Short Paper

Prevalence and clinical features of restless legs syndrome among Japanese pregnant women without gestational complications

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Ethical approval:
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by the Ethics Committee of Nagasaki University Graduate School of Biomedical Sciences (Approval No. 13032889).

Abstract

To determine the prevalence of restless legs syndrome (RLS) among Japanese pregnant women without complications, and to clarify the correlation between RLS and clinical outcomes, RLS screening was conducted using the Johns Hopkins Telephone Diagnostic Interview for 140 pregnant women in their third trimester. The frequency of positive RLS screening test was 15.7%. No significant differences were found in the hemoglobin, ferritin, and folate levels and in the delivery outcomes between the RLS and control groups. In the future, it will be necessary to clarify whether a similarly high prevalence of RLS exists in Japanese pregnant women with complications.

Key words: epidemiology, Japanese, pregnancy, restless legs syndrome

Introduction

The prevalence of restless legs syndrome (RLS) in pregnant women is known to be 2-3 times higher than in non-pregnant women in similar geographic and/or ethnic populations [1]. In Asian countries, a prevalence of RLS in pregnant women of 2.9-19.9% has been reported [1-4]. The majority of RLS cases in pregnant women develop during pregnancy, with peaks in the prevalence and severity of RLS found in the third trimester. Moreover, most symptoms that appear during pregnancy are alleviated within a few days postpartum [1].

More than half of all pregnant women with RLS experience severe and very severe RLS symptoms [5]. Furthermore, in pregnant women with RLS, it has been reported that gestational hypertension and caesarian section were more common compared to in pregnant women without this condition [1,2]. However, these previous reports are from countries other than Japan, and to the best of our knowledge, little is currently known about pregnancy-associated complications and delivery outcomes in pregnant women with RLS in Japan, where the management of pregnant women differs from in other parts of the world.

Accordingly, this study was conducted to clarify the prevalence and severity of RLS among Japanese pregnant women attending an obstetrics institution in Japan, with the

aim of determining if the presence of RLS affects the delivery outcomes.

Methods

Pregnant women in their third trimester (around 30 weeks' gestation) attending a maternity hospital in Nagasaki, Japan, providing care from the antenatal stage to delivery, were included in the present study. All participants had a normal pregnancy, with no complications, and a single fetus. Data collection was conducted from July 2013 to October 2014. Informed consent to participate was received from 140 out of 141 eligible participants. A blood sample was taken at the time of the RLS screening interview for hematology and biochemistry testing. The delivery medical records were checked to determine the delivery outcomes.

RLS screening was conducted using the Johns Hopkins Telephone Diagnostic Interview (TDI) [6]. At the first step of the RLS diagnostic algorithm for the TDI, the main symptom, that is, the urge to move the legs or unpleasant abnormal sensations, is selected. Subsequently, cases of cramping of the legs mimicking RLS and surface numbness are eliminated. When the following 3 items are fulfilled: (1) alleviation of symptoms by moving, (2) symptoms worsening when resting, and (3) symptoms

worsening at night, the case is evaluated as “definite RLS”; if 2 items are fulfilled, it is considered “probable RLS”, while the presence of only one or none of these items is rated as “none”. The face-to-face interviews were conducted by graduate students in the midwifery course who had studied RLS and TDI.

The severity of RLS was evaluated using the Japanese version of the International Restless Legs Syndrome Rating Scale (version 2.2) [7]. Total scores of <10, 10-19, 20-29, and ≥30 were graded as “mild,” “moderate,” “severe,” and “very severe,” respectively.

The groups assessed by the TDI as definite and probable RLS were assigned to the RLS group, while the remaining women were assigned to the control group. The results for these 2 groups are presented as the mean ± standard deviation. The participants’ demographic factors, test results, and delivery outcomes were analyzed for differences between the RLS and control groups using the unpaired t-test and Fisher’s exact test. All statistical analyses were conducted using IBM SPSS Statistics version 22.0. The level of statistical significance was set at $p<0.05$.

Results

In the TDI, 11 women (7.9%) were each characterized as definite RLS and probable RLS. Hence, the RLS group comprised 22 women (15.7%). Of those, 14 participants

(63.6%) had RLS symptoms at least twice a week. Thirteen (59.1%), 7 (31.8%), 2 (9.1%), and 0 (0%) participants were classified as having mild, moderate, severe, and very severe RLS, respectively.

No significant difference was found between the RLS group and the control group in terms of age. There were more multiparas in the RLS group compared to in the control group, but this was not statistically significant. Moreover, regarding the hemoglobin and serum iron levels, no significant differences were found between the groups. There were 16 participants with a serum ferritin level of 5 ng/ml or less, which is below the serum ferritin measurement range. When the serum ferritin level was divided into 2 categories (<25 vs. ≥25 ng/ml) and compared between the RLS and control groups, no significant difference was seen (Table 1).

Finally, no significant differences were seen between the RLS group and control group in the delivery outcomes (Table 2). There was no case of deformity in either group.

Discussion

The frequency of positive RLS screening tests among pregnant Japanese women with normal pregnancy courses was found to be 15.7% in the present study, which is clearly a higher rate compared to in non-pregnant women of the same age groups. However, it

should be noted that, in this study, screening was only performed using the TDI, and examination by specialists was not conducted. It has been reported that the sensitivity and specificity of TDI by non-clinicians' face-to-face interviews are 75% and 71%, respectively [6]. If the sensitivity and specificity in this study are similar, the true prevalence of RLS might be equivalent to our result. Nevertheless, to confirm the prevalence of RLS, examination by specialists is required.

The occurrence frequency of symptoms strongly influences the result of RLS prevalence. Two previous studies focusing on Japanese pregnant women have been reported. In the study by Suzuki et al., the occurrence frequency criteria of symptoms was not used, resulting in a high prevalence rate of 19.9% [4]. In the following report by Harano et al., the occurrence frequency of symptoms, ranging from 'sometimes' to 'always,' was taken into account, resulting in a low prevalence rate of 2.9% [3]. A similar tendency was observed in our study, indicating that, in studies of RLS prevalence, adding the symptoms occurrence frequency is an important element.

Our study had some limitations. First, other than the iron, ferritin, and folate levels, we did not include data on other factors that may affect the RLS condition such as family history of RLS, obesity, smoking, and caffeine consumption. Second, the correlation between iron supplementation and symptoms has not been confirmed. Third, we could

not determine the onset and the variability of RLS symptoms from before pregnancy to lactation period. In the future, it will necessary to conduct research into RLS in pregnant women including evaluations of these problems, changes in symptoms as the pregnancy progresses, and periodic limb movement, a common complication associated with RLS.

In conclusion, it is noteworthy that the frequency of positive RLS symptoms during pregnancy in Japanese women with a good clinical course in the present study, using the exclusion criteria to discriminate RLS mimics, was found to be as high as those reported in Western countries. However, further studies of pregnancies with a variety of gestational complications are needed in the future to confirm our findings in different populations. As transient RLS during pregnancy confers an approximately 4-fold increased risk of developing future chronic idiopathic RLS [8], providing information about RLS to pregnant women and taking action against gestational RLS are needed.

Compliance with Ethical Standards:

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Conflict of Interest: All authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national

research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by the Ethics Committee of Nagasaki University Graduate School of Biomedical Sciences (Approval No. 13032889).

Informed consent: Informed consent was obtained from all individual participants included in the study.

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Table 1. Demographic and clinical characteristics in subjects with (n=22) and without (n=118) RLS

		N (RLS/Controls)	RLS	Controls	t-value	p-value
Age	Years	22 / 118	30.6±4.1	30.3±5.0	-0.298	0.766
Parity	Primipara	22 / 118	5 (3.6)	53 (37.9)		0.061
	Multipara		17 (12.1)	65 (46.4)		
Hemoglobin	g/dl	21 / 117	10.8±0.9	10.8±0.9	-0.185	0.854
Iron	µg /ml	20 / 104	51.8±23.3	53.3±29.9	-0.221	0.825
Ferritin	<=25ng/ml	20 / 102	19 (15.6)	99 (81.1)		0.516
	>25ng/ml		1 (0.9)	3 (2.5)		

Mean ± SD or number (%); Results from unpaired t-test or Fisher's exact test.

Table 2. Birth outcomes in subjects with (n=22) and without (n=118) RLS.

	N (RLS/Controls)	RLS	Controls	t value	p-value
Gestational week (weeks)	20 / 114	39.6±1.1	39.7±1.0	0.328	0.743
Duration of delivery (hours)	19 / 103	7.5±6.2	10.3±6.6	1.626	0.087
Blood loss (ml)	20 / 113	550±225	679±439	1.983	0.053
Mode of delivery					
Vaginal	20 / 114	18 (13.5)	103 (77.4)		1.000
Caesarian		1 (0.8)	11 (8.3)		
Induction of labor					
negative	19 / 108	18 (14.2)	100 (78.7)		1.000
positive		1 (0.8)	8 (6.3)		
Augmentation of labor					
negative	19 / 108	17 (13.4)	91 (71.7)		0.736
positive		2 (1.6)	17 (13.4)		
Contraction after birth					
good	19 / 105	17 (13.7)	103 (83.1)		0.111
not good		2 (1.6)	2 (1.6)		

Mean ± SD or number (%); Results from unpaired t-test or Fisher's exact test.