



## Restless legs syndrome in pregnancy and risk of gestational hypertension in a low risk population

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### ABSTRACT

It has been reported a relationship between Restless Legs Syndrome (RLS) and pregnancy-induced hypertension (PIH). In this brief paper we report the association between RLS and PHI observed in a study conducted in Italy.

This is a cross sectional study. Eligible for the study were women aged >18 years who delivered in randomly selected days to the Department of Obstetrics of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, the largest maternity hospital in Milan, Italy during 3 bimonthly periods in 2013-2015. The study protocol did not include any exclusion criteria. The researchers identified eligible women in the obstetric wards on randomly selected days within 3 days from delivery. Each woman who met the inclusion criteria agreed to be interviewed. A total of 648 women (median age 35, interquartile range 32-38) were identified. A questionnaire was administered during a face-to-face interview. This questionnaire included information about demographic characteristics and personal behavior. Diagnosis of RLS was established on the basis of the International Restless Legs Syndrome Study Group criteria.

Out of the 648 interviewed women, 132 (20,4%, 95% CI: 17,3-23,5) met the criteria for diagnosis of RLS. Considering the 132 with and the 516 without RLS, 7(5,3%) and 29(5,6%) respectively had diagnosis of PHI (Odds Ratio adjusted for age: 0.89, 95% confidence interval 0.38-2.10). In conclusion despite the limitations our study suggests that the relationship between RLS syndrome and gestational hypertension should be more carefully analyzed in different populations.

### SOMMARIO

È stato segnalato un rapporto fra la Restless Legs Syndrome (RLS) e l'ipertensione gestazionale (PIH). In questo breve documento Analizziamo l'associazione tra RLS e l'ipertensione gestazionale osservata in uno studio condotto in Italia.

Questo è uno studio trasversale. Ammissibili per lo studio sono state le donne di età > 18 anni che hanno partorito in giorni selezionati in modo casuale al dipartimento di ostetricia della Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico durante 3 periodi di due mesi tra il 2013 ed il 2015. Il protocollo di studio non prevedeva alcun criterio di esclusione. I ricercatori hanno identificato le donne ammissibili nei reparti ostetrici nei giorni scelti casualmente entro 3 giorni dal parto. Ogni donna che ha soddisfatto i criteri di inclusione ha accettato di essere intervistata. Sono state identificate complessivamente 648 donne (età media 35 anni, intervallo interquartile 32-38). Un questionario è stato somministrato durante l'intervista faccia a faccia. Delle donne intervistate 648, 132 (20, 4%, 95% CI: 17,3-23,5) ha soddisfatto i criteri per la diagnosi di RLS. Considerando le 132 con e le 516 senza RLS, rispettivamente 7 (5,5%) e 29 (5,6%) hanno avuto una diagnosi di ipertensione gestazionale (Odds Ratio aggiustato per età 0,89, 95% intervallo di confidenza 0,38-2,10). In conclusione malgrado le limitazioni il nostro studio non conferma la possibile relazione tra la RLS ed il rischio di ipertensione gestazionale.

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## INTRODUCTION

Restless legs syndrome (RLS) is a common, distressing movement disorder. It is characterised by discomfort of, and urge to, move the legs, primarily during rest or inactivity<sup>(1)</sup>. RLS has been associated with cardiovascular disease (CVD), hypertension, diabetes, and related disorders. A systematic review<sup>(2)</sup> has found that over half of the existing studies supported a positive association between RLS and hypertension, and that the variation in findings was primarily due to differences in participant demographics and disease assessment.

In etiologic terms, it has been suggested that individuals with RLS are more likely to develop hypertension because of the presence of periodic limb movements of sleep (PLMS)<sup>(3)</sup>, thus underlining the association between sleep disorders, and RLS. Recently, it has been reported a relationship between RLS and pregnancy-induced hypertension (PIH)<sup>(4,5)</sup>, a predictor of subsequent CVD and diabetes. However, the association between RLS and gestational hypertension remains little explored.

Pregnancy is a well recognized risk factor for the development of RLS and sleep disorders<sup>(6-8)</sup>. Thus in consideration of the contribution to maternal and perinatal morbidity and mortality of hypertension in pregnancy, the potential association between RLS and hypertensive disorders in pregnancy deserves attention.

In this brief paper we report the association between RLS and gestational hypertension observed in a study conducted in an European Caucasian population, a population characterized by a lower rate of hypertensive disorders in pregnancy<sup>(9)</sup> and not considered in the previous published studies on the association between RLS and hypertension in pregnancy.

## METHODS

This is a cross sectional study.

Eligible for the study were women aged >18 years who delivered in randomly selected days to the Department of Obstetrics of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, the largest maternity hospital in Milan, Italy, during 3 bimonthly periods in 2013-2015. The study protocol did not include any exclusion criteria.

The researchers identified eligible women in the obstetric wards on the randomly selected days within 3 days from delivery. Each woman who met the inclusion criteria agreed to be interviewed.

A total of 648 women (median age 35, interquartile range 32-38) were identified.

A questionnaire was administered during a face-to-face interview. This questionnaire included information about demographic characteristics (age, height, body weight, education, number of previous pregnancies), personal behavior (physical activity, smoking, alcohol drinking) and information on the newborn including centiles of weight according to Parazzini et al<sup>(10)</sup>.

Diagnosis of RLS was established on the basis of the International Restless Legs Syndrome Study Group criteria<sup>(1)</sup>. Gestational hypertension was defined according to the ACOG criteria<sup>(11)</sup>.

Odds ratios (OR) and corresponding 95% confidence interval (CI) of gestational hypertension were computed. We used unconditional multiple logistic regression, with maximum likelihood fitting including terms for age and parity.

This study was approved by the Institutional Review Board. Informed consensus was obtained.

## RESULTS

Out of the 648 interviewed women, 132 (20.4%, 95% CI: 17.3-23.5) met the criteria for diagnosis of RLS. The risk of RLS increased with age (**Table 1**).

Considering the 132 with and the 516 with and without RLS, 7 (5.3%) and 29 (5.6%) respectively had diagnosis of PHI (Odds Ratio adjusted for age: 0.89, 95% confidence interval 0.38-2.10).

This finding was consistent strata of age: the corresponding OR estimates were: 1.1, 0.9 respectively in women aged <35 and ≥ 35.

## DISCUSSION

Few previous studies have suggested a possible link between RLS and hypertensive disorders in pregnancy. In a study conducted in Peru and including 218 consecutive expectant mothers preeclampsia was more common in women with RLS<sup>(4)</sup>. In a large Chinese study including 3,781 pregnant women PHI was more common among the 453 patients with RLS<sup>(5)</sup>. However no difference was observed in the prevalence of chronic hypertension in pregnancy between women with and without RLS.

Further, it has been shown that a history of PHI was positively related to RLS later in life in a study of primary care patients<sup>(12)</sup>.

We did not confirmed this association. Potential limitations of our study could explain the lack of association between RLS and gestational hypertension observed in this study.

First of all, the limited numbers may explain our findings. Further, interviewed women were a sample of all women who delivered in the study period in the study center and not a random sample of all pregnancies in the study area. The interviewers identified the subjects in random sampled days during all the study period. Major selection bias, however, should not act in the identification of study subjects: the observed prevalence of RLS in our population is largely consistent with that reported in another Italian study<sup>(6)</sup>. The information were collected in a vis a vis interview and the potential association between gestational hypertension and RLS was not known to the pregnant women and the diagnosis of gestational hypertension was checked with clinical records.

Among other limitations we have to

consider that we did not analyze the severity of hypertension. Among the strengths of the study we have to include the fact that we considered the main potential confounding.

However, some differences among published studies should also be discussed. We have considered only gestational hypertension. The South American study<sup>(4)</sup> considered preeclampsia and not hypertension. In preeclamptic women renal impairment may play a role and some studies have suggested that RLS is associated with renal diseases.

Further, in the largest study conducted in China<sup>(5)</sup> the prevalence of gestational hypertension was slightly higher than in our population and in that study an association (OR 1,35) between RLS and gestational hypertension, but not chronic hypertension was observed.

In conclusion despite the limitations our study suggests that the relationship between RLS syndrome and gestational hypertension should be more careful analyzed in different populations.

**Table 1.**

*Distribution of interviewed women according to diagnosis of RLS and selected characteristics.*

	Rest Legs Syndrome				OR*	95% CI
	Yes		No			
	No.+	(%)	No.	(%)		
<u>Age (years)</u>						
< 35	47	(35.6)	249	(48.3)	1°	
≥ 35	85	(64.4)	267	(51.7)	1.69	(1.14-2.51)
<u>Pre-conception BMI (kg/m<sup>2</sup>)</u>						
≤ 20.2	42	(31.8)	167	(32.7)	1°	
20.3-23.0	44	(33.3)	170	(33.3)	0.99	(0.62-1.60)
≥ 23.1	46	(34.8)	174	(34.1)	1.02	(0.64-1.64)
<u>Education (years)</u>						
≤ 13	73	(55.3)	253	(49.0)	1.36	(0.92-2.00)
≥ 14	59	(44.7)	263	(51.0)	1°	
<u>Weight gain in pregnancy(kg)</u>						
≤ 15	99	(75.0)	408	(79.1)	1°	
> 15	31	(23.5)	103	(20.0)	1.24	(0.78-1.97)
<u>Parity</u>						
0	69	(52.3)	282	(54.7)	1°	
1	49	(37.1)	201	(39.0)	1.03	(0.72-1.51)
≥ 2	14	(10.6)	33	(6.4)	1.61	(0.81-3.19)
<u>Smoking</u>						
No	109	(82.6)	426	(82.6)	1°	
Yes	23	(17.4)	90	(17.4)	1.06	(0.64-1.77)
<u>Alcohol drinking in pregnancy</u>						
No	100	(75.8)	397	(76.9)	1°	
Yes	32	(24.2)	119	(23.1)	1.02	(0.65-1.60)

OR odds ratio; CI Confidence interval

\*Multivariate estimates adjusted for age

° Reference category °°Reference category: no

In some cases the sum does not add up to the toll due to missing values

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