A CROSS-SECTIONAL RESEARCH ON RESTLESS LEGS SYNDROME (RLS) IN THE PATIENTS OF END STAGE RENAL DISEASE (ESRD) AND IT’S ASSOCIATED RISK FACTORS IN THE LIGHT OF REVISED INTERNATIONAL RLS CRITERIA (2012)

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Abstract:
Objective: The research design was cross sectional survey which was carried out to find out the Restless legs syndrome (RLS) prevalence in the patients of end stage renal disease (ESRD) on hemodialysis (HD).
Methods: We obtained this data from a total of 250 patients through chronic maintenance HD. For the assessment of the RLS prevalence, RLS criteria for the clinical diagnostic was made through the research group of international RLS.
Results: Research sample size was 250 cases with the male and female proportion of 153 males (61.2%) and 97 females (38.8%) respectively. The factor of mean age was observed as (45.27) years. HD mean duration was (26.10) months. We found a total of 162 RLS cases (64.8%). In the total of 153 males, 87 cases (56%) were diagnosed with RLS and among in the 97 females, 75 cases (77.3%) were diagnosed with RLS. We observed in this research that significant involvement of the gender was present in the research outcomes which was linked with RLS as p-value was observed as (0.001). Concerning to group of age 159 cases (63.6%) were under 51 years of age; in this number 102 cases (64.1%) were diagnosed with RLS; whereas, 91 cases (36.4%) were above or equal to 51 years and in the patients of this group 60 cases suffered from RLS (65.9%). It was noticed that no significant link was present in age group and RLS with a significant p-value as (0.776).
Conclusions: The patients undergoing routine HD are observed with a common incidence of RLS. Females are commonly observed in this incidence and dominate males.

Key Words: Restless legs syndrome (RLS), End stage renal disease (ESRD) and Hemodialysis (HD).

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INTRODUCTION:
In the literature of medical science, the term Restless legs syndrome (RLS) was first used in 1944 by K. A. Ekbom [1]. The leading causes and factors that add in the development of the RLS are decrease in the intracortical excitability dopaminergic modulation, having an increased spinal cord excitability and reduced supraspinal inhibition [1]. In the South Asia it is estimated that the number of ESRD cases is about 1.5 million.

On the grounds of the facilities of healthcare and ESRD incidence availability is likely to be more than actual reported when compared with the industrialized world. According to the research of Jha V Dida the assessment of age adjusted ESRD incidence in 232 patients was carried out in the South Asian population. Developed countries were observed more involved in the RLS incidence such as 10 – 15 percent [3, 4]. In ESRD the RLS prevalence was observed high against the general population with a higher degree variability where the range of the prevalence was in the range of 13.3% – 28% [5, 6]. Estimated possible reasons behind are RLS diagnostic criteria variation and various populations variations in the genetics. Clinical features help in the diagnosis of the RLS on the grounds of revised international RLS criteria (2012) [7]. Studies have also proved that there is an association of quality of life style with the RLS and increased rate of mortality [8]. Sleep disorders are also evinced in the patients of RLS such as excessive day sleeping and insomnia [8, 9]. RLS prevalence is observed generally in the old age and females. While considering the population of ESRD, the predisposed factors that may lead to the incidence of RLS include the deficiency of iron, under dialysis and anemia [12].

We carried out this research for the ESRD suffering patients on hemodialysis (HD) for the frequency determination in the population of Pakistan.

METHODS:
Research was cross-sectional survey which was carried out at CMH, Lahore in the timeframe of October, 16 to March, 17. Sample of 250 patients was selected through non-probability purposive sampling technique (CI as 95% and Error margin 5%) with an RLS percentage of (20.3%) in the cases of ESRD on HD [13]

The age group selected in the research was in the age limit of 14 – 85 years of age of both the genders and all the patients diagnosed with ESRD on HD and all the cases undergoing four hours HD twice in a week were made a part of the research. Pregnant cases having Parkinson’s disease, venous stasis, myalgia, arthritis, leg edema, leg cramps, habitual foot tapping and positional discomfort were not included in the research paper.

Diagnosis of the RLS was made on the criteria of (2012) about the RLS [7]. Five cardinal symptoms present in the RLS diagnoses patient are stated below:

(i) Movement of the legs because of the unpleasant sensation and discomfort in the legs as felt by the patients.
(ii) This urge becomes worse in the time of sitting, lying, inactivity and rest.
(iii) Movement bring relieve in the patients such as stretching and walking till the time of the activity.
(iv) Legs movement urge and accompanied restlessness is increased in night than the day because the inactivity is increased in the night time.
(v) In the presence of the above-mentioned features are primary to other related conditions of the behavior and medical such as myalgia, leg edema, venous stasis, leg cramps, arthritis, habitual foot tapping and positional discomfort.

Misunderstandings were cleared at the time of Performa filling by the participants specially about the questions. Analysis of the data was carried out through SPSS – 20. Chi-square test was also carried out for the observation of any pertinent variation specially in males and females with a significant p-value of (< 0.05).

RESULTS:
Research sample size was 250 cases with the male and female proportion of 153 males (61.2%) and 97 females (38.8%) respectively. The factor of mean age was observed as (45.27) years. HD mean duration was (26.10) months. We found a total of 162 RLS cases (64.8%). In the total of 153 males, 87 cases (56%) were diagnosed with RLS and among in the 97 females, 75 cases (77.3%) were diagnosed with RLS.

We observed in this research that significant involvement of the gender was present in the research outcomes which was linked with RLS as p-value was observed as (0.001). Concerning to group of age 159 cases (63.6%) were under 51 years of age; in this number 102 cases (64.1%) were diagnosed with RLS; whereas, 91 cases (36.4%) were above or equal to 51 years and in the patients of this group 60 cases suffered from RLS (65.9%). It was noticed that no significant link was present in age group and RLS with a significant p-value as (0.776).
Table – I: Comparison of different studies on RLS

<table>
<thead>
<tr>
<th>Study</th>
<th>Year of publication</th>
<th>Country</th>
<th>No. of patients</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Araujo SM et al. [17]</td>
<td>2010</td>
<td>Brazil</td>
<td>400</td>
<td>21.5</td>
</tr>
<tr>
<td>Al-Jahdali HH et al. [16]</td>
<td>2009</td>
<td>Saudi-Arabia</td>
<td>227</td>
<td>50.22</td>
</tr>
<tr>
<td>Sikandar R et al. [25]</td>
<td>2009</td>
<td>Pakistan</td>
<td>271</td>
<td>30</td>
</tr>
<tr>
<td>Kim JM et al. [6]</td>
<td>2008</td>
<td>Korea</td>
<td>164</td>
<td>28</td>
</tr>
<tr>
<td>Kawauchi A et al. [15]</td>
<td>2006</td>
<td>Japan</td>
<td>228</td>
<td>23</td>
</tr>
<tr>
<td>Mucsi I et al. [8]</td>
<td>2005</td>
<td>Hungary</td>
<td>333</td>
<td>14</td>
</tr>
<tr>
<td>Siddiqui S et al. [19]</td>
<td>2005</td>
<td>UK</td>
<td>277</td>
<td>45.8</td>
</tr>
<tr>
<td>Our study</td>
<td>2017</td>
<td>Pakistan</td>
<td>250</td>
<td>64.8</td>
</tr>
</tbody>
</table>

DISCUSSION:
The research determined the RLS frequency in ESRD patients on HD. The outcome of our research proves that there is a remarkable prevalence of the RLS (64.4%) in ESRD cases on HD and it is repeatedly observed in the female cases. Numerous other research studies carried out on the same topic also studies the RLS frequency in general population which has been reported in the limit of 10 – 15 percent in ESRD cases on HD [4 – 6].

There are three main reasons behind this frequency variation including research heterogeneity (genetic variation), RLS definitions (syndrome diagnostic tools) and most important is the third reason also known as deficiency of iron which leads to the incidence of the RLS in the patients including diabetes mellitus (DM), HD inadequacy and peripheral neuropathy. In the comparative analysis of our research with the other research studies it can be
observed that the used criteria were IRLSSG criteria, we have also observed some significant variations [7]. RLS frequency as observed in our research was observed as (64.8%), 121 cases (6%) were made a part of the study in a research that was carried out in India, in Japan 223 cases (23%) and in Saudi population as (22%) [13 – 16]. These number suggest that population heterogeneity which is genetic may be the possible reason behind the RLS frequency [18].

Anemia, level of serum calcium and iron deficiency have been associated to the incidence of RLS; however, in the recent research studies the confirmation have not been built about the earlier outcomes confirmation [19]. However, female frequency was dominant in the patients who suffered with RLS. This has been proved in many other research studies which can be linked with the sex hormones of the females followed by circadian rhythms [19]. Old age is also considered as the RLS risk factor [20]. However, in the previous research studies this point is not true every time specially in the patients underwent dialysis [21].

It is also proved through research studies that the association of the risk may also contribute in the RLS frequency also stated the link of RLS with smoking and excessive coffee consumption had a negative link with the RLS [22]. According to Gigli GL et al. two groups were made out of the patients experiencing dialysis; one group was RLS affected and second group was not linked with RLS, they also found that dialysis period was significantly linked with the negative RLS group.

There was no difference in the use of drugs in both the groups, an exception was considered for the phosphorus binders intake and antihypertensive drugs in the patients of RLS [23]. The reasons behind the RLS frequency in the population of our research were inadequate HD, malnutrition and anemia. For the provision of the adequate analysis to ESRD cases is of vital importance as the dialysis inadequacy leads to an increased rate of mortality and morbidity [22]. The measurement of HD adequacy is made in Kt/V, a minimum of (1.2 Kt/V) is provided / session of HD session to patients with a glomerular filtration rate (below 2 ml/min). It is recommended to take at least three sessions in a week. An inadequate dialysis (Kt/V lower levels) was observed linked with the RLS [22]. Most of the Pakistani dialysis centers are providing HD two time a week without the measurement of the value of Kt/V, same results were observed in our research as they underwent two-time HD in the dialysis centers that may also lead to the RLS incidence as observed in other research studies.

**CONCLUSION:**

It is confirmed through our research that patients undergoing HD were diagnoses with RLS. The dominance of females over males was also evident. Under an HD dose, poor iron deficiency management anemia because of the low economic status is one of the common reasons behind the incidence of RLS in the population of our research. Quality of life was also linked with the incidence of RLS and mortality. Routine assessment that diagnosis the RLS in those patients who underwent HD for ESRD is also mandatory. An early and prompt diagnosis and disease management is helpful in the overall development of the life quality.

**REFERENCES:**


