Restless Legs Syndrome in Hemodialysis Patients

Mehrdad Sharifi 1, Hamidreza Samimagham 2, Javad Golmirzaei 3, Maryam Baghban 4, Saed Hosseini 3, Abbas Paknahad 4, Payam Sadeghi 4, Mohadese Unesi 4, Hamidreza Mahboobi 4, Roksana Borran 5, Fatemeh Ostai 5, Tahereh Khorgoei 4

1. Department of Psychiatry, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
2. Department of Internal Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
3. Research Center for Behavioral and Neurologic Sciences, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
4. Student Research Committee, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
5. Infertility and Reproductive Health Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.


Corresponding author: Dr Javad Golmirzaei, Research Center for Behavioral and Neurologic Sciences, Hormozgan University of Medical Sciences, Bandar Abbas, Iran. E-mail: javadgolmirzaei@yahoo.com, Tel. 0098-9127125123.

Abstract

Background: Restless legs syndrome (RLS) is a disease with an unknown etiology and pathogenesis and is a complication of hemodialysis. The prevalence of RLS is 6% to 60% in the general population and 15% to 40% among hemodialysis patients. This study was conducted to assess the prevalence of RLS and its associations with the status of the patient.

Method: All of the hemodialysis patients of Shahid Mohammadi hospital of Bandar Abbas were enrolled. Eighty patients were examined for RLS by using the international RLS study group (IRLSSG) criteria and their demographic, biochemical and clinical status were examined to find the associations between them and RLS. Data was entered in the SPSS 16 software and descriptive statistics, chi-square, t-test, independent sample test and mantel-haenszel test were used to analyze the data.

Results: Eighty patients participated in our study which 39 (48.8%) of them were females and 41 (51.2%) were male. The average age of the participants was 49.13±17 years. The prevalence of RLS was 57.5%. The mean BMI was 21.77±5 Kg/m2 and the mean duration of dialysis was 41.5±32.28 months. Hypertension was seen in 81.2%, diabetes mellitus in 31.2%, smoking in 16.3%, the average Kt/V was 0.99±0.72. Significant relations were seen between RLS and Kt/V (p-value=0.015) and systolic blood pressure (p=0.021).

Conclusion: Our results showed a high prevalence of RLS in the hemodialysis patients. This may be because of low Kt/V, anemia, high Cr, low length dialysis. RLS highly effects on the life quality of the
patients, understanding the risk factors of RLS and preventing them and improving the efficacy of hemodialysis must be a high priority in these patients.

Keywords: Amniotic Restless Legs Syndrome, Renal Dialysis, Prevalence

Introduction:

Restless legs syndrome (RLS) is a disease with an unknown etiology and pathogenesis (1-3). In this disease, the patients develop an unpleasant feeling in their legs which relieves by shaking and activity (2-4). The incidence of RLS is strongly associated with low renal function and studies suggest that RLS may be associated with higher mortality in these patients (5, 6).

RLS is a complication of hemodialysis and affects patients who undergo hemodialysis more than it affects the general population (1, 3, 7). Since the prevalence of RLS in some races and monozygote twins is higher than the general population, it has been suggested that genetic plays a role as an underlying cause (8).

Hypertension, sex, dialysis, uremia, abnormal biochemistry, decreased parathyroid hormones, increase in age, BMI, low income, low activity, low exercise, smoking, alcohol consumption, low serum iron, pregnancy, diabetes, low hemoglobin, low serum phosphor and ferritin seem to be associated with RLS (1, 2, 9).

The aim of this study was to determine the prevalence of RLS among hemodialysis patients in Bandar Abbas and examine the associations between demographic, biochemical and clinical status of the patients with RLS.

Method:

In this descriptive study, the prevalence of restless legs syndrome was assessed in Shahid Mohammadi Hospital of Bandar Abbas in 2009. All of the patients who underwent hemodialysis in the hospital were enrolled. Those who didn’t undergo the treatment for more than 6 months, patients who were mentally or physically disabled or patients who weren’t conscious or had difficulty in speaking or hearing were excluded from the study.

According to the exclusion criteria, 28 patients were excluded and 80 patients participated in our study. All of the patients underwent hemodialysis 2 to 3 times a week. Data was collected by direct interview and by using restless legs syndrome questionnaire.
Demographic and biochemical data were collected: Age, sex, marital status, education level, alcohol use, smoking, past medical history, drug history, the start date of hemodialysis, the amount of time that hemodialysis took, history of previous transplantation, BMI and blood pressure.

Also, biochemical data was taken from their medical records: Parathormone (PTH) level, Ferritin, hemoglobin (Hb), creatinine (Cr), blood sugar (BS), Thyroid stimulation hormone (TSH), C-reactive protein (CRP), albumin, calcium (Ca), K/TV and phosphor (P) were collected from the medical records of the patients.

RLS was diagnosed according to the IRLSSG criteria; if the patient feels the need to move his/her limbs to overcome the unpleasant feeling that is commonly described as dysesthesias or paresthesias, sensory syndromes, that are started by resting or relieved with movement, and if the symptoms get worse at night and fade on morning. All of these symptoms must be present.

Data was entered in the SPSS v.16 software and descriptive statistics test, chi-square, t-test and independent sample test were used to analyze them. A p-value below 0.05 was considered as significant.

Results:

Eighty patients participated in our study which 39 (48.8%) of them were female and 41 (51.2%) were male. The average age of the participants was 49.13 ± 17 years. The mean BMI was 21.77 ± 5 Kg/m² and the mean duration of dialysis was 41.5 ± 32.28 months.

Forty six patients (57.5%) were diagnosed with restless legs syndrome. Out of these patients, 24 (52.2%) were female and 22 (47.8%) were male. Most of the patients who had RLS were between 41 to 70 years old (73.9%), 6 (13%) of them were between 21 to 40 years old, 4 (8.7%) were more than 70 and 2 (4.4%) were less than 20 years old.

About 87% (40) of the RLS patients never smoked in their lives, 4 (8.7%) were ex-smokers and only 2 (4.3%) smoked at the time. Among the RLS patients, 27 (58.7%) were dialyzed for 12 to 48 months, 8 (17.4%) were dialyzed between 49 to 80 months, 6 of them (13%) were dialyzed less than a year and 5 (10.9%) of them were dialyzed for more than 80 months.

Sixteen patients (34.8%) had a BMI less than 20, 18 (39.1%) had a BMI of 20 to 25, 7 (15.2%) had a BMI of 25 to 30 and 5 (10.9%) had a BMI higher than 30.

About 22 (47.8%) of the patients never went to school, 11 (23.9%) only went to school until the 5th grade and 13 (28.3%) went to school until they reached high school. None of the patients entered high school or finished school.
Among all the RLS patients, 18 (39.1%) patients with RLS had a systolic blood pressure (SBP) less than 140 and 28 (60.9%) had a high SBP at the time of admission. On the other hand the diastolic blood pressure (DBP) was higher than 90 in 40 (87%) patients.

Among the patients, 44 of them (95.7%) had an Hb above than 11 and the level of Hb was below 11 in 2 of the patients. A ferritin level more than 200 was seen in 25 (54.3%) of the RLS patients and it was below 200 in 20 (43.5%) of them. The PTH level of 26 (56.5%) of the patients was higher than 300, but below 300 in 20 (43.5%) of the patients.

Out of all the patients, 23 (50%) had a normal level of P, 18 (39.1%) had a higher level and 5 (10.9%) had a lower level. Also 25 (54.4%) of the patients had a normal Ca level, 7 (15.2%) had a higher level and 14 (30.4%) had a lower Ca level.

The albumin level of 45 (97.8%) of the patients was normal and only 1 (2.2%) patient had an albumin level below normal. The Kt/v level was below 1.2 in 33 (73.3%) of the patients and it was more than 1.2 in 12 (26.7%) of the patients. There was a significant association between the Kt/v level and RLS (p-value=0.015).

The TSH level was normal in 28 (60.9%) of the cases, below normal in 7 (15.2%) and higher than normal in 11 (23.9%). The mean level of CRP was 30.1 ± 18.7, the mean level of Cr was 8.6±3.2 and the mean level of BS was 114±45.

Among the medical conditions, hypertension had the highest prevalence with a 81.2% rate. Reflux nephropathy was only seen in 1 (1.2%) patient and had the lowest prevalence rate. Table 1 shows the prevalence of the medical conditions seen among all of the participants and among the patients.

Table 1- Frequency of medical conditions among the participants and among the RLS patients

<table>
<thead>
<tr>
<th>Medical condition</th>
<th>Prevalence among all</th>
<th>Prevalence among RLS patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>65 (81.2%)</td>
<td>37 (80.4%)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>25 (31.2%)</td>
<td>18 (39.1%)</td>
</tr>
<tr>
<td>Lupus</td>
<td>3 (3.8%)</td>
<td>1 (2.2%)</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>1 (1.2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Pylonephritis</td>
<td>7 (8.8%)</td>
<td>5 (10.9%)</td>
</tr>
<tr>
<td>Reflux nephropathy</td>
<td>1 (1.2%)</td>
<td>1 (2.2%)</td>
</tr>
<tr>
<td>Renal stone</td>
<td>4 (5%)</td>
<td>2 (4.3%)</td>
</tr>
<tr>
<td>Congenital disease</td>
<td>8 (10%)</td>
<td>3 (6.5%)</td>
</tr>
<tr>
<td>Unknown renal disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other renal conditions</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Anti-osteoporosis drugs and erythropoietin drugs were used more often than other drugs; 70 (90%) of the patients used them. However, analgesics were used less than other drugs 7 (11.2%). Table 2 shows the frequency of drugs used in all of the participants and in the patients.

Table 2 – Frequency of drug usage among the participants and among the RLS patients

<table>
<thead>
<tr>
<th>Drug</th>
<th>Prevalence among all</th>
<th>Prevalence among RLS patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-hypertensive</td>
<td>65 (81.2%)</td>
<td>37 (80.4%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>25 (31.2%)</td>
<td>18 (39.1%)</td>
</tr>
<tr>
<td>Analgesic</td>
<td>9 (11.2%)</td>
<td>6 (13%)</td>
</tr>
<tr>
<td>Ferro sulfate</td>
<td>36 (45%)</td>
<td>20 (43.5%)</td>
</tr>
<tr>
<td>Multi vitamin</td>
<td>14 (17.5%)</td>
<td>6 (13%)</td>
</tr>
<tr>
<td>Anti osteoporosis</td>
<td>72 (90%)</td>
<td>39 (84.8%)</td>
</tr>
<tr>
<td>Erythropoietin</td>
<td>72 (90%)</td>
<td>40 (87%)</td>
</tr>
</tbody>
</table>

The odds of catching RLS was 6.4 times higher than patients with a Kt/v > 1.2 (CI = 33.24 ± 1.25, OR=6.4, P-value=0.026). Table 3 shows the frequency of RLS among diabetic and non diabetic patients according to Kt/V.

Table 3- Frequency of RLS among diabetic and non diabetic patients according to Kt/V

<table>
<thead>
<tr>
<th>RLS</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Diabetics</td>
<td></td>
</tr>
<tr>
<td>Kt/v &lt; 1.2</td>
<td>19 (44.2%)</td>
</tr>
<tr>
<td>Kt/v &gt; 1.2</td>
<td>7 (77.8%)</td>
</tr>
<tr>
<td>Total</td>
<td>26 (50%)</td>
</tr>
<tr>
<td>Non diabetics</td>
<td></td>
</tr>
<tr>
<td>Kt/v &lt; 1.2</td>
<td>14 (63.6%)</td>
</tr>
<tr>
<td>Kt/v &gt; 1.2</td>
<td>5 (100%)</td>
</tr>
<tr>
<td>Total</td>
<td>19 (70.4%)</td>
</tr>
</tbody>
</table>

Conclusion:

In our study, the prevalence of RLS was 57.5% and 52.2% of these patients were female and 47.8% were male. Salman reported that the frequency of RLS was 20.3% in his study (4). Araujo and coauthors reported a 21.5% prevalence of RLS among hemodialysis patients (9).

The prevalence of RLS is reported to be 5-15% in the general population and 6-60% in the ESRD patients. The difference seen in the prevalence may be because of using different criteria. However, a difference
is also seen in the studies that used the same criteria that we used in our study. The prevalence of RLS was 14% in Hungry (10), 18.4% in Italy (11), 14.8% in Brazil (12), 34.1% in Turkey (13), 6.6% in India (2), 50.22% in Saudi Arabia (14) and 28% in Korea (15).

The mean age of the RLS patients was 50.5 ± 15 and no significant relations were seen between age and RLS. Other studies results were similar to ours (2, 10, 13-16). As seen in other studies, Mucsi I and colleagues found a significant relation between the female gender and RLS (10, 13, 15-17). Our study didn’t confirm this result. We didn’t find any significant relations between smoking and RLS. Some other studies confirm this (10, 16).

Although Szentkiralyi and colleagues didn’t find any relations between education and RLS (16), our results showed a significant relation between these two. Many studies confirmed our results in not finding a significant relation between the length of dialysis and RLS (2, 10, 13-15).

Xiang Gao and colleagues suggested that RLS may increase with a raise in BMI (18), a result that wasn’t supported by other studies including ours (10, 13). In our study, no significant relations were found between RLS and any other medical conditions. Al Jahdali and colleagues and Mucsi and colleagues found a significant association between DM and RLS (10, 14) while Filho and colleagues found a significant relation between RLS and glumerolonephritis (12).

However, since some other surveys didn’t find any relations between DM and RLS, we suggest that peripheral neuropathy might not play an important role in the pathophysiology of RLS. The significant relation found between RLS and SBP confirmed Bhowmik’s findings (2). However, Berger and colleague didn’t find any relation between SBP and RLS in the general population (19).

A low Kt/v is associated with RLS. This is a finding of Al Jahdali’s study (14) which was confirmed by our results. But many other studies didn’t confirm this issue (2, 10, 15). Recent studies including our study didn’t find any relations between Cr level and RLS (2, 12, 13). Also no significant relations were seen between iron level and anemia with RLS (2, 10, 12-15). This may be because of the wide erythropoietin and ferro sulfate usage in the participants. This finding was confirmed by many other studies.

PTH, Ca and P were not related to RLS. Other studies also found the same results (15). According to these results, since Ca and P of all of the participants were similar regardless of having RLS or not, it can be concluded that hyperparathyroidism does not play a role in RLS (12, 15).

This study showed a lower TSH level in RLS patients (15.2% against 9.4%), however this difference wasn’t significant. Since hypothyroidism is a cause of secondary RLS, evaluating the T3 and T4 level of the RLS patients is necessary. Berger didn’t find any relations between TSH level and RLS in the general population (19). As other studies, we didn’t find any significant relations between albumin levels and RLS (10).
Our results showed a high prevalence of RLS in the hemodialysis patients. This may be because of low Kt/V, anemia, high Cr, low length dialysis. RLS highly effects on the life quality of the patients, understanding the risk factors of RLS and preventing them and improving the efficacy of hemodialysis must be a high priority in these patients.

Acknowledgements: The authors of this study would like to thank all the patients who agreed to participate in this study.

Conflicts of Interest: The authors of this article declare that they have no conflicts of interest.

References:

