RESTLESS LEGS SYNDROME DURING PREGNANCY AND EARLY PUERPERAL PERIOD IN WOMEN OF BOSNIA AND HERZEGOVINA

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Objective: To investigate the prevalence of restless legs syndrome (RLS) during pregnancy and early postpartal period among Bosnian women and to identify factors associated with RLS during pregnancy.

Methods: A total of 1282 pregnant women reporting to the clinic for the first time were interviewed. Only those patients who prenatally met the RLS criteria were reinterviewed four to seven days postpartum.

Results: A total of 291 (22.7%) participants reported RLS during pregnancy (7.2% during first, 42.2% during second and 50.6% during third trimester - first and second trimesters: p<.05; first and third trimesters: p<.05; second and third trimesters: p>.05). Multiparity was more common among women with RLS (p<.0.05). 53 patients (10.7%) met all four RLS diagnostic criteria after their delivery.

Conclusion: RLS prevalence during pregnancy was 22.7%, more than a half of which exhibited symptoms during their third trimester. Multiparity was an independent risk factor of RLS occurrence in pregnancy.

INTRODUCTION

Restless legs syndrome (RLS) is a sensorimotor disorder whose primary sensory symptom is a strong, often irresistible, urge to move the legs (1) resulting in sleep disruption, particularly in moderate-to-severe cases (2). For the purpose of addressing matters of stigma and title inaccuracy, in recent years, there has been a shift from using the name 'Restless Legs Syndrome' to 'Willis-Ekbom Disorder'. RLS is diagnosed in accordance with four criteria (2) and can be classified as either primary or secondary based on the presence of associated conditions (3). The primary form is the most common one. It has an inherent pattern and affects patients with no underlying disorder (3). On the other hand, pregnancy is the major secondary cause, together with iron deficiency and end-stage renal disease (4). Prevalence of RLS in pregnancy has been found to range between 19 and 30% (1,5,6). There are no published reports on RLS prevalence during pregnancy from the Balkans.

The aim of this study was to assess the prevalence of pregnancy related RLS in a sample of pregnant women in Bosnia and Herzegovina in the course of their pregnancy and early postpartum period as well as to identify factors associated with RLS during pregnancy.

MATERIALS AND METHODS

This was a cross-sectional study conducted in the period between November 2012 and January 2014 at the Clinic for Ob/Gyn of the University Clinical Center Tuzla and the Mostar University Hospital in Bosnia and Herzegovina, both of which provide public services. The study subjects were recruited from a population of pregnant women attending prenatal services at the Tuzla and Mostar clinics. For the purpose of ruling out possible causes of secondary RLS other than pregnancy, only women with no underlying diseases were recruited. Having requested participation from a total of 1589 women, 1282 consented. The study, approved by the ethics committee of the University Clinical Center Tuzla, included consecutive pregnant women aged 18-35 admitted to either of the two clinics. The questionnaire was distributed on the day of admission (for pregnant women) and four to seven days after delivery. Its primary concern was to address the four essential RLS diagnostic criteria ⟨2⟩: the urge to move the limbs is usually associated with parasthesias/dysesthesias; the onset or the exacerbation occurs during periods of rest or inactivity; the urge is partially or totally relieved by activity; the onset occurs or worsens during night. Interviewees were positively diagnosed with RLS once they affirmatively answered all four questions. Other relevant

data regarding sociodemographics, medical and drug history was collected via face-to-face interviews conducted on the day of admission. Other necessary material such as serum concentrations of hemoglobin was retrieved from medical charts. Only one interview was conducted with each patient reporting to the clinic for the first time. However, in the postnatal period, only those patients who prenatally met the RLS criteria were reinterviewed four to seven days after delivery. The statistical analysis was conducted using the SPSS statistics software (SPSS V.11.5SPSS Inc., Chicago, IL, USA) with the level of significance set at 0.05.

RESULTS

Among the 1282 pregnant women enrolled in the study, 11.3% were in their first trimester of pregnancy, 36.4% in their second and 52.3% in their third. The mean age was 25.7 ± 3.2; in regards to the number of pregnancies 53.4% of women were primigravida and 46.6% multigravida. Education level data showed that 76.9% had completed elementary and middle school while 23.1% had completed high school (Table I).

From the total of 1282 examined women, 291 were positively diagnosed with RLS, resulting in a prevalence

Table I. Demographic data				
	All sample (pregnancy) 1282 (100.0)	1st Trimester 149 (11.3)	2nd Trimester 467 (36.4)	3rd Trimester 666 (52.3)
Age	25.7 ± 3.2	25.4 ± 5.1	26.1 ± 6.2	25.6 ±3.2
Primigravida/para	684 (53.4)	90 (13.1)	245 (35.8)	349 (51.0)
Multigravida/para	598 (46.6)	59 (9.9)	222 (37.1)	317 (53.0)
Level of education				
High	296 (23.1)	33 (11.2)	120 (40.5)	143 (48.3)
Low/Moderate	986 (76.9)	116 (11.8)	347 (35.2)	523 (53.0)

Age in years (mean ± standard deviation); other number (percentage)

of 22.7%. Prevalence of 7.2% was found in the first trimester, 42.2% in the second and 50.6% in the third (first and second trimesters: p<.05; first and third trimesters: p<.05; second and third trimesters: p>.05) (Table II).

Table II. Prevalence of RLS in pregnant women				
	All sample 291 (22.7)	1st Trimester 20 (7.2)	2nd Trimester 123 (42.2)*	3rd Trimester 148 (50.6)*
Age	26.3 ± 6.4	25.6 ± 0.4	24.9 ± 4.1	25.1 ± 4.3
Primigravida/para	149 (51.2)	9 (6.1)	65 (43.6)	75 (50.3)
Multipara/para	142 (48.8)	11 (7.7)	58 (40.9)	73 (51.4)
Level of education				
High	63 (21.6)	3 (4.8)	26 (41.3)	34 (53.9)
Low/Moderate	228 (78.4)	17 (7.4)	97 (42.5)	114 (50.1)
Cigarette smoking	33 (11.3)	3 (9.1)	16 (48.5)	14 (42.4)
Hemoglobin, mg/dl	12.3 ± 2.4	12.4 ± 4.4	12.2 ± 0.5	12.0 ± 1.1
Iron therapy	172 (59.4)	7 (4.1)	70 (40.7)	95 (55.2)
Vitamins	118 (40.7)	13 (11.0)	55 (46.6)	50 (42.4)

Age and hemoglobin: in years (mean ± standard deviation); other number (percentage);
* Statistical significance (p<.05) to 1st x 2nd and to 1st x 3rd trimester

No significant differences in RLS prevalence were found for the whole sample and among the trimesters regarding education level, cigarette smoking, iron and vitamin supplementation and hemoglobin concentration while multiparity was more common among women with RLS (p<.0.05) (Table III).

Table III. Association between restless legs syndrome and analyzed factors during pregnancy (multivariate analysis)

Variable	Odds ratio	95% CI	p value
Lower level of education	1.451	0.64 – 7.21	NS
Iron supplementation	2.029	0.46 – 4.76	NS
Vitamins supplementation	1.83	0.75 – 2.68	NS
Hemoglobin <12 mg/dl	0.515	0.30 – 1.87	NS
Multiparity	3.12	1.01 – 5.12	.05

NS – no significance

From the 291 participant who prenatally met the RLS criteria only 53 remet those criteria after delivery as well which resulted in an RLS prevalence of 10,7%. Noteworthy is the fact that RLS prevalence during pregnancy was significantly different from that in the postpartum period (p < .05).

DISCUSSION

The present research showed that RLS prevalence during pregnancy was 22.7% as well as that it decreased in the early postpartum period to 10.7%. However, no data about the prevalence and RLS associated features for the general population of the Balkans is available. Since this was a multicenter study, the population included in it can be representative of the majority of Bosnian pregnant women. Accordingly, the sample of postpartum women included in this study represents the general population of women with RLS prevalence of 10.7%. Therefore, it can be assumed that the prevalence of pregnancy-related RLS in this study's population was 22.7%. This is lower than the prevalence reported in some of the previous studies that are methodologically comparable (1,7,8). Results of the present study confirmed the considerably higher prevalence of RLS in pregnant women in comparison to the reported general women population (4,7,9). RLS prevalence among the pregnant women of Brazil was 13.5% (5) and up to 34% in Norway (1). A wide range of RLS prevalence during pregnancy, in the general population as well (6), can be associated with different research methodologies, recall bias and genetic predisposition (10,11,12,13). It is also widely known that epidemiological studies in RLS have often been limited by misdiagnosis (6). However, the condition is a common neurological disorder which may negatively affect the health of pregnant women (3), but most women are without symptoms sometime after delivery (1), as confirmed by the results. Therefore, pregnancy is mostly associated with transient RLS (7).

Results from this study showed increasing prevalence of RLS during pregnancy peaking in the third trimester. RLS prevalence increased from 7.2% in the first trimester to 50.6% in the third. Therefore, as previously described (5,7,14), RLS occurrence was strongly related to the third trimester of pregnancy. Authors agree that the highest number of women are affected in the last trimester and those with pre-existing RLS often complain of worsening symptoms during pregnancy (7,14,15). Epidemiological evidence suggests that the majority of affected pregnant women had not experienced RLS before pregnancy (7). This study also aimed at identifying the predisposing factors of RLS occurrence in pregnancy. RLS in pregnancy was first described 58 years ago, but the etiology of the disorder remains unclear (1). The etiopathogenetic hypothesis of higher RLS prevalence during pregnancy involves iron and folate deficiency, hormonal changes and heredity (16,17,18). Iron and folate requirements during pregnancy are, respectively, up to 10 times higher compared to the non-pregnant state due to increased fetal demand and hemodilution. Accordingly, the development of RLS during pregnancy could be related to iron deficiency anemia and folate insufficiency (19,20). Iron and folate deficiency are well known conditions associated with RLS (21,22), but studies regarding the preventive effects of iron and folate supplementation during pregnancy have been inconclusive (1,7,19). In the present study, the risk of RLS associated with the supplemental intake of iron and vitamins was estimated by multivariable logistic regression adjusted for education level and multiparity. There was no association between RLS in pregnancy and the supplemental intake of iron and vitamins. Manconi et al. (7) (2004) also found no relationship between RLS in pregnancy and the supplemental intake of iron and folate. In this study and as previously reported (3), there was no association between pregnancy-related RSL and hemoglobin level. Education level was also found to be unassociated with RLS in pregnancy, as already observed by other studies (3). Furthermore, in prior studies (5,7), parity was not associated with an increased risk of RLS development during pregnancy while present results indicate that multiparity was an independent risk factor of RLS occurrence in pregnancy.

The questionnaire was not formally validated, but was based on the essential RLS criteria (2), therefore, it is unlikely that other diagnoses could be responsible for the symptoms. Lack of evaluation of the severity of RLS symptoms by using the International RLS study group rating scale (IRLS) (23) could be considered a limitation of the study. Another limiting factor is that no prospective follow-up of the pregnant women with RLS was performed for some months after childbirth.

In conclusion, RLS is a frequent movement disorder during pregnancy with a 22.7% prevalence calculated for the population enrolled in the study with more than half of the women presenting symptoms in their third trimester. The present results showed that multiparity was an independent risk factor of RLS occurrence in pregnancy. Lastly, screening pregnant women for RLS should be considered.

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