

Restless Legs Syndrome in Pregnant Women: Survey Of 504 Women and Literature Review

Rajaa EL QASSEH^{1*}, Houssine BOUFETTAL¹, Mohamed HAMIRIFOU¹, Hajar BELLAKHDER¹, Mohamed Abdou RAFAI²

¹Department of Gynecology - Obstetrics 2 Neurology Department

^{1,2}Ibn Rochd University Hospital, Faculty of Medicine and Pharmacy, Hassan 2 University, Casablanca, Morocco

*Corresponding author: Rajaa EL QASSEH, Department of Gynecology-Obstetrics 2 Neurology Department, Morocco. Email: rajaaelqasseh@gmail.com

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Abstract

Restless Legs Syndrome (RLS) is common in pregnancy. It is often unrecognized, undiagnosed, poorly managed and source of morbidity. The aim of this study is to assess the frequency, the clinical presentation and the impact of this syndrome in pregnant women in Morocco.

This is a prospective study carried out among 504 parturients of the CHU Ibn Rochd of Casablanca, between 2015 and 2016. It is based on a questionnaire. The sample is divided into two groups. The study is comparative between cases with RLS and free cases. The frequency of RLS is 10%. The mean age of the cases affected by RLS is 32 [20 - 43] years. The frequency of RLS increases markedly with age. Multiparous female represents 35 (68.6%) cases. Anemia is common in RLS. The symptoms appeared in the third trimester in half of the cases and in the second quarter in 16 (31.4%) cases. The mean score according to the criteria of the IRLSSG rating scale is 18.3 [7 - 30]. The intensity of RLS symptoms was moderate in 29 (56.9%) cases and mild in 22 (43.1%) cases. An impact on the quality of life is found in more than half of the cases. Patients who consulted a physician accounted for 16 (31.4%) cases. Half of them received no treatment.

Pregnancy can trigger or aggravate the symptoms of RLS. Pregnant women are two or three times more likely to develop RLS than the general population. The rate of RLS during pregnancy can reach 42%. It increases with age and parity. Symptom management in RLS includes hygiene rules, correction of ferritinemia and prescription of dopaminergic drugs. The RLS prognosis during pregnancy is good. Childbirth may be the cause of exacerbation of the symptoms. Thus, RLS is common in pregnant women. It needs to be defined, diagnosed and well- managed to avoid the resulting morbidity.

Keywords: Restless leg syndrome; pregnancy, L-DOPA; ferritinemia; sleep disorder.

Introduction

Restless Legs Syndrome (RLS) is characterized by extremely unpleasant sensations, preferentially affecting the lower limbs at the end of the day or during sleep, accompanied by a compelling need to move [1]. It is a sensorimotor syndrome characterized by the presence of a sensitive component: tingling, paresthesia, tingling, drawing, burning and a motor component: the irresistible need to move the limbs [2]. It remains one of the most common neurological conditions in Western countries, but its exact prevalence remains difficult to specify, given the subjective nature of the symptoms but also its frustrated and intermittent discomfort [3]. The pathophysiology of this syndrome remains unclear. Nevertheless, an iron deficiency seems to be a determining factor. This explains the high prevalence of RLS in pregnant women [4].

Pregnancy is one of the major causes of RLS, affecting a large number of parturients with a resolution of the symptomatology within the month following delivery [5,6]. He is often misunderstood by obstetricians. His diagnosis is exclusively clinical based on the functional signs reported by the patient and meeting the criteria of the International Restless Legs Syndrome Study Group (IRLSSG) [7,8]. In order to assess the severity of Restless Legs Syndrome, the IRLSSG developed a questionnaire (IRLSSG rating scale) [9].

The RLS developed during pregnancy is rarely evoked, poorly researched and poorly managed, which can be a source of anxiety and fatigue, and even obstetric complications that alter the mode of delivery [10].

The objective of this work is to study epidemiological, clinical data and the impact of this syndrome in pregnant women in Morocco.

Materials and methods

This is a prospective study carried out among 504 women admitted to the gynaecology and obstetrics department of the Ibn Rochd University Hospital of Casablanca, between October 2019 and January 2020.

A questionnaire was established for the conduct of this survey. Patients with RLS were defined according to the International Restless Legs Syndrome Study Group (IRLSSG) score criteria for positive diagnosis. The sample of patients was divided into two groups: a G1 group of patients with RLS and a G2 group of RLS-free women. The two samples were matched according to other confounding factors, including patient age, parity number, etc.

The investigation included any parturient transiting the gynecology-obstetrics department. Non-pregnant women,

patients with ectopic or maternal pregnancies, and post-partum women were excluded from this study. Le recueil des informations était sous la responsabilité d'un même enquêteur. Les données de l'enquête comportaient la fréquence du SJSR, les données socio-démographiques et les données obstétricales (Annexe). Pour comparer entre les deux groupes quant aux facteurs de morbidité associés à ce syndrome. Le test chi carré était utilisé pour comparer les résultats.

Results

During the period of inclusion, 504 female respondents were interviewed. Of these, 51 patients with RLS were identified. The RLS frequency was thus 10%.

The average age of women with RLS was 32 [20-43] years. The incidence of RLS increased significantly with age. The majority of patients (73% of cases) were over the age of 30. Nullipares accounted for 16 (31.4%) cases. Multiparous accounted for 35 (68.6%) cases (Table 1).

Age (ans) et parité	N et % G1	N et % G2	OR	p
Age - 17 - 24	3 (7)	63 (14)	0.415 [0.133 - 1.293]	0.129
- 24 - 29	8 (20)	273 (61,5)	0.148 [0.071 - 0.308]	<0.0005
- ≥ 30	30 (73)	111 (24,5)	3.678 [2.181 - 6.203]	<0.0005
Parité				
- Nullipares	16 (31,4)	238 (52,5)	2.223 [1.263 - 3.911]	0.006
- Multipares	35 (68,6)	215 (47,5)	0.450 [0.256 - 0.792]	0.006
Total	51 (100)	453 (100)		

Table 1: frequency of RLS by age and parity.

RLS is less common when there is a threat of premature delivery (p 0.002, 0.308 [0.114- 0.837]). On the other hand, it is more common in the presence of a congenital malformation (p 0.004, 14.094 [2.298-86.447]) or oligoamnios (p0.004, 9.375 [1.841-47.742]).

Furthermore, there was no difference in the other pathological areas associated with pregnancy for the two study groups (Table 2).

Reason for hospitalization	n and% G1	n and% G2	OR	p
Childbirth	25 (49)	256 (55)	0.74 [0.493-1.284]	0.308
Preeclampsia	5 (10)	20 (5)	2.083 [0.907-4.780]	0.083
Threatened preterm birth	4 (7)	105 (24,5)	0.308 [0.114-0.837]	0.021
Twin pregnancies	3 (6)	10 (2)	2.361 [0.844-6.660]	0.102
Breech presentation	3 (6)	9 (2)	2.573 [0.931-7.108]	0.068
Premature rupture of membranes	3 (6)	30 (7)	2.578 [0.933-7.123]	0.068
Congenital malformation	3 (6)	2 (0,5)	14.094 [2.298-86.447]	0.004
Oligohydramnios	3 (6)	3 (0,5)	9.375 [1.841-47.742]	0.007
Gestational diabetes	3 (6)	11 (2)	2.511 [0.677-9.316]	0.169
Cerclage of the uterine cervix	1 (2)	0	-	-
Termination of pregnancy	1 (2)	7 (1,5)	1.274 [0.154-10.570]	0.822
Thalassemia	1 (2)	0	-	-
Total	51	453	-	-

Table 2: Distribution of the parturientes according to the pathological ground associated with the pregnancy.

Anemia is defined by a hemoglobin level less than 11g/dl. It was present in 28 (54.9%) G1 cases and 95 (21%) G2 cases (p0.0005, OR 3.487[2.116-5.748]. No patients were tested for ferritinemia. There was no history of peripheral neuropathy in any of the RLS participants. Symptomatology appeared in the third quarter in 26 (51%) cases, in the second quarter in 16 (31.4%) cases and in the first quarter in nine (17.6%) cases.

The average score according to the criteria of the IRLSSG rating scale was 18.3 with extremes of 7 to 30. No parturient had a very severe form. The intensity of RLS symptomatology was moderate in 29 (56.9%) cases and mild in 22 (43.1%) cases. Work stoppage secondary to this syndrome was observed in eight (15.7%) cases, with an average duration of five days [1-15]. Impacts on household and work tasks were noted in 45 (88.2%) cases. Sleep need was reported by 37 (72.5%) cases.

Symptoms of RLS first appeared during pregnancy in 46 (90.2%) cases. In six (11.8%) cases, symptomatology existed during previous pregnancies. No parturient showed symptoms outside of pregnancy.

Patients who had consulted a physician (general practitioner, gynecologist or rheumatologist) for the symptomatology of RLS accounted for 16 (31.4%) cases. The diagnosis of RLS was not made in any of them and the symptomatology was related to the small ailments of pregnancy. Half of these patients had no treatment. For the second half, the treatments prescribed were paracetamol, magnesium or vitamin complexes.

Etudes	Pays	Année	Prévalence (%)
Hübner et al [14]	Suisse	2013	11,58
Chen et al [26]	Taiwan	2012	10,41
Uglane et al [15]	Norvège	2011	33,86
Manconi et al [21]	Italie	2012	26,57
Neau et al [16]	France	2010	32,25
Suzuki K et al [17]	Japon	2003	19,9
Notre étude	Casablanca, Maroc	2015	10,11

Table 3: Frequency of RLS in pregnant women.

The pathophysiological mechanisms that generate the symptomatology of RLS suggest the roles of L-Dopa and iron [31-34]. Iron and folic acid deficiency and hormonal alteration are implicated in the genesis of RLS during pregnancy [35,36]. A low level of ferritin in early pregnancy is considered a predictor of RLS [11]. Symptoms of RLS decrease rapidly after childbirth, regardless of iron and folate levels [12]. In our study, almost half of pregnant patients developed these symptoms in the third trimester.

Discuss

Restless legs syndrome, or Willis-Ekbom's disease, is a sensory disorder that is characterized by an irresistible need to move the limbs (typically the legs) typically associated with unpleasant sensations (tingling, tension, tingling) and sometimes painful (electric shocks, burns, crushing) [1,11]. It occurs electively at rest, improves with voluntary movement of limbs (especially walking) and worsens in the evening and at night [3,12]. It can be primary or secondary to peripheral neuropathy, chronic kidney failure, martial deficiency or pregnancy [4,13].

The prevalence of RLS in the general population is highly variable in the literature between 2.9% and 32% [7,14]. In the general adult population of Western Europe and North America, it is 7-11%, with twice as many women as men and an increase in prevalence in both sexes with age [7,15-17]. In the French population, the annual prevalence of RLS is 8.5% [18]. The prevalence of RLS in the Asian and South American population remains lower, ranging from 0.3% to 3.9% [20]. Pregnancy may be considered an initial or aggravating risk factor for RLS symptoms. Pregnant women are two to three times more likely to develop RLS compared to the general population [21-25].

The incidence of RLS in our survey was 10.1%, which is close to the prevalence rate reported in the Swiss study of Hübner et al. [14] and the Taiwanese study of Chen et al. [26] (Table 3). The high frequency of RLS justifies better defining this pathology among practitioners and proposing adequate management in order to reduce its consequences, particularly on the quality of sleep [27-30].

It is estimated that 22-92% of patients with primary RLS have a positive family history [34]. First-degree relatives of RLS patients are five to six times more likely to have RLS compared to a control group [35].

The diagnosis of RLS is primarily clinical based on four criteria reported by the patient and which must all be present in order to carry the positive diagnosis. In addition to these mandatory criteria, there are three additional optional signs [37]. These criteria were defined by the RLS International Study Group in 1995 and revised in 2002 [7,8] (Table 4).

A. Mandatory criteria for diagnosis	<ol style="list-style-type: none"> 1. Urgent need to move the legs, often accompanied or caused by unpleasant sensations (electric shocks, twisting, pulling, burning, etc.) or discomfort (tingling, pins and needles, etc.) in the legs (this motor impatience may not be accompanied by the discomforting sensations, and the arms or other parts of the body may be reached with the legs) 2. The urge to move and the uncomfortable sensations begin or worsen during periods of rest or inactivity, such as while lying or sitting 3. The urge to move and unpleasant sensations are partially or completely relieved by movement, such as walking or stretching, at least as long as the activity continues 4. The urge to move or unpleasant sensations worsen in the evening and at night or occur only in the evening and at night (when symptoms are very severe, the worsening at night may not be observed, but should have been presented previously)
B. Supporting clinical criteria	<ol style="list-style-type: none"> 1. Family history of RLS 2. Positive response to dopaminergic therapy 3. Periodic leg movements during sleep (SJMS) or wakefulness (VJMS)
C. Clinical characteristics	<ol style="list-style-type: none"> 1. Natural clinical course: RLS can occur at any age. The course is usually progressive. In some patients, RLS may be intermittent and spontaneous remissions of one month or more may be observed. 2. Sleep disturbances (insomnia, daytime sleepiness, fatigue, etc.) 3. Clinical workup and physical examination usually normal.

Table 4: Diagnostic Criteria for Restless Legs Syndrome [7,8].

Neurological examination is strictly normal [38]. These were the criteria used to conduct our study. Once the diagnosis is made, it is necessary to assess the severity of the syndrome [39]. There are two validated clinical scales of severity of RLS. The John Hopkins Group Scale [34] and the international IRLSSG Rating scale [7,8]. This latter scale is a 10-question self-assessment that allows patients to be classified into four groups according to whether the syndrome is mild (score 1 to 10), moderate (score 11 to 20), severe (score 21 to 30) or very severe (score 31 to 40) [7]. It is also used to monitor patients and to judge the effect of treatment [9]. In our study no form, severe or very severe, is found. Light and moderate forms account for 43% and 57% of cases, respectively.

Moderate forms of RLS are the most common. The average score ranges from 17.4 +/- 6.2 [39-41]. In our study, we found an average score of 18.4.

The determination of ferritinemia, electromyography, nerve biopsy are sometimes useful for investigating etiology or eliminating an organic cause [42-45]. In our study, no specific paraclinical examination was requested.

Symptoms of RLS are frequently reported during pregnancy, with prevalence rates that vary widely from survey to survey, up to 42% [38,46]. The pathogenesis of RLS related to pregnancy is unclear, although the degree of improvement in RLS symptoms appears to be correlated with improvements in ferritinemia [45]. A high

concentration of the soluble transferrin receptor found in pregnant women with RLS would decrease the bioavailability of free serum iron and thus be the cause of the syndrome. This parameter is considered a more relevant marker of martial deficiency than ferritin [46].

The correlation with age is quite significant in most works. The population of pregnant women affected by this syndrome is generally older [41] In our work, the average age of women with RLS is 32 years and 73% of women are over the age of 30.

Studies show that the prevalence of RLS in pregnant women is strongly associated with the number of children [10-15]. This can be explained by the increase in iron losses as pregnancies accumulate [17]. Finally, the relative risk of developing RLS increases from 1.98 in a primipare to 3.04 in a second pregnancy and 3.57 in a third or more pregnancy [16]. In our study, multiparous accounted for 68.6% of cases (p0.006).

Symptom management of RLS begins with a non-pharmacological approach, including mental deviation activities such as crossword puzzles, caffeine abstinence, tea, nicotine, alcohol and elimination, if possible, medications known to aggravate RLS such as antidepressants, neuroleptics, antiemetics and antihistamine sedatives [47-49]. Sports should also be practised in the morning rather than in the evening [50]. Given the failure of these measures, the pharmacological

approach is justified. In our study, only 26.3% of female respondents consulted for this symptomatology, but none were adequately treated. The RLS is a condition still unknown to practitioners.

A balanced diet must be able to cope with the iron requirements of a normal pregnancy in a woman who is not deficient before conception. Inadequate dietary intake of iron justifies intake during the last two quarters to decrease the prevalence of iron deficiency anemia in late pregnancy and to improve symptoms of RLS [12,13].

The drug prescription must take into account the teratogenic effect of certain drugs. Controlled studies of RLS during pregnancy are limited. As a result, most evidence of therapeutic outcomes comes from cases or small series of reported cases. Drugs that have been studied include iron intake, dopaminergic agents, benzodiazepines, opiates and antiepileptic agents [51-60].

The prognosis of RLS during pregnancy is good. Symptoms disappear a few days after delivery in 97% of cases [1]. The occurrence of RLS during pregnancy is a significant risk factor for the development of a chronic idiopathic form of RLS in the future. In one study [11], RLS in pregnant women increases the risk of developing chronic RLS four times in the future [4].

Childbirth may be the cause of exacerbation of symptomatology. Stress, insomnia, prolonged immobilization and the use of dopaminergic antagonists in surgery are factors that promote this exacerbation. It is manifested by diffuse painful paresthesias that can affect the whole body leading to painful akathisia and involuntary shaking of the legs or even agitation that can compromise childbirth [10]. The motor signs of exacerbation involve an unquenchable need to move the legs even as the surgeon operates and periodic sudden and involuntary movements when awake [41]. On the sensory level, the initial paresthesias of the legs characteristic of the syndrome transform during exacerbation into painful sensations, their territory extends from the legs to the whole body and the affective component associated with pain is referred to as 'may lead to a suicidal act [42]. Agitation also causes surgical complications.

Situations at risk of exacerbation include treatment breakdown, forced or prolonged immobilization, lack of sleep and acute iron deficiency, but especially the administration of dopaminergic blocking agents (droperidol, hydroxyzine) [43]. For example, a parturient with RLS may compromise the healthy completion of her delivery during an epidural or spinal anaesthesia [20]. Post-operative follow-up can be difficult for these patients [31]. In order to prevent these exacerbations, it is necessary to control the level of ferritinemia, to supplement iron according to severity, to avoid stopping the treatment of RLS, to temporarily increase the doses of drugs against RLS in postoperative, to counter-indicate the administration [6].

Concluding Remarks

Restless legs syndrome in pregnant women is a frequent

situation, underestimated by parturients and doctors. It is a complex disorder related to several mechanisms, involving iron deficiency and hormonal mechanisms. This syndrome is responsible in pregnant women for significant sleep disorders and alteration of the quality of life. The exacerbation of the symptoms by the use of certain drugs during delivery, which cause significant pain and agitation, can endanger the vital prognosis of the mother and child, hence the need for preventive measures by the health care team in the case of any pregnant woman. The prognosis is generally good, with the symptoms disappearing within a month after delivery.

However, there is a risk of developing idiopathic RLS later on. Restless legs syndrome remains a poorly understood condition among clinical practitioners, hence the importance of making them aware of this entity, particularly in pregnant women.

"Conflicts of interest: **none**

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