PREVALENCE OF RESTLESS LEG SYNDROME AND QUALITY OF LIFE AMONG FEMALES WITH REPRODUCTIVE AGE

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ABSTRACT:

The aim of this study was to determine the prevalence of restless leg syndrome among non-pregnant females of reproductive age and to find effect of RLS on quality of life of females. An observational cross-sectional study was conducted on the general population of District Gujrat, Pakistan. A sample of 304 non-pregnant females of reproductive age (15-49 years) were interviewed face to face and data was collected regarding presence and RLS severity and quality of life using Restless Legs Syndrome Short Form 2 diagnostic questionnaire (CH-RLSQ13), Self-administered version of international restless leg syndrome study group rating scale(sIRLS) and Restless leg syndrome quality of life instrument (RLS-QLI). All data was analysed with SPSS (Social Sciences Statistical Package) version 21. Among 304 participants, mean age was 28.16 ± 14.167 years (range 15-49). According to CH-RLSQ13 score prevalence of RLS was 45.4%. Out of 138 participants, 8.9% out of 138 participants, 8.9% had severe RLS 28% moderate RLS and 11(3.6) % mild RLS. According to scores obtained from RLS severity scale. According to RLS-QLI means scores for QOL domains were social functioning (63.76 ± 19.24), daily functioning (63.75 ± 18.17), sleep quality (43.48 ± 5.36) and emotional well-being (46.07 ± 21.37). High prevalence (45.4%) of RLS was found among non-pregnant females of reproductive age. with moderate to severe severity. Reduced quality of life was found among RLS positive females with sleep quality and emotional well-being greatly affected

Keywords: Restless Legs Syndrome, Willis Ekbom Syndrome, Quality of Life, Reproductive age,

INTRODUCTION

Restless legs syndrome(RLS) Or Ekbom syndrome is a common sensorimotor neurological disorder that is characterized by an urge to move the legs due to unpleasant sensations. The symptoms occur at rest, are relieved by movement, and usually worsen in the evening.[1] it is very underdiagnosed and very commonly occurring complaint[2]. Restless legs syndrome (RLS) affects 5% of the population[2].It more commonly occurs in females than males[2]

Patients suffering from RLS usually face difficulty in describing their symptoms they often have funny explanations like creeping or crawling sensation, or they may describe their symptoms as pain, fluttery, moving worms, bubbling soda like feeling in veins, and feeling like their bones are itching. A study conducted in Pakistan has shown a RLS point prevalence of 23.6% with female preponderance.[3]Reproductive age according to WHO (world health organization) is 15-49 years[4].

Restless leg syndrome (RLS) may be primary or secondary. The primary type can be hereditary and have early onset and is slowly progressive. However exact cause of primary RLS is unknown .Secondary RLS develops as a result of any underlying condition or drugs , it have fast progression and late onset[5]

RLS places significant impact on an individual's quality of life (QOL)[6]. The increase in RLS symptoms at night causes sleep disturbances, this may result in chronic sleep deprivation, drowsiness during daytime and stress, this places a negative impact on daily life functioning, social life, family life, work, enjoyment and other aspects of life. For example , it is difficult for RLS patients to participate in prolonged sitting activities(travel or watching movies) as this may exacerbate their symptoms.[6]

According to scientific literature, Increased incidence of RLS in women may be due to estrogen and other hormonal changes[7]. Vitamin d deficiency may be related to RLS and according to a study conducted in Pakistan, 73% of women of child bearing age were vitamin d deficits so vitamin D deficiency is found to be highly prevalent among women of child bearing age[8,9]. Many studies have demonstrated the association of RLS and iron deficiency[10], iron deficiency is also more common in women of reproductive age [11]. Comorbidities like migraine, depression, anxiety have major association with high prevalence in women. These disorders are more common in women than men[7].

To the best of my knowledge only one study is available regarding prevalence of prevalence of restless leg syndrome specifically in women of reproductive age and according to that study which was conducted in Saudi Arabia RLS is found to be common among women of child bearing age with a prevalence of 24[12]. An older study conducted in Sweden in 2010 assessed prevalence of RLS and health related quality of life(HRQOL) in women[13].

As no research data is available regarding prevalence of RLS specifically among non-pregnant women of reproductive age and impact this disease places on their QOL in Asia, so our study aims to address this research gap. So, with the availability of data through our research better health services for RLS can be developed in future, better preventive measures can be defined, and further measures and better interventions can be developed to improve quality QOL affected by RLS.

MATERIAL AND METHODS:

Study design, duration and setting

A descriptive cross-sectional study was conducted between august 2022 and November 2022. A sample of 304 non-pregnant females of reproductive age 15-49 years were selected from General population of Gujrat district of Pakistan who agreed to participate in the study.

Sampling technique and sample size calculation

Nonprobability convenient sampling technique was used. Sample size n=304 was calculated using below mentioned formula10 and WHO recommended calculator

$$n = (Z1\text{-}\alpha/2)^2 \ (p)(1\text{-}p)/(d)^2$$

$$n = (1.96)^2(0.22)(0.78) \ / \ (0.05)^2$$

$$n = 264 + 14\% \ dropout(40) = 304 \ total \ sample \ size$$

Participants

Non pregnant females of reproductive age 15-49 years were included in the study. Exclusion criteria included women with diagnosed conditions that may mimic RLS symptoms including [12,14].Peripheral neuropathy, Radiculopathy, Akathisia (hypotensive, neuroleptic induced), Arthritis (involving lower limb), Reported psychiatric disorders ,those who are taking antidepressants, sleep disorder (Periodic limb movement disorder).

Ethical approval and Consent

Ethical approval was taken from Institutional Review Board (IRB) of University of Lahore, Punjab, Pakistan. An informed was taken from the participants before collecting data. Ensured that data would be used for only research purpose.

Data collection procedure and outcome measures

The participants were interviewed face to face, informed consent was taken from all the participants. The research project was approved by research and ethics committee of University of Lahore. Collected data comprised of demographics, for RLS data Cambridge- Hopkins Restless Legs Syndrome Short Form 2 diagnostic questionnaire (CH-RLSQ13) was used. Demographics data included participants age and marital status. Cambridge- Hopkins Restless Legs Syndrome Short Form 2 diagnostic questionnaire (CH-RLSQ13)[15] was used for diagnosis of Restless Leg Syndrome(RLS) which is a structured questionnaire for RLS diagnosis Self-administered version of international restless leg syndrome study group rating scale(sIRLS)[16] to determine the RLS severity in those participants who were diagnosed of having RLS. Restless leg syndrome quality of life instrument (RLSQLI)[17], was used to collect data regarding RLS effect on quality of life of RLS positive participants.

Self-administered version of international restless leg syndrome study group rating scale(sIRLS)[16] to determine the RLS severity in those participants who were diagnosed of having RLS. RLS severity questionnaire had 10 questions and according to scoring criteria provided RLS severity is categorized into very severe, severe, moderate, mild and none.

Restless leg syndrome quality of life instrument (RLS-QLI)[17] was used to collect data regarding RLS effect on quality of life of RLS positive participants. Restless leg syndrome, quality of life instrument (RLSQLI)[17] contains 17 questions, QOL domains are social function, daily function , sleep quality and emotional well-being. Individual domain scores are transformed on a scale of 0-100 according to scoring criteria provided. Closer the score is to mean poor QOL and closer to 100 means good QOL.

Statistical analysis

Data were entered and analysed using Statistical Package for Social Sciences (SPSS) software version 20. For descriptive analysis, mean and standard deviation was calculated for

quantitative variables whereas frequencies and percentages were calculated for qualitative variables. For inferential statistics, Chi-square test was applied. All results were calculated at 95% confidence interval and p-value ≤ 0.05 was considered as significant value.

RESULTS

During this study period, 304 non pregnant women of mean reproductive age in years 28.16 ± 14.167 years who agreed to participate in the study were interviewed face to face and data was collected related to RLS diagnosis, severity and impact on quality life. Out of 304 females 86(28.3%) were in age group 15-21 years, 103(33.9%) in 22-28 years, 59(19.4%) in 29-35 years, 31(10.2%) in 36-42 years and 25(8.2%) in 43-49 years. Of 304 participants 150(49.30%) were unmarried and 154(50.70%) were married. Table.1 shows demographic characteristics of participants described above

Table 1. Socio-demographic characteristics

Variables	Responses	n (%)	Mean ± S.D
Age of respondent (years)	15-21	86(28.3)	28.16 ± 14.167
	22-28	103(33.9)	
	29-35	59(19.4)	
	36-42	31(10.2)	
	43-49	25(8.2)	
Marital status of respondent	Unmarried	150(49.3)	
	Married	154(50.7)	
Total		304(100.0)	

Table 2. shows that out of total of 304 non- pregnant females of reproductive age participated in the study. The presence of RLS was confirmed in 138(45.4%) of the participants according to CH-RLSQ-13 diagnostic questionnaire and 166(54.6%) didn't have RLS. According to scoring criteria of CH-RLSQ13 89(29.3%) had definite RLS ,4(1.3%) had probable RLS, and 45(14.8%) had clinically significant RLS. Prevalence of RLS is shown in Figure 1.

Of the non-pregnant females of reproductive age who had RLS,11(3.9%) had mild severity, 85(28%) moderate severity, 27(8.9%) had severe severity and 3(1%) experienced very severe severity., while 12 of the participants didn't experience any symptoms in the past 7 days so they had no severity

Out of the 304 RLS positive females, 10(3.3%) experienced RLS symptoms on daily basis, 10(3.3%) experienced four to five times per week, 38(12.5%) of the participants

experienced 2-3 days per week,43(14.1%) experienced once a week, 23(7.650 experienced 2 days per month and1 14(4.6%) experienced these symptoms once a month.

Table 2. Restless Leg Syndrome prevalence, Diagnostic categories and Severity

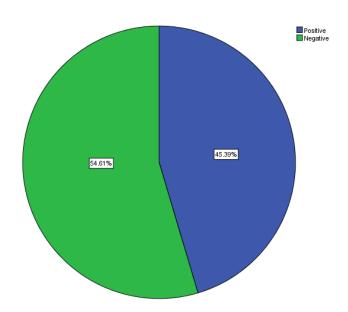| Variable	Responses	n (%)
Restless Leg Syndrome	Positive	138(45.4)
	Negative	166(54.6)
RLS diagnostic categories	Definite RLS	89(29.3)
	Probable RLS	4(1.3)
	Not RLS	166(54.6)
	Clinically significant RLS	45(14.8)
Severity of RLS	Very severe	3(1.0)
	Severe	27(8.9)
	Moderate	85(28.0)
	Mild	11(3.6)
	None	12(3.9)
	N/A	166(54.6)
Frequency of RLS symptoms	Every day	10(3.3)
	4-5 days per wk	10(3.3)
	2-3 days per wk	38(12.5)
	1 day per wk	43(14.1)
	2 days per month	23(7.6)
	1 day per month or less	14(4.6)
	N/A	166(54.6)
Total		**304100.0**

Figure 1. Prevalence of Restless leg syndrome

Table 3. shows association of marital status and age with prevalence of RLS was not found to be statistically significant.

Table 3. Association of age and marital status with prevalence of RLS

			Prevalence of Restless leg syndrome		Total	Chi-square	P value
			Positive	Negative			
Association of Marital status and Restless Leg Syndrome	Marital status of respondent	Unmarried	60(43.50%)	90(54.20%)	150(49.30%)	3.477	0.062
		Married	78(56.50%)	76(45.80%)	154(50.70%)		
Association of age and Restless leg syndrome	Age of respondent (years)	15-21	35(25.40%)	51(30.70%)	86(28.30%)	3.568	0.468
		22-28	49(35.50%)	54(32.50%)	103(33.90%)		
		29-35	24(17.40%)	35(21.10%)	59(19.40%)		
		36-42	18(13.00%)	13(7.80%)	31(10.20%)		
		43-49	12(8.70%)	137.80%	25(8.20%)		
Total			138(100.0%)	166(100.0%)	304(100.0%)		

Table 4. shows that, In RLS positive females, mean scores for QOL domains for social functioning (63.76±19.24), daily functioning (63.75±18.17), sleep quality (43.48±5.36) and emotional well-being (46.07±21.37) were found

Table 4. Quality of Life domain scores

QOL Domains	Prevalence of RLS	
	RLS Positive	RLS Negative
	Mean ± SD	
Social Function	63.76±19.24	N/A
Daily Function	63.75±18.17	
Sleep Quality	43.48±5.36	
Emotional Well-being	46.07±21.37	

DISCUSSION:

The purpose of this descriptive cross-sectional study was to find out prevalence of RLS among non-pregnant females of reproductive age and impact of RLS on quality of life of these females. According to previous studies, RLS is found to be more prevalent among females[3,18,19]. Mahmood K et al reported that prevalence of RLS was twice high in females as compared to males[3]. Ishaq M, Riaz SU, Iqbal N, Siddiqui S, Moin A, Sajjad S et al. also found that RLS occurs more in females in a population of medical students in Karachi . Anand S et

al. also found that RLS occurs more in females. In our study we selected non pregnant female of reproductive age as RLS prevalence needs to be evaluated in this population due to scarcity of data regarding this. We excluded other conditions that mimic RLS so to accurately diagnose RLS.

First major finding of our study was that, we found high prevalence of RLS 45.4% among non-pregnant females of reproductive age of Gujrat, Pakistan, which is almost twice higher as compared the study conducted in Saudi Arabia in 2020 by Almeneessier AS et al, they found a prevalence of 24% in a sample of 271 non-pregnant Saudi females of childbearing age. They used International Restless Legs Syndrome Study Group criteria (IRLSSG) for diagnosis of RLS, but current study used a validated structured questionnaire for RLS diagnosis so that muscle cramps and positional discomfort like condition that mimic RLS were excluded and more accurate diagnosis of RLS was made. High prevalence found in our study might be due to vitamin D deficiency and anemia. As Iron deficiency anemia is previously found to be a risk factor for RLS[20-22]. High prevalence of anemia has been found among females of reproductive age in Pakistan by Ali SA, Abbasi Z, Shahid B, Moin G, Hambidge KM, Krebs NF et al[23]. Vitamin D deficiency has been previously found to be associated with RLS[24] .High prevalent of Vitamin d deficiency has been found in Pakistan according to a study by Junaid K et al[25].

Some studies conducted in Pakistan on RLS prevalence are, Saleem S et al. in 2020 reported a frequency of RLS in pregnant females to be 54% [26]. Mahmood K et al. found high prevalence of RLS (23.6%). They used IRLSSG criteria for RLS diagnosis and no measures were takes to exclude mimics of RLS in this study[27]. Fasih A et al. found prevalence of RLS in industrialized area of Pakistan to be 31.90%. Another study conducted by Mubeen SM et al. in 2022 in a sample of 478 pregnant women they found low prevalence(11%)[28].but our study is focused on non-reproductive age females of Pakistan and prevalence was found to be higher(45.4%) than in studies conducted in Pakistan described above.

Of 304 participants, majority of the females 89(29.3%) had definite RLS while only 4(1.3%) had probable RLS 4(1.3%), clinically significant RLS was found in 45(14.8%) which can either be definite or probable RLS. Most of the participants had definite RLS.

Out of the 304 RLS positive females, most of the participants experienced RLS symptoms two to three times per week 38(12.5%) and 43(14.1%) experienced once a week while equal no of participants 10(3.3) experienced symptoms of RLS on daily basis and four to

five times per week, , 23(7.6) experienced these symptoms bimonthly and(4.6%) experienced these symptoms once per month. In a study by Didriksen M, Rigas AS, Allen RP, Burchell BJ, Di Angelantonio E, Nielsen MH et al. most of the participants 46.0% experienced RLS symptoms once in a week, 18.5% experienced the symptoms two to three times a week, and 10.1% experienced the symptoms more than four times a week. participants who reported no experience of RLS symptoms for the past 12 months prior to inclusion were not classified as suffering from RLS.

Severity of RLS was found to be moderate to severe in most of the participants of our study. Only 3(1%) of the RLS positive females had very severe RLS, 27(8.9%) had severe RLS, 85(28.0%) had moderate RLS severity and only 11(3.6%) had mild RLS. RLS severity among non-pregnant child bearing age females found by Almeneessier AS et al, was mild to moderate in majority(85%) of the participants, but our study reports a higher severity as compared to this[12]. Högl B, Kiechl S, Willeit J, Saletu M, Frauscher B, Seppi K et al. also found moderate to severe RLS among two third of the participants in a community based study[29]. Ataide MF et al. found RLS severity to be moderate to severe among MG patients[30]

Another major finding of our study is the impact of RLS on quality of life of the population under study. On a scale of 0-100 in which closer the score is to 100 means good quality of life and closer to 0 means poor quality of life. QOL domains assessed in our study are social function, daily function, sleep quality and emotional well-being. Mean scores of QOL obtained for RLS positive females are 63.76±19.24SD, 63.75±18.17, 43.48±5.36, 46.07±21.37 for social function, daily function, sleep quality and emotional well-being respectively. These findings suggest that QOL of patients suffering from RLS is significantly reduced. Daily and social functioning domains of QOL are almost equally affected by RLS with fair quality of life scores but higher scores as compared to sleep quality and emotional well-being scores. Poor QOL scores were found for sleep quality and emotional well-being.

These finding are found to be consistent with previous studies which assessed impact of RLS on QOL in different population[31-35].Pinheiro T et al. in 2022 reported that RLS resulted in poor sleep quality and affected overall quality of life in diabetics[35]. Tuna Oran N et al. in 2021 also reported reduced quality of life in pregnant females suffering from RLS as compared to those who don't suffer from RLS[32]. As higher impact of RLS was found on sleep quality ,Turk AC et al. also confirmed the adverse impact of RLS on sleep quality and fatigue[33].

An older study conducted on women ,found that mental aspects of HRQOL are impaired among women having RLS as compared to those who don't have RLS while physical HRQOL is very minimally affected.[13] ,similarly emotional well-being is also found to be significantly affected by RLS in our study. Kutlu R et al. (2018) found that physical aspects of life are affected by this syndrome in chronic hemodialysis patients [31] similarly our study confirmed that RLS impacts daily functioning of participants

Poor sleep quality has been found to be associated with physical fitness performance females. i.e. subjects with poor sleep quality had decreased cardiovascular fitness ,muscle endurance, and flexibility[36].

Association of RLS with age was not found to be statistically significant with p-value >0.05, similarly Wali SO et al. found no association of age and prevalence of RLS[37]. Our study contradicts Almeneessier AS et al. found significant association of age with RLS. Our finding of no association of age with prevalence of RLS[12]. Marital status of the participants was also not found to be associated with prevalence of RLS

In summary, approximately half of the non-pregnant females of reproductive age had RLS in the current study. Majority of participants had severe and moderate levels of RLS. QOL is also found to be reduced in RLS positive females with sleep quality and emotional well-being were greatly affected, social function and daily function suggested fair QOL scores as compared to sleep quality and emotional well-being scores.

This study has strengths and limitations. Strengths include a large sample size and use of a structured questionnaire for diagnosis of RLS, so that RLS is not misdiagnosed due to mimics like positional discomfort and muscle cramps like conditions that mimic RLS were excluded from the study.

Limitations include that study was conducted in one district only due to limited resources and lack of time. Additionally, risk factors that contribute to prevalence of RLS were also not assessed in our study

High prevalence found in current study suggests that further studies are recommended to assess the possible risk factors of high prevalence of RLS among study population, clinical trials are recommended to define better treatment measures to cope with RLS symptoms and regain better QOL and its severity. Patients with RLS should be advised to seek physician

consultation for early recognition and treatment. More awareness regarding RLS is needed in general population.

CONCLUSION:

High prevalence of RLS was found among non-pregnant females of reproductive age. Severity of RLS was predominately moderate and severe. All QOL domain scores were reduced among RLS positive females. Scores were higher (fair QOL) for social and daily functioning as compared to sleep quality and emotional well-being scores, which were lower with poor QOL.

Conflict of interest: There was not any conflict of interest.

Data Availability: Data will be provided on demand by corresponding author.

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