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Research Article

**ASSOCIATION BETWEEN RESTLESS LEG SYNDROME (RLS) AND  
HYPERTENSION (HTN) IN ADULTS AT TAIF CITY, SAUDI ARABIA****Dr. Suzan Atia Alsaid <sup>\*1</sup>, Dalal Owith Al-osimi <sup>2</sup>, Fatima Moeesh Altalhi <sup>2</sup>,  
Nada Mohammed Al-Sufyani <sup>2</sup>, Reham Faleh Algethami <sup>2</sup>, Rana Adel Alkhalidi <sup>2</sup>,  
Norah Talal Alqarashe <sup>2</sup>**<sup>\*1</sup> Associate Professor, Taif University, College of Medicine, Taif City, Saudi Arabia.<sup>2</sup> Taif University, College of Medicine, Taif City, Saudi Arabia.**Abstract:**

**Introduction:** Restless leg syndrome (RLS) is a common neurological disorder in the community that is characterized by irresistible urge to move the extremities especially leg that is usually experienced during rest or at night. The study is aimed to assess the association between restless legs syndrome (RLS) and hypertension (HTN) among Saudi Arabia population.

**Materials and Method:** A pre-tested and validated questionnaire was used for data collection after identifying the participants who had RLS through hospital records. An online questionnaire was sent to 528 people who had RLS and we got completed responses from 386 participants thus giving a response rate of 73.1%. The questionnaire recorded socio-demographic details, presence of systemic diseases and common symptoms related to RLS. Data analysis was done using SPSS version 23 and Pearson's Chi-square test was used to find an association between categorical variables.

**Results:** The prevalence of hypertension among people with RLS was found to be 17.6%. The symptoms of RLS were predominantly seen more commonly among females than males and this showed a statistical significance ( $p < 0.05$ ). Also, most of the symptoms were seen more in the hypertensive patient than people those who didn't have the disease ( $p < 0.05$ ). The relationship between the presence of insomnia and hypertension showed a statistically significant association ( $p < 0.05$ ).

**Conclusion:** The findings of the study show a primary level of evidence of association with hypertension with Rest Leg Syndrome. People who suffered insomnia had also shown an association with RLS. There is a need for more analytical prospective studies to explore a causal relationship between hypertension and RLS.

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**INTRODUCTION:**

Restless leg syndrome (RLS) also called Willis-Ekbom disease (WED) is a neurological disorder that characterized by an irresistible urge to move the leg or other body parts usually accompanied by uncomfortable sensation that partially or totally relieved by movement. RLS mostly occurs during rest and at night. (1) RLS is idiopathic, but it can be secondary to pregnancy, diabetes mellitus (DM), end stage renal disease (ESRD) and iron deficiency anemia. (2) RLS is common among Saudi population where the prevalence of RLS in adults was estimated to be 5.2% - 8.4% of the Saudi general public. (1, 3)

The risk of RLS increased in individuals with chronic medical conditions such as cardiovascular disease, multiple sclerosis, Parkinson's disease, spinal cord disease, and neuropathy, HTN. (4) Hypertension (HTN) is a major public health problem in the Kingdom of Saudi Arabia (KSA) with a reported prevalence of 15.2%. (5)

The relationship between RLS and hypertension has been accumulating. A recent study done in Korea reported a significant association between them. (6) A meta-analysis study has also reported a relationship between RLS and HTN. (7) And 30% of hypertensive patients had RLS. (2) Furthermore, A study done by batool-Anwaratal. showed that Asian adults women with RLS were more likely to have hypertension by 95%. (8) However, a previous study done in Germany had reported a controversial result. It reported that RLS is not a significant indicator of hypertension. (9) In addition, A cross sectional studies demonstrated that people with RLS may develop cardiovascular disease as a complication of hypertension (10, 11). Furthermore, RLS and hypertension were not associated after adjustment for possible confounding factors. (12)

Published studies that have assessed the association between RLS and HTN among Saudi population are scarce. In this study, our aim is to assess the association between restless legs syndrome (RLS) and hypertension (HTN) in adults at Taif city, Saudi Arabia.

**MATERIALS AND METHODS:**

A cross-sectional study was conducted using a pre-tested and validated questionnaire among people who are diagnosed with restless legs syndrome (RLS). The age of the participants ranged between 18-60 years old with no gender discrimination. The study was conducted during the period of November 2019 and April 2020.

Participants were identified through hospital records who were diagnosed with RLS and contacted to participate in the study. The questionnaire was distributed as an online survey form. Patients were informed about the nature of study and those who gave consent to use their data was included for our analysis. Ethical clearance for the study was obtained from the Research Ethics Committee of Taif University.

The questionnaire consisted two parts: Part A included socio-demographic details and also had items that recorded systemic diseases prevalent in the participants. Part B had 10 closed end items that had dichotomous responses (YES/NO), which recorded symptoms related RLS. Participants were ensured confidentiality of their data and all the ID details were blinded during our analysis.

A minimum sample size of 252 was calculated for our study using the formula given below. Where  $Z=1.96$  at 95% confidence interval,  $p$  = proportion of the study population ( $P_0$ ) was 0.022 (2.2%), sample proportion ( $P_\alpha$ ) was 0.052 (5.2%) and  $d$  = degree of accuracy (0.05). Hence the sample size ( $n$ ) 246 was calculated applying the above values for our study. We finally included a sample size of 386 for our analysis.

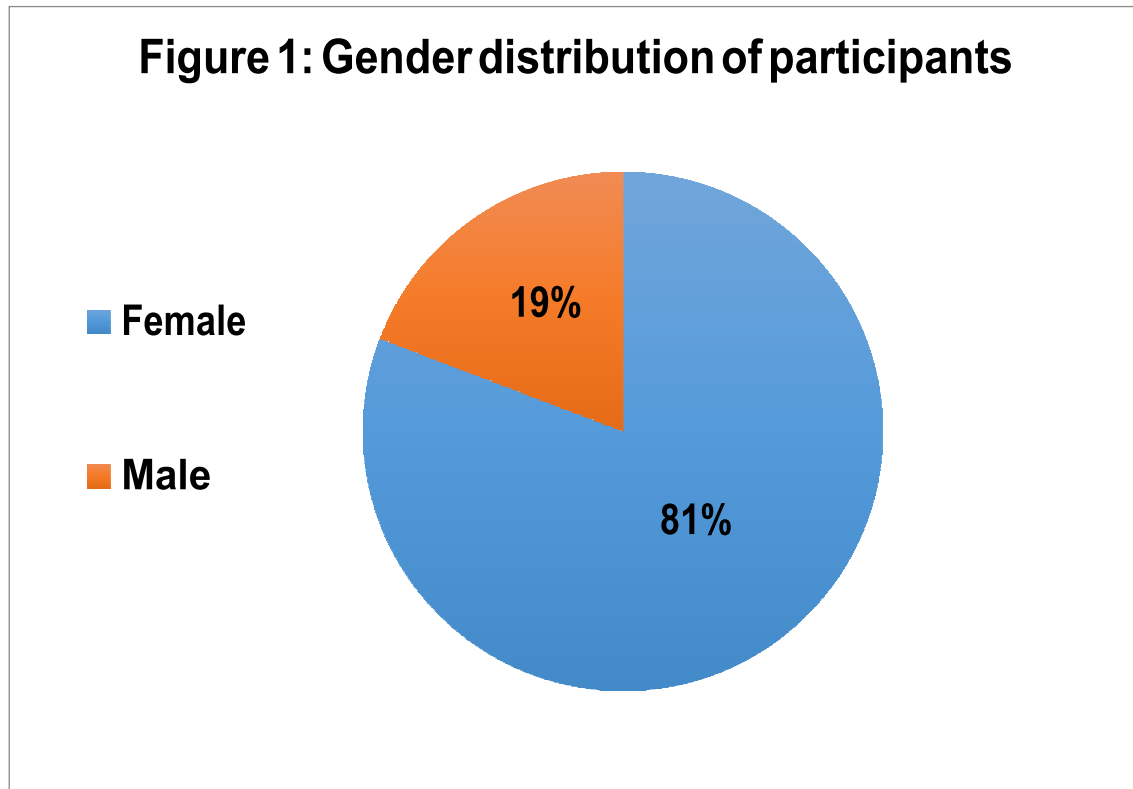
$$n = \frac{\{Z_{1-\frac{\alpha}{2}}\sqrt{P_0(1-P_0)} + Z_{1-\beta}\sqrt{P_\alpha(1-P_\alpha)}\}^2}{(P_\alpha - P_0)^2}$$

**Data management and Statistical analysis:**

Data collected were entered in MS excel and tabulated accordingly by one of the independent investigators. The statistical analysis was done using SPSS ver 23. A significance value ( $\alpha$ )  $p < 0.05$  were considered to be statistically significant and confidence interval was set at 95% with a power of test ( $\beta$ ) of 80%. Frequencies and percentages were used for categorical variables in descriptive analysis. Continuous variables were presented as mean with standard deviation. Pearson's Chi-square test was used for testing any statistically significant association of categorical variables. (3)

**RESULTS:**

The final analysis of our study included a sample included 386 participants who satisfied our study criteria that had 80.8% females ( $n=312$ ) and 19.2% males ( $n=74$ ) (Figure 1). The prevalence of Hypertension and diabetes mellitus was found to be 17.6% and 12.4% respectively (Table 1). The smoking status of participants showed that 7.3% were smokers and 2.8% were reported to be ex-smokers (Table 1).



When the relationship of symptoms of RLS with the gender of participants was analyzed it was observed that some symptoms were more predominant among females than males. The participants who reported that they repeatedly moved the legs while sitting or lying down were 85% females and this was statistically significant ( $X^2=5.99, p<0.014$ ) and also it was 86.4% females who reported that they had a 'frequent need' to move their legs while sitting or lying down [ $X^2=8.87, p<0.003$ ]. (Table 2). It was also reported that these symptoms showed improvement when getting up, on moving and/or doing any physical activity among 48.4% ( $n=187$ ) participants, of which 85.6% of them were females [ $X^2=5.24, p<0.022$ ] (Table 2). 22.8% of the participants reported that they had these symptoms repeated daily and there was no statistically significant association observed with gender ( $p=0.512$ ).

The relationship between the prevalence of hypertension with the RLS symptoms showed that most of them had a statistically significant association (Table 3). 22.1% of the participants who reported that

they moved the legs repeatedly while sitting or lying down had hypertension [ $X^2=7.632, p=0.006$ ] and also these symptoms were felt during rest comparatively more in people in hypertension [ $X^2=6.484, p<0.011$ ]. The repeated movement of legs was seen among 26.16% participants when they were physically active and it was observed among 31.7% of the participants who had hypertension [ $X^2=18.650, p<0.001$ ]. 27.3% of participants who had these symptoms repeated daily were hypertensive ( $X^2=7.323, p=0.007$ ) and 27.9% of participants who suffered from snoring had hypertension [ $X^2=5.247, p=0.022$ ]. It was also observed that 40.15% [ $n=155$ ] of the participants had insomnia and this showed a statistically significant association with hypertension (24.5%) [ $X^2=8.495, p=0.004$ ] (Table 3)

When the relationship of diabetes mellitus with the symptoms related to RLS was seen, there was no statistically significant association observed except with participants who suffered from snoring [ $X^2=12.66, p<0.001$ ] and insomnia [ $X^2=7.533, p=0.006$ ] (Table 4).

		Frequency	Percent
<b>Smoking status</b>	Ex. smoker	11	2.8
	No	347	89.9
	Yes	28	7.3
<b>Sports</b>	No	254	65.8
	Yes	132	34.2
<b>Dyslipidemia</b>	No	337	87.3
	Yes	49	12.7
<b>Diabetes Mellitus</b>	No	338	87.6
	Yes	48	12.4
<b>Hypertension</b>	No	318	82.4
	Yes	68	17.6

		Gender		Total	Pearson Chi-Square	P value	
		Female	Male				
Do you want to move the legs repeatedly while sitting or lying down?	No	N	120	40	160	5.992	0.014
		%	75.0%	25.0%	100.0%		
	Yes	N	192	34	226		
		%	85.0%	15.0%	100.0%		
Do you have a frequent need to move your legs while sitting or lying down:	No	N	134	46	180	8.872	0.003
		%	74.4%	25.6%	100.0%		
	Yes	N	178	28	206		
		%	86.4%	13.6%	100.0%		
Are you more likely to feel this feeling during rest (either sitting or lying down):	No	N	152	44	196	2.761	0.097
		%	77.6%	22.4%	100.0%		
	Yes	N	160	30	190		
		%	84.2%	15.8%	100.0%		
Are you more likely to feel this way when you are physically active:	No	N	227	58	285	0.978	0.322
		%	79.6%	20.4%	100.0%		
	Yes	N	85	16	101		
		%	84.2%	15.8%	100.0%		
If you experience this feeling during rest, do you feel any improvement when getting up, moving, or doing any physical activity:	No	N	152	47	199	5.243	0.022
		%	76.4%	23.6%	100.0%		
	Yes	N	160	27	187		
		%	85.6%	14.4%	100.0%		
Are you more likely to feel this in the morning:	No	N	238	63	301	2.730	0.098
		%	79.1%	20.9%	100.0%		
	Yes	N	74	11	85		
		%	87.1%	12.9%	100.0%		
Are you more likely to feel this at night:	No	N	198	51	249	0.778	0.377
		%	79.5%	20.5%	100.0%		
	Yes	N	114	23	137		
		%	83.2%	16.8%	100.0%		
Are these symptoms repeated daily:	No	N	243	55	298	0.431	0.512
		%	81.5%	18.5%	100.0%		
	Yes	N	69	19	88		
		%	78.4%	21.6%	100.0%		
Do you suffer from snoring:	No	N	273	52	325	13.345	0.000
		%	84.0%	16.0%	100.0%		
	Yes	N	39	22	61		
		%	63.9%	36.1%	100.0%		
Are you suffering from insomnia:	No	N	183	48	231	0.960	0.327
		%	79.2%	20.8%	100.0%		

	Yes	N	129	26	155		
		%	83.2%	16.8%	100.0%		

**Table 3: Relationship between Hypertension and rest leg syndromes symptoms**

		Hypertension			Total	Pearson Chi-Square	P value
		No	Yes				
Do you want to move the legs repeatedly while sitting or lying down?	No	N	142	18	160	7.632	0.006
		%	88.8%	11.3%	100.0%		
	Yes	N	176	50	226		
		%	77.9%	22.1%	100.0%		
Do you have a frequent need to move your legs while sitting or lying down:	No	N	160	20	180	9.835	0.002
		%	88.9%	11.1%	100.0%		
	Yes	N	158	48	206		
		%	76.7%	23.3%	100.0%		
Are you more likely to feel this feeling during rest (either sitting or lying down):	No	N	171	25	196	6.484	0.011
		%	87.2%	12.8%	100.0%		
	Yes	N	147	43	190		
		%	77.4%	22.6%	100.0%		
Are you more likely to feel this way when you are physically active:	No	N	249	36	285	18.650	0.000
		%	87.4%	12.6%	100.0%		
	Yes	N	69	32	101		
		%	68.3%	31.7%	100.0%		
If you experience this feeling during rest, do you feel any improvement when getting up, moving, or doing any physical activity:	No	N	170	29	199	2.622	0.105
		%	85.4%	14.6%	100.0%		
	Yes	N	148	39	187		
		%	79.1%	20.9%	100.0%		
Are you more likely to feel this in the morning:	No	N	258	43	301	10.499	0.001
		%	85.7%	14.3%	100.0%		
	Yes	N	60	25	85		
		%	70.6%	29.4%	100.0%		
Are you more likely to feel this at night:	No	N	212	37	249	3.674	0.055
		%	85.1%	14.9%	100.0%		
	Yes	N	106	31	137		
		%	77.4%	22.6%	100.0%		
Are these symptoms repeated daily:	No	N	254	44	298	7.323	0.007
		%	85.2%	14.8%	100.0%		
	Yes	N	64	24	88		
		%	72.7%	27.3%	100.0%		
Do you suffer from snoring:	No	N	274	51	325	5.247	0.022
		%	84.3%	15.7%	100.0%		
	Yes	N	44	17	61		
		%	72.1%	27.9%	100.0%		
Are you suffering from insomnia:	No	N	201	30	231	8.495	0.004
		%	87.0%	13.0%	100.0%		
	Yes	N	117	38	155		
		%	75.5%	24.5%	100.0%		

Table 4: Relationship between Diabetes Melites and rest leg syndromes symptoms							
			Diabetes Melites		Total	Pearson Chi-Square	P value
			No	Yes			
Do you want to move the legs repeatedly while sitting or lying down?	No	N	146	14	160	3.408	0.064
		%	91.3%	8.8%	100.0%		
	Yes	N	192	34	226		
		%	85.0%	15.0%	100.0%		
Do you have a frequent need to move your legs while sitting or lying down:	No	N	163	17	180	2.770	0.096
		%	90.6%	9.4%	100.0%		
	Yes	N	175	31	206		
		%	85.0%	15.0%	100.0%		
Are you more likely to feel this feeling during rest (either sitting or lying down):	No	N	170	26	196	0.251	0.615
		%	86.7%	13.3%	100.0%		
	Yes	N	168	22	190		
		%	88.4%	11.6%	100.0%		
Are you more likely to feel this way when you are physically active:	No	N	251	34	285	0.255	0.613
		%	88.1%	11.9%	100.0%		
	Yes	N	87	14	101		
		%	86.1%	13.9%	100.0%		
If you experience this feeling during rest, do you feel any improvement when getting up, moving, or doing any physical activity:	No	N	178	21	199	1.337	0.248
		%	89.4%	10.6%	100.0%		
	Yes	N	160	27	187		
		%	85.6%	14.4%	100.0%		
Are you more likely to feel this in the morning:	No	N	268	33	301	2.719	0.099
		%	89.0%	11.0%	100.0%		
	Yes	N	70	15	85		
		%	82.4%	17.6%	100.0%		
Are you more likely to feel this at night:	No	N	225	24	249	5.039	0.025
		%	90.4%	9.6%	100.0%		
	Yes	N	113	24	137		
		%	82.5%	17.5%	100.0%		
Are these symptoms repeated daily:	No	N	265	33	298	2.225	0.136
		%	88.9%	11.1%	100.0%		
	Yes	N	73	15	88		
		%	83.0%	17.0%	100.0%		
Do you suffer from snoring:	No	N	293	32	325	12.660	0.000
		%	90.2%	9.8%	100.0%		
	Yes	N	45	16	61		
		%	73.8%	26.2%	100.0%		
Are you suffering from insomnia?	No	N	211	20	231	7.553	0.006
		%	91.3%	8.7%	100.0%		
	Yes	N	127	28	155		
		%	81.9%	18.1%	100.0%		

**DISCUSSION:**

The primary objective of our study was to assess the relationship of hypertension with Restless Leg Syndrome (RLS). Epidemiological data have shown that the prevalence of RLS in the population is between 5-15%, which slightly increased with age (14-16). The disorder is currently reported more among females than males and the prevalence is found to be more in pregnant women that range from 11-29% (17,18). American and European populations showed a higher prevalence of RLS compared to Asia. (14,19) The exact etiology of RLS is still unclear and is considered as both a sensorimotor and a sleep disorder that is suggested to have a genetic basis of autosomal genetic inheritance (20). Several medical conditions have shown a consistent association with RLS such as pregnancy, iron deficiency, renal failure, anxiety disorders, attention-deficit/hyperactivity disorder (21). Some of the systemic disorders such as coronary heart diseases (CHD) and stroke have also shown positive association with RLS (22-24).

Even though the exact mechanism of an increased risk of CHDs in RLS is not clear, the periodic limb movements (PLMS) during sleep may elevate blood pressure thus causing hypertension in such instances(25,26). The association of hypertension is not well documented in the scientific literature and our study findings showed that the prevalence of hypertension among people who had RLS was about 17.6%. Our findings are consistent with previous literature suggesting a possible role of hypertension in the pathophysiology of RLS (27-29). Most of the people with RLS have the PLMS during sleep that is a rhythmic extension of the legs (toe and dorsiflexion of the ankle), which would lead to elevations in heart rate and blood pressure (30-32). This elevation of blood pressure at night leads to the development of hypertension during the daytime (33). It is also reported that the prevalence of PLMS in patients with grade 3 hypertension is double than those with grade 1 and 2 (34). This suggests that antihypertensive drugs could reduce the frequency of RLS indirectly by decreasing the risk of Coronary heart diseases (35). The suggested first line of treatment for RLS are dopaminergic drugs such as pramipexole and ropinirole as a large number of clinical findings and pharmacological studies have shown strong evidence in the role of dopaminergic system dysfunction in RLS (36,37). But other dopamine agonists such as Pergolide and cabergoline are not recommended as these have an increased risk of coronary heart diseases (38).

Our study also assessed the prevalence of type 2 Diabetes Mellitus (T2DM) among RLS patients and it was found to be 12.4%. Studies show that the prevalence of T2DM among RLS patients in the

general population ranges from 5-10% (39). Evidence shows that high blood sugar levels often cause nerve damage that may lead to diabetic peripheral neuropathy thereby contributing to RLS (40). In Saudi Arabia, the prevalence of hypertension (25- 27%) and T2DM (23-28%) is comparatively higher and this could be a pre-disposing to RLS among this population (41-43). We also found that the prevalence of RLS was comparatively more in women than men, which suggests that the female gender is a predisposing factor for RLS. Pieces of evidence show that the prevalence of RLS among woman is twice as men and our results support those findings (44). But our findings are not concurrent with another study done at the primary health care setting in Saudi Arabia, even though there was more prevalence of RLS among aged female patients (13). In another study done in Kingdom also showed that the prevalence of RLS among pregnant women is more than non-pregnant women (45). This increased pre-disposition could be explained based on the elevated levels of sex hormones (especially estrogen) that increase the severity of RLS symptoms and this is found to be in peaks in the early morning hours (2 am - 4 am) (46-48).

Several limitations of this study should also be considered before interpreting the findings. Our study design was cross-sectional and it is challenging to generalize the findings to the whole Saudi population. Secondly some of the findings (especially symptoms of RLS) of our study depend on self-reports and there could be a possibility of recall bias. It is not always possible to assess all the predisposing factors to RLS in our questionnaire by including more items as it could have decreased the response rate. Hence we focused more on our primary objective to assess the association between hypertension and RLS. Thus the possibility of confounding bias is also not limited to our study. All these limitations should be considered before drawing up a conclusion.

**CONCLUSION:**

The findings of our study show that there is a shred of primary level evidence that patients with RLS have a higher chance of getting hypertension or vice versa. The prevalence of T2DM is also found to be comparatively higher in RLS patients. Most of the time it has become difficult for the primary care physician to diagnose and manage RLS. Identifying the co-morbidities and other predisposing factors should be identified for proper management of this disorder. More comprehensive analytic studies are required to show a confirmatory casual relationship between RLS and hypertension.

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