Background: Restless legs syndrome (RLS) is a common neurological disorder characterized by painful or disturbing sensations leading to an irresistible urge to move. Pregnancy is a risk factor for RLS. The association between RLS and pregnancy was examined in this study.

Methods: One hundred seventy-four pregnant and 30 non-pregnant healthy control females were included in the study. International RLS Study Group criteria were applied to all participants in the diagnosis of RLS. Week of gravidity, demographic and medical history were recorded. Depression, daytime sleepiness, and insomnia were also assessed.

Results: The median patient age was 27.5 in the pregnant group and 31.5 in control group. RLS was present in 35% of pregnant women and in 3% of women in the control group (p<0.001). Depression, insomnia severity, and sleep quality scores were correlated with RLS in pregnant women. Beck depression scores were significantly higher in pregnant women (9/63 - 5,5/63, p=0.008). Epworth Sleepiness Scale scores were significantly lower in pregnant patients than in the control group (median scores of 2 vs. 4.5) (p=0.002). PSQI was also significantly higher in pregnant subjects than in healthy control subjects (median score 7.1 vs. 5.3) (p=0.028). Insomnia occurred more frequently in pregnant patients (p=0.03).

Conclusion: The RLS rate in pregnant women in the current study was comparable with other findings in the literature. Despite an unclear etiopathogenesis of RLS, secondary factors may aggravate symptoms. Pregnant women who were diagnosed with RLS had prominent anxiety, sleep disorder and depression symptoms in the current study. Regression analyses demonstrated that pregnancy was not the only risk factor for RLS.

INTRODUCTION
Restless legs syndrome (RLS), or Willis-Ekbom disease, is a common neurological disorder characterized by uncomfortable and painful sensations accompanied by an irresistible urge to move to temporarily relieve the symptoms [1-3]. Symptoms primarily occur at a state of rest at night [1-3]. The pathogenesis of the disease involves disruption of dopaminergic function in the central nervous system, dysfunction of subcortical areas and abnormal metabolism of iron in the brain [3-5]. Etiologically, RLS can be classified into two groups: idiopathic or secondary [3,4]. Secondary factors that may contribute to RLS include uremia, rheumatoid arthritis, cigarette smoking, hypo or hyperthyroidism, diabetes mellitus, and acute intermittent porphyria [3,4]. The use of medications such as tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), lithium or caffeine may trigger symptoms [3,4]. Iron, folate, B12, and magnesium deficiency were also related to symptoms of RLS [6].

Pregnancy can be a risk factor for RLS. The general population exhibits an RLS prevalence of 6-15% [7]. RLS prevalence ranges between 10 and 34% in pregnant patients [8-10]. In this study, sleep disturbances, gestational age, depression scores and laboratory parameters were analyzed for possible association with RLS symptoms.

MATERIALS AND METHODS
One hundred seventy-four pregnant women and 30 healthy non-pregnant women were included in the study after signing written consent. The study design was cross-sectional. Data
from 169 patients in the pregnant group were used for statistical analyses. All patients were evaluated for the presence of RLS using the Restless Legs Syndrome Questionnaire [11,12]. Recent laboratory parameters were extracted from patient medical files. Symptoms of depression were evaluated with the Beck Depression Scale. Scores were assessed as: 0-7, no depression; 8-15, mild depression; 16-28, moderate depression; and ≥29, severe depression. Symptoms of anxiety were assessed with the Hamilton Rating Scale. The Hamilton S scale was used for the evaluation of somatic complaints, and the Hamilton P scale was used for the evaluation of psychiatric complaints. The Epworth Sleepiness Scale was used to quantify daytime sleepiness: normal range, 0-10; borderline, 10-12; abnormal, 12-24 points. Insomnia was analyzed through the use of the Insomnia Severity Index. Scoring was as follows: no clinically significant insomnia, 0-7; sub threshold insomnia, 8-14; moderate insomnia, 15-21; and severe insomnia, 22-28. Sleep quality was assessed through the use of the Pittsburgh Sleep Quality Index (PSQI), which consisted of 24 questions. Scores ranged from 0 to 21 points. An overall score of higher than five points was interpreted as having worse sleep quality. Insomnia rating scale scores, demographic data, medical history and smoking history were recorded. The present study was approved by Bursa Regional Ethics Committee. All procedures were in accordance with the Second Declaration of Helsinki.

Statistical analyses

SPSS was used for statistical analysis. Normal distribution of the data was confirmed using the Kolmogorov-Smirnov test. Continuous variables are presented as the mean±standard deviation, and categorical variables are presented as percentages. The differences between the groups for categorical variables were evaluated by the chi-square test. According to the distribution, the differences between two groups for continuous parameters were calculated by Student’s t test or the Mann-Whitney U test. For the multivariate analysis, possible factors were identified through univariate analyses.

RESULTS

One hundred sixty-nine pregnant women and 30 healthy control women were included in the study analyses. The median age was 27.5 years in the pregnant group and 31.5 years in the non-pregnant control group. The mean week of pregnancy was 28 (min: 6, max: 38 weeks). RLS diagnosis due to IRLSSG criteria was 35% in pregnant women and 3.3% in controls (p<0.001) (Table 1). The median overall Hamilton scores were 9 in pregnant women and 6 in non-pregnant controls and were not significantly different between the two groups (p=0.19). Hamilton P scores were the same in the two groups (median score: 4 vs 4) (p=0.515). Hamilton S scores were significantly higher in pregnant women than in control subjects (median score: 5 vs. 2) (p=0.009). Beck depression scores were significantly higher in pregnant women (9/63-5, 5/63, p=0.008) (Table 1). Epworth Sleepiness Scale scores were significantly lower in pregnant patients than in the control group (median scores of 2 vs. 4.5) (p=0.002). PSQI was also significantly higher in pregnant subjects than in healthy control subjects (median score 7.1 vs. 5.3) (p=0.028) (Table 1).

Insomnia occurred more frequently in pregnant patients (p=0.03). Poor sleep quality was also reported significantly more often in pregnant patients (p=0.002). Daytime sleepiness did not differ between both groups (p=0.711). No pregnant patients exhibited folate deficiency. Despite similar hemoglobin levels in both groups, pregnant subjects had anemia more frequently than control subjects (p=0.001) (Table 1).

Univariate analyses did not show any correlation between RLS diagnosis and hemoglobin levels (r=0.12; p=0.077). Scores on the following assessments exhibited a trend toward correlating with RLS diagnosis: Hamilton P scores (r=0.24; p=0.002), Hamilton total scores (r=0.35; p=0.001), Beck Depression scores (r=0.26; p=0.001), insomnia scores (r=0.26; p=0.001), Pittsburgh Sleep Quality Index (PSQI), and Pittsburgh Insomnia Rating scores (r=0.25; p=0.001). Hamilton S scores also trended toward a correlation with RLS diagnosis (r=0.41; p=0.001).

DISCUSSION

RLS prevalence was shown to be up to 15% in the normal population [7]. In a prospective study, Manconi et al. revealed the presence of RLS symptoms in 26% of pregnant women throughout their pregnancy [8]. In the same study, RLS primarily occurred in the third trimester, and patients had lower hemoglobin and mean corpuscular volume (MCV) levels despite folate and iron replacement therapy [8]. In another study consisting of 524 pregnant patients, RLS prevalence was shown to be 13.5%, and RLS symptoms were seen in the third trimester in 90% of pregnant subjects [9]. Another RLS study revealed that 34% of subjects fulfilled criteria for the diagnosis of RLS in a cohort of 521 pregnant women [13]. RLS prevalence was reported as 35% in our study, which was comparable to previously reported data. RLS prevalence during specific weeks of pregnancy was consistent with the third trimester frequency data in the literature.

Research evidence indicates that there are strong positive relationships between a healthcare team member’s communication skills and a patient’s care givers.

Table 1: Depression, insomnia, insomnia severity ratios of both groups.

<table>
<thead>
<tr>
<th></th>
<th>Pregnant (n=169)</th>
<th>Control (n=30)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>RLS presence</td>
<td>62 (35.9%)</td>
<td>1 (3%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Epworth B</td>
<td>2 (1.2%)</td>
<td>0 (0%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Insomnia</td>
<td>29 (17.8%)</td>
<td>1 (3.3%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Pittsburgh (PSQI)</td>
<td>102 (60.4%)</td>
<td>9 (30%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>11.3 (6-14)</td>
<td>12 (11-14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EPWORTH Sleepiness Scale</td>
<td>2 (0-15)</td>
<td>4.5 (0-12)</td>
<td>0.002</td>
</tr>
<tr>
<td>Hamilton P score</td>
<td>4 (0-17)</td>
<td>4 (0-13)</td>
<td>0.515</td>
</tr>
<tr>
<td>Hamilton S score</td>
<td>5 (0-28)</td>
<td>2 (0-12)</td>
<td>0.099</td>
</tr>
<tr>
<td>Hamilton Total score</td>
<td>9 (0-41)</td>
<td>6 (0-25)</td>
<td>0.19</td>
</tr>
<tr>
<td>Pittsburgh (PSQI) total score</td>
<td>7.1 ± 4.1</td>
<td>5.3 ± 3.7</td>
<td>0.028</td>
</tr>
<tr>
<td>Beck Depression Scale score</td>
<td>9(0-39)</td>
<td>5.0(0-26)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

*:* standard deviation

RLSǂ presence

‡: Restless Legs Syndrome.
chronic disease is one of the most important challenges for the health system. Management of a chronic disease such as RLS requires that patients take a more active role in their day-to-day decisions about the management of their illness [14].

Several pathophysiological mechanisms have been proposed for the increased prevalence of RLS during pregnancy, distinct from mechanisms of RLS in the general population. These mechanisms have been classified as hormonal factors, iron metabolism, folate metabolism and other mechanisms. Pregnant RLS patients have been reported to possibly exhibit higher estradiol levels in the third trimester, [13] but insufficient data exist to support this conclusion. Other studies have suggested that during pregnancy, the thyroid gland is overstimulated, and the increase of thyroid hormone levels may lead to dopamine dysregulation[15]. Increased progesterone levels were observed in the third trimester, but the influence of progesterone on RLS is not yet clear [15]. As another possible mechanism, iron or folate deficiency can decrease levels of tetrahydrobiopterin, which may contribute to decreased dopamine synthesis [15, 16]. Despite the iron deficiency or low hemoglobin levels observed in our patients, significant differences were not apparent.

Anxiety, emotional stress, tension and insomnia can provoke or worsen RLS symptoms [16]. RLS patients may experience more severe symptoms during pregnancy [16]. Sikandar et al. determined that previous RLS during pregnancy, a positive family history of RLS, and hemoglobin levels<11 were independent risk factors for the development of RLS during pregnancy [17]. Multiparity and family history were identified as predictive factors for RLS progression in the same study [17]. Our study did not evaluate parity or family history as primary risk factors. Another study reported that pregnancy induced hypertension occurred more frequently than chronic hypertension in pregnant RLS patients [18]. Sleep disorders and excess daytime sleepiness were reported to be more common in pregnant patients with RLS [18]. In our study, daytime sleepiness did not differ significantly between groups, but sleep quality and depression scores were correlated with RLS symptoms.

The current study had some limitations. The study design was cross-sectional; a prospective design could be more informative. The lack of multi-parity and family history data prevented a complete risk analysis. Large scale studies are needed to evaluate risk factors for RLS and to characterize the pathophysiological mechanisms of RLS in pregnancy.

REFERENCES