



Scholars Research Library

Der Pharmacia Lettre, 2015, 7 (11):313-317  
(<http://scholarsresearchlibrary.com/archive.html>)



## Relationship between Chemical Parameters and Restless Legs Syndrome in Hemodialysis Patients of Zabol City

Elham Shahraki Moghaddam<sup>1</sup>, Azizollah Arbabisarjou<sup>2</sup>, Aziz Shahraki Vahed<sup>1\*</sup>, Elaheh Asadi Bidmeshki<sup>1</sup>

<sup>1</sup>Educator, School of Nursing and Midwifery Zabol University of Medical Sciences, Zabol, Iran.

<sup>2</sup>Health Promotion Research Center, Zahedan University of Medical Sciences, Zahedan, Iran.

### ABSTRACT

*Restless Legs Syndrome (RLS) is a sensory-motor disorder occurring in 20-30 percent of hemodialysis patients. This syndrome causes confusion, inability to rest and impaired quality of life for hemodialysis patients. This study was carried out to investigate the relationship between chemical parameters in hemodialysis patients and RLS. This cross-sectional study was conducted on 37 patients with chronic hemodialysis at a hospital affiliated to Zabol University of Medical Sciences. The patients have passed from start of their hemodialysis at least six month and they have been under hemodialysis three times a week and three and four hours in each time. Restless legs syndrome questionnaire was used as tool of study to collect data. Simultaneous with completing the questionnaire, the patients were sampled to measure biochemical parameters. The data were analyzed by SPSS software version 16.0. The results showed that 83.7 % of hemodialysis patients had RLS in which 24.3% of patients suffered from mild disorder, 40.5 % of them suffered from moderate disorder, and 18.9% of them suffered from severe disorder. According to the findings of this study, hemoglobin, uric acid, Iron, CRP, urea, creatinine, TSH, T4, phosphorus, albumin had no significant correlation with RLS, while calcium, T3 and PTH had significant correlation with restless legs syndrome ( $P = 0/026, 0/013, 0/001$ ). Considering the high prevalence of RLS in hemodialysis patients, identifying risk factors for this syndrome and providing guidelines to reduce clinical symptoms of this syndrome appears to be necessary.*

**Keywords:** biochemical parameters, restless legs syndrome, Hemodialysis

### INTRODUCTION

Chronic kidney disease is one of the major health problems [1] and the annual growth rate of this disease in Iran is approximately 11 % based on statistics of Management of Transplant and Specific Diseases of Health Ministry Center, and it reached to approximately fourty thousand people in 2009. The annual incidence of this syndrome is 53 person per one million people in Iran and its prevalence is 250 cases per one million people. These figures are respectively 200 and 975 people in America per million people [2]. Currently, the most common treatment for advanced kidney failure in the world is hemodialysis [3]. Based on report of Kidney Patients Support Community, among 40 thousand kidney patients, more than 15 thousand people of them are under the hemodialysis treatment and about 1,500 of them lose their lives due side effects of this disease [4]. Hemodialysis patients suffer from many problems that all of them lead to a decline in quality of life (QOL) [5]. Enhancing QWL and QOL have long explicit and implicit lifestyle and policy goal for individuals, communities, nations, and the world [6,7]. In addition to psychological stress, such as sleep disorders (6), depression, anxiety, social isolation and reduced quality of life, these patients are facing with neurological sensory problems such as burning sensation in the body, RLS, disability of legs and even full paralysis [8-7]. Bogan reported the prevalence of RLS in hemodialysis patients as 70 percent [9]. English physician Thomas Willis identified RLS for the first time in 1685, and it was

named in 1945 by Karl Ekbom [10]. The study conducted by Mollahoseini & Alidousti, it was reported that 5.61 and 3.57% of hemodialysis patients are suffering from RLS, respectively [12-11]. RLS is a neurological movement disorder, and patients of this syndrome have a strong tendency to move their legs during sleep and describe as adverse feeling that it is getting worse in periods of inactivity and often leads into insomnia [12]. RLS has been considered as one of the most common undetected diseases [13]. Special criteria for the diagnosis of this syndrome have been announced by restless leg IRLSSG (International Restless Leg Syndrome) Community, including a desire to move frequently associated with unpleasant symptoms with moving, the start or exacerbation of symptoms with rest or immobility, and start or exacerbation in the evening or night [14]. RLS prevalence is 15-5% in total population among and it is 30-20% among hemodialysis patients is [15]. Additionally, the prevalence of this syndrome has been reported 6-83 % in uremic patients [17-16]. RLS is a complex disease that a combination of genetic and biochemical factors contribute to its development [18]. This syndrome can be occur in the form of idiopathic or secondary due to factors such as diabetes, renal failure, Iron deficiency anemia, pregnancy and MS. Symptoms of the syndrome include insomnia, excessive daytime sleepiness and depression [15]. Results of the study conducted by Hemati *et al.* also showed a direct relationship between this syndrome and lower QOL in hemodialysis patients [5]. Although the etiology of RLS is unknown [19] yet, investigation of the factors associated with this syndrome can contribute to the development of medical knowledge in this area. Based on the results of a study in Ireland, RLS was more common in patients with Iron deficiency [20], while in another study no significant relationship was found between chemical parameters such as Fe, serum ferritin, hematocrit and dialysis adequacy with RLS [21]. According to the principle of "prevention is better than cure", identifying the effective factors in the process of a disease is one of the most basic steps to explain the treatment process. On the other hand, due to the adverse effects of the syndrome on the quality of life for hemodialysis patients and few and contradictory studies conducted on risk factors in occurrence of RLS in these patients, it is important to know about risk factors of RLS. This study investigated the relationship between experimental results and RLS in hemodialysis patients of Zabol city.

## MATERIALS AND METHODS

In this study, the prevalence of RLS and its relationship with biochemical parameters were investigated on 37 patients referred to hemodialysis sections of hospitals affiliated to Zabol University of Medical Sciences in 2011-2012. Characteristics of studied patients were as follows:

1. Willingness to participate in research
2. Having at least 18 years of age and at least one year of dialysis experience
- 3- Having file in hemodialysis sites of studied hospitals (Amirolmomenin and Imam Husain Hospitals).
- 4- Being on the weekly list of dialysis and doing it 2 or 3 times a week and every 3 to 4 hours
5. The lack of mental and physical disabilities
6. Having a complete alertness, listening and speaking ability to answer questions
7. Having no experience of of smoking, hypnotics or sedatives

However, all people, whether male or female, illiterate or literate, could participate in this research. Tools to collect data in this study included demographic information form, lab results form, and questionnaire for restless legs syndrome. The questionnaire had questions about RLS and its severity was measured through a four-point Likert scale. The questionnaire related to demographic characteristics of the participants included questions about gender, age, marital status, family size, education level, physical activity, income, history of kidney disease, duration of hemodialysis and history of the underlying disease. The scientific validity of research tools was assessed using content validity and reliability of the questionnaire for restless legs syndrome was determined by re-test. After determining the validity and reliability (95%) of tools, information was collected by interviews and based on the mentioned questionnaire. Before the start of dialysis, five milliliter of blood was taken from a peripheral vein of the upper limb of patients and it was sent to laboratory. The results of experiment were followed and they were attached to file. The abnormal cases were reported to nurse in charge of information. To analyze the data, SPSS Version 16 was used. Data were analyzed using descriptive and inferential statistics and significance level was considered as  $P < 0.05$ .

## RESULTS

The results showed that 62.2 percent of patients were male and 73 percent of them were married. The mean of age of the subjects of study was  $45.1 \pm 18.1$ . Most of the subjects (37.8 %) had secondary school education and 32.4 % of them had high school education level. Considering the living place of subjects, 62.2 percent of them were rural. The monthly income of most of the subjects was between 2000000 and 4000000 Rials, and 67.7 percent of subjects had no physical exercises. Most hemodialysis (9/45%) was conducted in the morning shift. Based on the findings, 83.7 % of hemodialysis patients were diagnosed with restless legs syndrome (Table 1).

**Table 1: Distribution of frequency of RLS in subjects**

Restless Legs Syndrome	n	percentage
Healthy	6	16/2
Mild	9	24/3
Moderate	15	40/5
Severe	7	18/9

**Table 2: Distribution of frequency of subjects in terms of gender in both healthy and patient groups regarding RLS**

Restless Legs Syndrome	Male	Female
healthy	(%17/4)4	(%14/3)2
patient	(%82/6)19	(%85/7)12

**Table 3: Comparison of subjects' scores based on experiments**

Variables	Mean $\pm$ Healthy SD	Mean $\pm$ Patient SD	P-value
Dialysis duration (in hours)	2/83 $\pm$ 0/41	4/82 $\pm$ 5/42	0/662
Hemoglobin	2/28 $\pm$ 1/36	9/91 $\pm$ 1/5	0/679
Fe	686/5 $\pm$ 231/3	539/0 $\pm$ 322/1	0/295
Calcium	9/63 $\pm$ 1/32	4/82 $\pm$ 1/24	0/026
CRP	2/28 $\pm$ 0/82	1/03 $\pm$ 0/75	0/289
Urea	11/08 $\pm$ 2/5	47/21 $\pm$ 34/05	0/877
Creatinine	2/83 $\pm$ 0/41	8/3 $\pm$ 4/14	0/124
uric acid	6/57 $\pm$ 1/57	5/7 $\pm$ 2/543	0/409
TSH	3/35 $\pm$ 0/68	3/05 $\pm$ 1/37	0/612
T4	9/47 $\pm$ 1/37	13/73 $\pm$ 28/66	0/7216
T3	132/67 $\pm$ 22/1	92/56 $\pm$ 66/6	0/013
Phosphorus	686/5 $\pm$ 231/3	539/0 $\pm$ 322/1	0/295
Albumin	4/92 $\pm$ 0/57	4/66 $\pm$ 0/69	0/399
PTH	686/189 $\pm$ 168/231	512/1 $\pm$ 217/78	0/001

The above table shows that the amount of calcium, T3 and PTH has significant relationship with RLS.

## CONCLUSION

Based on the results of this study, the majority of hemodialysis patients (83.7%) had RLS. Additionally, a significant correlation was found between calcium, hormone Triiodothyronine (T3) and PTH with RLS. In addition, in studies conducted by Hemati et al. titled as the relationship between quality of life and restless leg syndrome in hemodialysis patients, results showed that 98 (57.3 %) of subjects had RLS and 73 (42.7 %) of them did not have this syndrome. The mean age of patients in the group who had this syndrome was  $59.27 \pm 16.86$  and it was  $55.20 \pm 17.95$  in the group who had no this syndrome, and the difference between the mean age of both groups was not statistically significant ( $p=0.131$ ) (5). In this study, the non-syndrome patients was 16.2 %. In the present study, there was significant correlation between physical activity and RLS ( $P < 0/05$ ). In addition, 66 percent of people who had RLS, they had hemodialysis treatment for 6-10 years, so that there was significant difference between duration of hemodialysis and RLS.

Based on the results of study conducted by Ansarian et al. it was found that there was significant positive difference between duration of dialysis in dialysis patients and RLS ( $51 \pm 6.7$  months and  $34 \pm 2.5$  months with  $P = 0.025$ ). In line with the present study, the results of Al-Jahdali were also indicated that approximately 80 % of dialysis patients' had RLS (23). In the study of Salimipour et al. 33.1 % of hemodialysis patients had restless leg syndrome and this syndrome had no correlation with amount of ferritin (18). In the study conducted by Walker, increase in urea and creatinine before the dialysis was considered as the cause of this syndrome (16) incompatible with results of the current study. In this study, the amount of Iron in healthy subjects was  $686.5 \pm 231.3$ , while it was  $539.0 \pm 322.1$  in patients with restless legs syndrome, which was not statistically significant ( $p = 0/295$ ) correlation. Unlike our results, study of Habibzade et al. titled as the relationship between Iron deficiency and restless legs syndrome in hemodialysis patients, results showed that 38.7 % of hemodialysis patients with restless legs syndrome complained that the mean Iron of their serum was  $78 \pm 29.3$   $\mu\text{g/dl}$ . In this study, the serum levels of Iron and ferritin in hemodialysis patients with RLS was significantly lower than hemodialysis patients without RLS and statistical tests showed a significant difference in this case ( $p < 0.05$ ) (13). Additionally, in the study conducted by Salimipour et al. titled as RLS in dialysis patients of Bushehr province and its relationship with serum ferritin level, results showed that 43 of the studied subjects were diagnosed with restless leg syndrome (33.1 percent), including 18 women (41.9%) and 25 men (58.1 %).

Family history has positive significant relationship with RLS ( $P < 0.016$ ) and these group of people had 3.39 times than other people (confidence interval 1.25-9.21) to have RLS. Factors of age, gender, serum ferritin, period of renal failure course and BUN were not correlated with RLS (18). Results of Okeeffe et al. showed that RLS is more common in people with Fe deficiency anemia (20). According to results of study conducted by Altanoglu on patients with RLS, ferritin, and vitamin B12 levels were low, but no significant relationship was found between level of fasting blood sugar (FBS), and folic acid and creatinine and RLS [24]. In a study to evaluate the correlation between biochemical correlations RLS in patients with Parkinson's, Guerreiro reported no statistically significant relationship between age, duration of dialysis, urea, ferritin, creatinine, hemoglobin was observed with RLS [25] which is consistent with the results of this study.

In this study, the mean of calcium in both groups (with and without RLS) was different significantly, and the calcium level in the RLS group was lower. It was in line with our study results ([26]). In addition, in a study conducted by Ansarian et al, the relationship between RLS in patients with chronic renal failure and ferritin, Iron, and serum hemoglobin showed that there was no significant correlation between mean of hemoglobin level ( $p = 9.7 \pm 0.18$  g/dl and  $10.1 \pm 0.31$  g/dl), Fe ( $p = 0.75$  with  $72.2 \pm 6.3$  and  $74.3 \pm 6.6$ ) and ferritin ( $p = 0.34$  with  $684 \pm 97.4$  and  $519.8 \pm 138$ ) in two groups of chronic renal failure patients with and without RLS. The relationship between RLS and severity of daytime sleepiness were significantly increased in patients. Thus, according to the results of this study, in patients with restless legs syndrome associated with chronic renal failure, serum ferritin, serum Iron anemia rate is [22] which is in line with the results. Korkmaz investigated the biochemical and clinical characteristics between the two groups of hemodialysis patients with and without RLS. He reported that the consumption of folic acid and B vitamins in patients with RLS was significantly lower than the control group. Additionally, no significant correlation was found between two groups in terms of mean of hemoglobin, phosphorus, iron, albumen, TIBC, ferritin, folic acid, vitamin B12 and calcium [27], whereas in our study, the mean of calcium correlated with RLS significantly.

In this study, mean of PTH was significantly different between two groups of with and without RLS ( $P = 0.001$ ); in a study conducted by Kim to determine the risk factors for RLS in hemodialysis patients, he reported that there was no relationship between PTH and RLS ( $P = 0.399$ ) [28]. The difference of results of this study with the results of other studies may be due to differences in diagnostic procedures of RLS, racial and social differences, and size of the sample. Therefore, it seems that trying to find factors related to RLS in hemodialysis patients can bring fruitful results. Therefore, considering that the studies produced conflicting results regarding blood biochemical factors and this syndrome, further studies with larger sample size is recommended.

### Acknowledgments

This study is extracted from a research project approved by Zabol University of Medical Science at Zabol. The researchers of study appreciate all patients and nurses of hemodialysis ward in hospitals affiliated to Zabol University of Medical Sciences for their cooperation this study.

### REFERENCES

- [1] Smeltzer S, Bare B, Hinkle J, Cheever K. Brunner & sodarth's, Text book of medical surgical nursing. 12<sup>th</sup> ed. Philadelphia: Lippincott; 2010.
- [2] Lesan Pezshki M, Matini M, Tagadosi M. *Fyze J*. 2001;17(2):82-7.
- [3] Kimmel PL, Peterson RA. *Semin Dial*. 2005; 18(2): 91-7.
- [4] Shafiapoor V, Jaafari H, Shafiapoor L. *Kowsar Med J* 2009;3:169-74. [Persian]
- [5] Hemati Z, Alidosti M, Reisi M. 2011. *Iran J Crit Care Nurs*. 2012;5(3):145-50. [Persian].
- [6] [6]. Constanza et al. *Surv. Percept. Integr. Envir. Sco.*, 2007, 1, 1-5.
- [7] [7]. Arabbisarjou A, Allame S M., Farhang A. *Life Science Journal*, 2012;9(4).<http://www.lifesciencesite.com>
- [8] Mucsi I, Molnar MZ, Ambrus C, Szeifert L, Kovacs AZ, Zoller R, et al. *Nephrol Dial Transplant*. 2005; 20(3): 571-7.
- [9] Winkelmann J, Prager M, Lieb R, Pfister H, Spiegel B, Wittchen UH, et al. *J Neurol*. 2005; 252(1): 67-71
- [10] Rangarajan S, D'Souza GA. *Sleep Med*. 2007;8(3):247-51.
- [11] Bogan RK. *Neuropsychiatr Dis Treat*. 2006; 2(4): 513-9.
- [12] Cotter PE, O'Keeffe ST. *Ther Clin Risk Manag*. 2006; 2(4): 465-75.
- [13] Molahosseini Sh, Mohammadzadeh Sh, Kamali P, Tavakkoli Shooshtari M. *Med Sci J Islamic Azad Univ Tehran Med Branch*. 2005; 15(1): 27- 30.
- [14] Alidosti M, Hemate Z, Reisi M. Feyz, *Journal of Kashan University of Medical Sciences*. 2013;17(1):85-90.
- [15] Habibzade H, Khalkhali H, Ghaneii R.. *Iran J Crit Care Nurs*. 2011;4(3):153-8.
- [16] Jadoulle V, Hoyois P, Jadoul M. *Clin Nephrol*. 2005;63(2):113-8.
- [17] Wali SO, Alkhouli AF. *Saudi Med J*. 2015;36(2):204-10.

- [18] Walker S, Fine A, Kryger MH. *Am J Kidney Dis.* **1995**; 26(5):751-6.
- [19] Holley JL, Nespor S, Rault R. *Am J Kidney Dis.* **1992**;19(2):156-61.
- [20] Samilipour H, Azizi F, Motamed N, Taiebi N, Delavar Kasmaie H, Karimi M. *Iranian South Medical Journal.* **2009**;12 (3):206-13
- [21] Chokroverty S, Jankovic J. *Neurology.* **1999**; 52:907-910.
- [22] O'Keeffe ST. *Age & Ageing.* **2005**; 4(4):349-52.
- [23] Shahidi AR, Abbaspour S, Namjoo M, Najafzadeh A. *Journal of Medical Council of Iran.* **2010**;28(1):29-35.
- [24] Ansarin Kh, Shabanpour J, Argani H, Airomlou H.. **2005**;128(4):383S.
- [25] Al-Jahdali HH, Al-Qadhi WA, Khogeer HA, Al-Hejaili FF, Al-Ghamdi SM, Al Sayyari AA. *Saudi J Kidney Dis Transpl.* **2009**;20(3):378-85.
- [26] Altunayoglu Cakmak V, Koc B, Nuhoglu I, Topbas M, Ucuncu SY, Deger O, et al. *Neurol Res.* **2015**;37(9):751-62.
- [27] Guerreiro TM, Nishikawa DR, Ferreira LC, Melo HA, Prado RC. *Arq Neuropsiquiatr.* **2010**;68(6):869-72.
- [28] Virga G, Mastrosimone S, Amici G, Munaretto G, Gastaldon F, Bonadonna A. *Int J Artif Organs.* **1998**;21(12):788-93.
- [29] Korkmaz S, Tokgoz B, Ismailogullari S, Kocyigit I, Kocyigit M, Aksu OB, et al. *Open Journal of Nephrology.* **2013**;3:44-50.
- [30] Kim JM, Kwon HM, Lim CS, Kim YS, Lee SJ, Nam H. *J Clin Neurol.* **2008**;4:153-7.