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Original Article

Risk factors and prevalence rate of restless legs syndrome among pregnant women in Taiwan

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ABSTRACT

Background: The goal of this study was to assess the prevalence and clinical correlates of restless legs syndrome (RLS) among pregnant Taiwanese women.
Methods: We enrolled 461 pregnant women (18–45 years) admitted at Mackay Memorial Hospital for delivery from September 2010 to May 2011. The face-to-face questionnaire used to gather data included assessment of RLS diagnostic criteria, and questions related to RLS.
Results: The overall prevalence rate of RLS among the study participants was 10.4%; 2.8% were categorized as having chronic RLS. Participants without RLS reported higher folate and iron supplement consumption than those with RLS. Multivariate analysis revealed significant associations of RLS with anemia and peptic ulcer disease. Participants with transient RLS during pregnancy reported more regular coffee consumption before pregnancy, and better sleep latency, duration, and efficiency, than those with chronic RLS. Overall, 81.2% of RLS sufferers reported sleep disturbances.
Conclusions: Our study revealed highly prevalent but poorly recognized RLS among Taiwanese pregnant women. The identification of predictors such as medical comorbidities, and protectors such as folate and iron supplements, is warranted for obstetric RLS. In most cases, symptoms began during the second or third trimester and resolved within a week after delivery. Restricted coffee consumption before pregnancy is encouraged, but further evidence is needed to support this recommendation.

1. Introduction

Restless legs syndrome (RLS), first given its name in 1945 by the Swedish neurologist Karl-Axel Ekbom [1], is a sleep and movement disorder characterized by unpleasant sensations in the legs occurring at rest and at night, with an irresistible urge to move. The diagnosis of RLS was upheld by the International Restless Legs Syndrome Study Group (IRLSSG), with four cardinal features based on the history of the patient [2]. It is one of the leading known causes of insomnia and common movement disorders. RLS affects 5–15% of the general population and it has an increased prevalence in older individuals [3,4]. The prevalence of RLS in Taiwanese adults was found to be 1.57%, suggesting substantially lower rates in Asian populations compared with Caucasians [5]. Collectively, findings to date offer evidence for an association between RLS and medical comorbidities such as osteoarthritis, varicose veins, type 2 diabetes, hypertension, hypothyroidism, fibromyalgia, rheumatoid arthritis, emphysema, chronic alcoholism, sleep apnea, chronic headaches, and injuries or diseases that affect the central nervous system [6]. However, the literature in this area is sparse and less consistent, so the possible relationships between these factors and RLS are not clearly defined.

The development of RLS during pregnancy has been long known; Ekbom noted in his original report that 11.3% of 486 pregnant women had RLS [7]. Thus, the prevalence of RLS among pregnant women was twice that reported by Ekbom among a sample of 230 healthy women (5.7%). Studies found that RLS prevalence rates in pregnant women are similar in Western and Eastern countries [3]. To the best of our knowledge, overall reported prevalence rates of RLS in pregnant women based on IRLSSG criteria with face-to-face interviews range from 10.5% in Turkey to 30% in Pakistan [8,9]. The main causes of association between RLS and pregnancy are not well known. Hypotheses for the higher prevalence of RLS during pregnancy involve reduced serum iron or folate levels and hormonal changes such as estrogen, progesterone, prolactin, and thyroid hormones [10–13]. However, previous studies have shown

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inconsistent results with respect to their close relationships [13–17].

To date, there have been no reports on the prevalence of RLS among Taiwanese pregnant women. In this study, the purposes are 2-fold: (1) to determine the prevalence of RLS in Taiwanese pregnant women, and (2) to explore the clinical correlates of RLS in pregnancy and its impact on sleep.

2. Methods

We prospectively enrolled pregnant women aged $\geqslant$18 years who were admitted to the Department of Obstetrics of Mackay Memorial Hospital for delivery from September 2010 to May 2011. Women were not included in the study if they had eclampsia, preeclampsia, or severe ankle edema. Specific diseases known to be causes of symptomatic RLS were not excluded. This study was approved by the Mackay Memorial Hospital Institutional Review Board and informed consent was obtained from each participant. A questionnaire was administered during the face-to-face interview. This questionnaire consisted of 20 questions, including demographic characteristics (age, height, body weight, education, race, number of previous pregnancies, number of children, etc.), personal behavior (exercise, smoking, drinking, caffeine, iron and vitamin supplement consumption), and past medical illnesses. Medical information was also obtained from the medical records of all participants, including demographic characteristics, previous pregnancies, drug history, and sleep disorders. Diagnosis of RLS was established on the basis of all four of the IRLSSG criteria. All participants were evaluated by the same neurologist (Chen P.H.), who reviewed all the completed questionnaires and interviewed the women either by phone or face-to-face if they responded positively to at least one of the four screening questions based on the IRLSSG criteria. There is a possibility of confusion between the symptoms of RLS and those of positional discomfort, hypnagogic jerks, nocturnal leg cramps, or musculoskeletal disorders. To prevent this confusion, we utilized the validated Hopkins telephone diagnostic interview [18] that contained 11 specific questions to confirm RLS and to eliminate potential false positives.

Participants who fulfilled the IRLSSG criteria were asked to fill in a form that included questions to assess their RLS history and the RLS history of their first-degree relatives, as well as questions based on the John Hopkins RLS Severity Rating Scale [19] and the Chinese version of Pittsburgh Sleep Quality Index (PSQI) [20]. The John Hopkins RLS Severity Rating Scale consists of one question regarding the usual (>50% of days) time of the day that symptoms started. Severity of RLS can be classified as minimal (score 0), mild (score 1), moderate (score 2), and severe (score 3). This crude severity rating scale rates most people with RLS fairly well, but it does not take into account the intensity of the RLS symptoms and their effect on daytime functioning. The Pittsburgh Sleep Quality Index measures components of sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, daytime dysfunction, and a global score. Scores range from 0 to 21, with scores greater than five indicating clinically significant sleep disturbance. Hemoglobin levels were obtained from routine blood tests between week 24 and week 28 of pregnancy. Women were considered anemic if hemoglobin levels were below 11 g/dL [21]. All participants affected by RLS underwent follow-up telephone interviews conducted by the same neurologist 1 and 3 months after parturition. In addition, 20 randomly sampled participants who had denied any symptoms in the screening questions were interviewed as controls. Women who fulfilled the IRLSSG criteria and had symptoms for at least 4 days/month were diagnosed as having RLS. RLS was further divided into transient or chronic forms, which were defined by the absence or presence of symptoms 3 months after delivery, respectively.

SAS version 9.2 for Windows was used for statistical analysis. For continuous variables, the Student's t test was used to compare the means. For categorical variables the χ^2 test was used to test the difference between groups. We used the Mann–Whitney U test or Fisher exact test when analyzing the smaller sample subgroup. Multivariate analysis was also performed using logistic regression models with RLS during pregnancy (yes/no) as the response variable and RLS predictors found significant by univariate analysis as covariates. Each covariate was tested independently and with the main interaction terms. Measures of association were odds ratios (ORs) with 95% confidence intervals (95% CIs). The continuous variables were expressed as the mean ± SD. All calculated p values were two-tailed, and we considered $p < 0.05$ to be statistically significant.

3. Results

3.1. Study participants

During the study period, 660 pregnant women fulfilled the requirements of the inclusion and exclusion criteria. After obtaining informed consent and the completed questionnaires, 461 questionnaires were considered valid. The principal demographic and clinical characteristics of participants with and without RLS during pregnancy are listed in Table 1.

3.2. Comparisons of participants with and without RLS during pregnancy

The frequency of RLS among pregnant participants was 10.4% (n = 48). Age, BMI, education level, race/ethnicity, gravida, and number of parities were not different between the RLS and non-RLS groups. Further, exercise habits, smoking, alcohol consumption, and coffee drinking history were not different between these two groups. Pregnant women without RLS had a higher overall rate of folic acid and iron supplement consumption (defined as self-report of at least twice-weekly supplementation for a month during the first and second trimester of pregnancy) than those with RLS. Participants with RLS reported more comorbidities, such as anemia, thyroid disease, or peptic ulcer disease, than those without RLS. Pregnant women without RLS had significantly higher serum hemoglobin levels than those with RLS (12.6 ± 1.74 mg/dL versus 11.6 ± 1.86 mg/dL, p = 0.001). Table 2 shows the results of multiple logistic regression analyses, listing significant covariates that were identified by univariate analysis. Multivariate analysis identified anemia (OR: 2.91, 95% CI: 1.47–5.76) and peptic ulcer disease (OR: 11.65, 95% CI: 2.84–47.83) was independent predictors of RLS during pregnancy. Multivariate analysis also revealed a trend towards the association of alcohol consumption and pregnancy-related RLS, but this did not reach statistical significance (OR: 2.98, 95% CI: 0.99–9.02).

3.3. Comparisons of participants with transient and chronic RLS

The comparisons of demographic data and medical history between pregnant women with chronic RLS and those with transient RLS are shown in Table 3. Among the participants with RLS, 13/48 (27.1%) had chronic RLS and 35 (72.9%) had transient RLS. The demographic characteristics of participants between both groups were not significantly different. Further, exercise habits, smoking history, and alcohol consumption history did not differ between these two groups. Participants with transient RLS during pregnancy reported more coffee consumption before pregnancy than