in 1945, Dr. Karl-Axel Ekbom used the terms "irritable legs" and "restless legs" and this syndrome was named as Ekbom syndrome.^[2] The patients have the urge of moving their legs because of paresthesia and disesthesia and express relief by moving their legs or walking. They describe odd sensations in the legs and express that they relieve moving their legs or swinging their legs down. The symptoms start with resting or at night and relieve during the day.^[3]

Although the etiopathogenesis of disease is not understood well yet, it is believed to result from central dopaminergic system dysfunction as the patients benefit from dopaminergic treatment.^[4] Pregnancy is considered as an important risk factor for appearance and/or worsening of RLS. It is thought to be a result of hormonal (prolactin, progesterone, estrogen levels), psychomotor and behavioral changes, changes in sleeping habits and folate-iron levels.^[5,6]

In this study we aimed to investigate possible factors that could induce restless leg syndrome during pregnancy.

Methods

Between January and March 2013, 500 pregnant women who admitted to the University hospital Gynecology and Obstetrics department and gave informed consent were included to the study. The questionnaire forms evaluating demographic and pregnancy characteristics and RLS symptoms were filled in with face to face interview technique. The questionnaire containing RLS diagnosis criteria consisted of 4 questions and diagnosis of RLS was established when all of the questions that were formed according to the International Restless Legs Syndrome Study Group (IRLSSG) based on patient history in 1995 were answered as 'yes'.^[7]

The questions are as follows:

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 the legs and any accompanying unpleasant sensations begin or worsen during periods of rest or inactivity such as lying down or setting
3. The urge to move the legs and any accompanying unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues
4. The urge to move the legs and any accompanying unpleasant sensations during rest or inactivity only are worse in the evening or night than during the day

Pregnant were divided into two groups as RLS and non-RLS groups. Parameters like age, number of gestation and birth, body mass index, week of gestation, hemoglobin value, thyroid stimulating hormone (TSH), creatinine and aspartate aminotransferase / alanine aminotransferase (AST/ALT) were compared between two groups.

For statistical analysis Pearson chi-square, Fisher's exact and independent two sampled t tests were used. Categorical varieties were given as numbers and percentages, means as means \pm standard deviations. Statistical significance was set as $p < 0.05$. Analyses were conducted by SPSS software (IBM SPSS Statistics 18; SPSS Inc., Chicago, IL, USA).

Results

Mean age of the pregnant was 27.0 ± 5.9 years. Mean age was 27.5 ± 6.6 for RLS and 26.9 ± 5.7 for non-RLS groups, and there was no statistical significance between two groups ($p > 0.05$). Seventy-seven pregnant women responded all the RLS diagnostic criteria questions positively and prevalence of RLS during pregnancy was found as 15.4%. Prevalence increased with the advancing trimester in these pregnant. The prevalence was 9.7%, 14.5% and 19.5% in the first, second and third trimester, respectively. Although the prevalence of RLS increased with advancing trimester, there was no statistical significance ($p = 0.744$).

There were no statistical significances between two groups based on numbers of pregnancy, birth and abortions (**Table 1**). Week of gestation, weight and BMI were significantly higher in RLS group ($p < 0.05$). Diabetes, hypertension and goiter rates were similar between two groups ($p > 0.05$). The rate of taking iron replacement was significantly higher in the RLS group

($p=0.009$), but no statistical significance was detected between hemoglobin and hematocrit values ($p>0.05$). There was no difference in terms of multivitamin use. As seen in **Table 2**, there were no significant differences between two groups based on TSH, thyroxin and AST/ALT levels ($p>0.05$).

Discussion

Restless leg syndrome which is characterized by an urge to move the legs and cause restlessness of the extremities can be seen in any age in the population but is more frequent with increasing age and pregnancy.^[8] In general population, the prevalence of RLS is reported as 10%.^[9] In epidemiologic studies, the frequency of RLS during pregnancy is reported as 11-22.5%.^[10-13] In our country, the frequency of RLS is reported as 19-26%.^[14,15] In our study, the frequency of RLS during pregnancy was found as 15.4% concordant with the present literature.

Şahin et al.^[14] found similar results between two groups based on number of age, pregnancy, birth and abortion in their study. We also did not find any significant differences between two groups based on these demographic characteristics. However, we detected increased week of gestation in pregnant with RLS. The week of gestation was 24.5±9.1 in RLS (+) and 22.1±9.9 in RLS (-) pregnant. In the studies performed up to date, the prevalence of RLS during pregnancy was found to increase in the third trimester and the symptoms worsened.^[10-12] Although not statistically significant, we found increased prevalence of pregnancy related RLS in the third trimester compared with the other two trimesters.

There is a close relation between obesity and frequency of RLS. There are studies reporting an increase in RLS prevalence with the increasing body mass index (BMI).^[16,17] This relation in pregnancy could not be well-depicted. However, in the studies investigating the relationship between RLS and pregnancy, no relation was found between RLS and body weight.^[14,18] In our study, we found increased body weight and BMI in RLS (+) pregnant.

In a lot of studies, iron deficiency is reported as an important factor in the pathogenesis of RLS. Serum ferritin level is the most important indicator of iron deficiency. A significant inverse proportion was reported between ferritin level and RLS severity, and the severity

Table 1. Comparison of demographic characteristics of pregnant women.

Characteristics	RLS (+) n=77	RLS (-) n=423	p value
Age (year)*	27.5±6.6	26.9±5.7	0.706
Gravida*	2.4±1.2	2.4±1.3	0.608
Parity*	1.0±0.9	1.1±1.1	0.785
Abortion*	0.3±0.7	0.3±0.7	0.650
Gestational week*	24.5±9.1	22.1±9.9	0.040
Weight (kg)*	71.5±13.1	66.8±12.3	0.003
Height (cm)*	161.3±5.5	161.9±29.9	0.700
BMI (kg/m2)*	27.3±5.6	25.8±4.6	0.037
Iron supplementation	53 (%68.8)	223 (%52.7)	0.009
Multivitamin supplementation	59 (%76.6)	294 (%69.5)	0.207
Diabetes	4 (%5.2)	16 (%3.8)	0.529
Hypertension	3 (%3.9)	10 (%2.4)	0.433
Thyroid dysfunction	7 (%9.1)	49 (%11.6)	0.694

*Mean±SD, BMI: body mass index, RLS: restless leg syndrome.

Table 2. Comparison of the laboratory findings of pregnant women.

Laboratory finding	RLS (+)	RLS (-)	p value
Hemoglobine (g/dl)	11.8±1.1	11.9±1.2	0.400
Hematocrite (%)	35.8±3.2	36.1±3.0	0.375
TSH (mIU/mL)	2.3±1.4	1.8±1.4	0.063
ft4 (ng/mL)	1.0±0.2	1.8±0.2	0.105
BUN (mg/dL)	7.6±2.9	8.5±3.4	0.329
Creatinine (mg/dL)	0.50±0.10	0.56±0.11	0.370
AST (IU/L)	20.5±14.6	17.0±8.3	0.621
ALT (IU/L)	14.2±5.4	16.1±13.9	0.796

AST/ALT: aspartat aminotransferase / alanine aminotransferase, BUN: blood urea nitrogen, ft4: free thyroxine, RLS: restless leg syndrome, TSH: thyroid stimulating hormone

had increased with decreasing ferritin level. Therefore, iron replacement along with the dopaminergic treatment was found to be beneficial in most of the patients.^[19,20] Tunç et al.^[15] found decreased hemoglobin levels in RLS (+) pregnant whereas there was not any difference between serum iron, ferritin and hematocrit levels in their study. Hübner et al.^[21] found similar levels of hemoglobin and serum ferritin levels in pregnant with and without RLS. We did not detect any difference between two groups in term of serum hemoglobin and hematocrit levels but there was an increased iron use in the RLS group. In the study of Chen et al.^[18] including 461 pregnant, the prevalence of RLS was found as

10.4% and the rate of folate and iron use in non-RLS group were higher than the RLS group.

On the other hand, closely related family members of the RLS diagnosed patients also had RLS and the inheritance was autosomal dominant in family-inherited RLS patients. The rate of family inheritance was 60-65%.^[22,23] Perdeci et al.^[24] stress that these patient families should be evaluated as a whole considering the high autosomal dominant inheritance.

The relief of symptoms of RLS with the dopaminergic L-DOPA (L-dihydroxyphenylalanine) use suggests a dopaminergic system dysfunction. The interaction of dopaminergic system with the thyroid is well known and thyroid function deficiency can affect RLS development.^[25] Clinical studies related to this show increased secondary hypothyroidism in females with RLS compared with controls.^[26] However, in another study, no significant difference was detected among RLS prevalence in the patients with and without a thyroid disease. So the relationship between RLS and thyroid disease is unclear.^[27] In our study we did not find difference between two groups in terms of thyroid hormone levels or a history of a thyroid disease.

Conclusion

As a conclusion, RLS during pregnancy is not a well-known and questioned condition in the gynecology and obstetrics practice and seen more frequently in advanced gestation weeks. We think that evaluation of patients in advanced gestation weeks, with increased BMI on iron treatment for RLS symptoms will be beneficial. Further studies are necessary to evaluate the etiological relationship between RLS and pregnancy.

Conflicts of Interest: No conflicts declared.

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