Jurnal Ners

Volume 19 Issue 2, May 2024, p. 240-272
http://dx.doi.org/10.20473/jn.v19i2.54993

ORIGINAL ARTICLE OPEN ACCESS

Meta-analysis of the prevalence of restless leg syndrome and associated risk factors in chronic kidney disease patients

Nur Aini[1,2,*], Fitria Endah Janitra[1,3], Alfiani Rahmi Putri[1], Nelsensius Klau Fauk[4], and Hidayat Arifin[1, 5]

[1] School of Nursing, College of Nursing, Taipei Medical University, Taipei, Taiwan

[2] Nursing Department, Faculty of Health Science, University of Muhammadiyah Malang, Malang, Indonesia

[3] Faculty of Nursing, Universitas Islam Sultan Agung, Semarang, Indonesia

[4] Centre for Public Health, Equity and Human Flourishing, Torrens University, Sydney, Australia

[5] Department of Basic Nursing, Faculty of Nursing, Universitas Airlangga, Surabaya, Indonesia

*Correspondence: Nur Aini. Address: Nursing Department, Faculty of Health Science, University of Muhammadiyah Malang, Indonesia. Email: nuraini_fikes@umm.ac.id

Responsible Editor: Laily Hidayati

Received: scan ya 9 Desember 2023○ Revised: 03 February 2024 ○ Accepted: 29 April 2024

ABSTRACT

Introduction: Restless legs syndrome (RLS) presents as a sleep-related issue in individuals with chronic kidney disease (CKD), contributing to heightened sleep disturbances and diminished quality of life. Consequently, this meta-analysis was conducted to assess the prevalence of RLS among CKD patients.

Methods: A comprehensive search for articles published between inception and September 2023 was conducted across CINAHL, Cochrane, Embase, Ovid-MEDLINE, PubMed, Scopus, and Web of Science databases. A Comprehensive Meta-Analysis (CMA) software version 3.0 with random effects models was used for pooled prevalence and prediction interval analysis. Heterogeneity was assessed using the I2 test and Cochran's Q-statistic. The quality of the studies was evaluated using Hoy's risk of bias. Additionally, moderator analyses were performed to investigate variations in the prevalence estimates among the included studies.

Results: A total of 97 studies were included in this meta-analysis with 315,875 participants. The pooled prevalence of RLS among CKD patients was 25% (95%CI: 20% to 32%). In terms of the demographic breakdown, the prevalence of RLS was nearly comparable in adults and children/adolescents at 25% and 21%, respectively. The prediction interval indicated a potential future RLS prevalence ranging from 1% to 88%. Notably, iron and phosphorus levels emerged as significant moderating factors influencing the prevalence of RLS.

Conclusions: Roughly 25% of individuals with chronic kidney disease (CKD) encounter restless legs syndrome (RLS). It is imperative to foster collaboration among healthcare professionals to facilitate proactive management and early assessment of RLS, thereby enhancing the overall quality of life for CKD patients.

Keywords: chronic kidney disease, meta-analysis, prevalence, renal disease, restless leg syndrome

Introduction

Patients diagnosed with chronic kidney disease (CKD) are susceptible to various sleep disorders, including conditions such as sleep apnea, insomnia, disturbed sleep, excessive daytime drowsiness, and restless leg syndrome (RLS) (Maung *et al.*, 2016, Tan *et al.*, 2022). Restless leg syndrome, also known as Willis-Ekbom Syndrome, is defined as a sensory-motor disorder marked by circadian rhythmicity. Patients frequently describe sensations of discomfort in their lower legs, such as achy, creeping, crawling, or itchy feelings, which are relieved by movement. Although symptoms of this disorder are typically heightened at night, they can occur at any time during periods of rest

© 2024 Jurnal Ners. This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/).

or inactivity (Novak *et al.*, 2015, Maung *et al.*, 2016). Previous meta-analyses conducted in Asian, American, and European countries revealed the prevalence of RLS in hemodialysis patients was 24% (Liu *et al.*, 2024), the prevalence of RLS in patients undergoing hemodialysis was 50% in Iranian and 30% in international databases (Ghanei Gheshlagh *et al.*, 2017), and the prevalence of RLS among CKD populations in East Mediterranean, Western Pacific, America, Europe, and Southeast Asia countries was 24.2% (Lin *et al.*, 2016). Although these prevalences are not too large, a systematic review found that RLS is two to three times more common in patients with CKD than in the general population (Safarpour *et al.*, 2023).

An imbalance in iron metabolism and dopamine neurotransmission among CKD patients is suspected as the cause of RLS (Novak *et al.,* 2015; (Maung *et al.*, 2016). Dopamine is a key neurotransmitter involved in the regulation of movement and motor control (Novak *et al.,* 2015). Additionally, electrolyte imbalances, for instance, potassium and calcium, can cause muscle cramps, restlessness, and discomfort, all of which can disrupt sleep. Furthermore, the accumulation of uremic toxins in the bloodstream can cause symptoms such as itching, restless legs, and general discomfort, making it difficult for people with CKD to get restful sleep (Maung *et al.*, 2016, Nigam *et al.*, 2018). RLS is linked to several risk factors, including female gender and alcohol users (Lin *et al.*, 2019). A meta-analysis by Lin *et al.* (2016) found that the prevalence of RLS increased with age, Kt/V or index of dialysis adequacy (dialyzer clearance of urea * dialysis time/volume of distribution of urea), and level of serum phosphate, and decreased with level of serum calcium, and hemoglobin, also associated with diabetes mellitus and hypertension. Other meta-analyses revealed no differences in gender, age, dialysis duration, body mass index (BMI), blood urea nitrogen (BUN), creatinine, albumin, phosphorus, parathyroid hormone, and calcium between dialysis patients with RLS and non-RLS (Liu *et al.*, 2024).

Previous research has confirmed that RLS in CKD is associated with increased cardiovascular risk (Chen *et al.*, 2022), increased risk of death, sleep disturbance (Novak *et al.,* 2015), and decreased health-related quality of life (HRQOL) among community-dwelling populations (Kubo *et al.*, 2016). Moreover, for hemodialysis patients grappling with RLS, the consequences are evident in elevated levels of fatigue, compromised sleep quality, heightened daily sleepiness, and symptoms of depression (Giannaki *et al.*, 2017). This emphasizes the complex implications of RLS in the context of CKD and underscores the need for comprehensive management strategies, commencing with addressing the prevalence of RLS.

Although several meta-analyses have been conducted on RLS, certain limitations were identified. These include: 1). limited moderator variables analyzed (Lin *et al.*, 2016, Ghanei Gheshlagh *et al.*, 2017, Liu *et al.*, 2024); 2). authors did not perform a moderator analysis (Kang *et al.*, 2022); 3). the search time was restricted and the meta-analysis study was not registered in the International Prospective Register of Systematic Reviews (Ghanei Gheshlagh *et al.*, 2017); 4). focused on adult CKD patients (Lin *et al.*, 2016); and 5). the inclusion of only hemodialysis patients in some analyses (Ghanei Gheshlagh *et al.*, 2017, Liu *et al.*, 2024). Therefore, our meta-analysis aims to address these gaps and build upon the existing evidence. This comprehensive examination evaluates the pooled prevalence of RLS in patients with chronic kidney disease, assesses the prevalence of RLS among children/adolescents and adults, and explores the associated risk factors for RLS.

Materials and Methods

Reporting standard

Our study adheres to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) (Page *et al.*, 2021). This study has been registered on the international Prospective Registered Systematic Review (PROSPERO) database under the registration number (CRD42022385009) and was designed following the Cochrane collaborations.

Eligibility criteria

The criteria for inclusion of studies in this meta-analysis were as follows: (1) reporting of data derived from observational studies employing cohort, cross-sectional, and case-control designs; (2) presentation of outcomes related to RLS; and (3) inclusion of a prevalence rate. Conversely, studies were excluded if they: (1) addressed irrelevant topics; (2) utilized irrelevant study designs; (3) involved irrelevant populations; (4) were meta-analyses or reviews; (5) represented study protocols; (6) constituted non-research articles; (7) exhibited insufficient data, even after attempts to contact the study authors; and (8) included participants identical to those in another study.

Search strategy

Two researchers performed a comprehensive literature search without time and language restrictions

from inception to September 2023 on the CINAHL, Cochrane, Embase, Ovid-MEDLINE, PubMed, Scopus, and Web of Science databases. Any differences were resolved through team discussion. A forward citation search was conducted to identify articles referenced in specific published studies and a backward citation search to review the reference lists of previously published systematic reviews and meta-analyses.

Furthermore, a manual search was conducted using Google Scholar to retrieve potential studies. Correspondingly, we reached out to the corresponding authors of eligible studies via email in case any information was absent from their published studies. A combination of Boolean and the following keywords were used to conduct a thorough search: Chronic Renal Insufficiency OR Chronic Kidney Disease OR kidney disease, Reltess Leg Syndrome OR Willis Ekbom Syndrome OR Wittmaack-Ekbom syndrome. The specific search terms used in each database are listed in Appendix 1.

Study selection

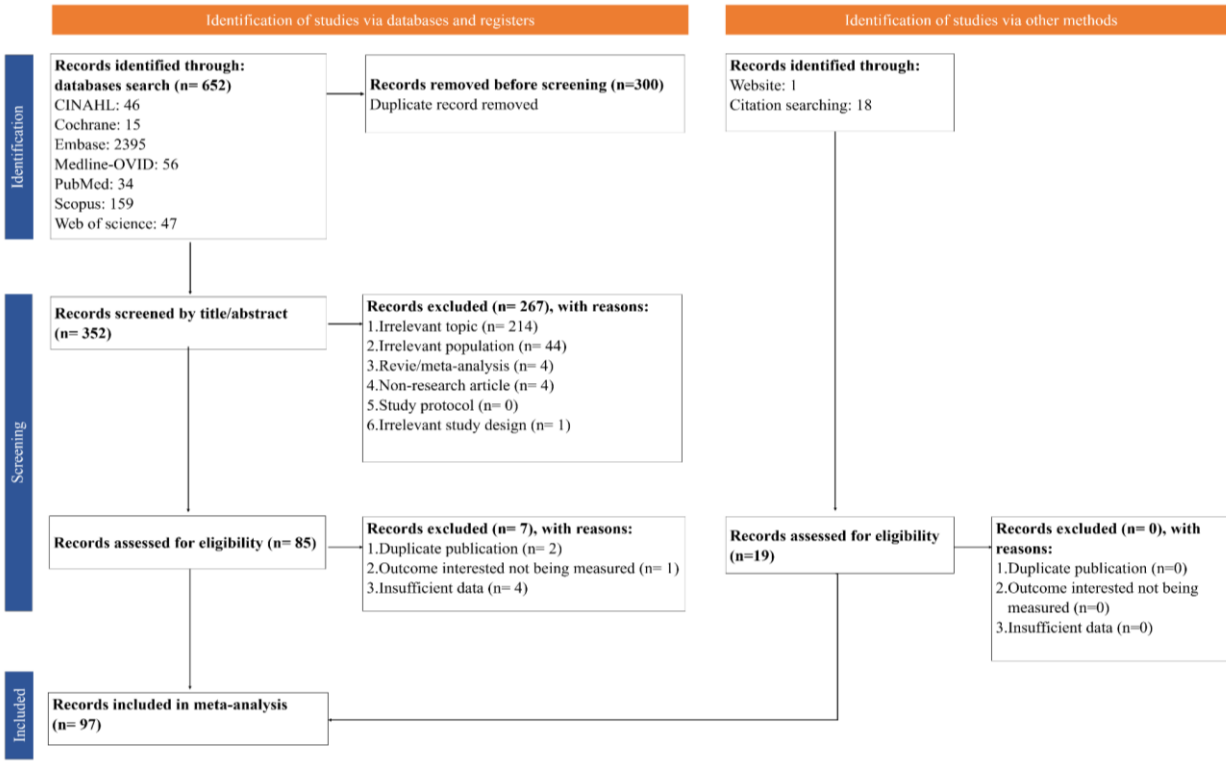
EndNote version 20.3 was employed for the comprehensive screening of studies based on inclusion and exclusion criteria through both database searches and manual searches. Manual and electronic methods were utilized to eliminate duplicate entries. Subsequently, two independent reviewers evaluated the titles and abstracts of each study to identify those eligible for full-text review. In cases where the full manuscript was not accessible, authors were contacted via email. Any inconsistencies identified during the screening process were addressed by consulting a third expert reviewer

Data extraction and risk of bias

To ensure the quality and validity of the data, two independent researchers conducted the data extraction, resolving disagreements through team discussions. The extracted data encompassed various categories, including authors, country, study design, population, sample size, RLS events, population characteristics, laboratory parameters, medical comorbidities, and other sleep problems. If data were missing from published studies, authors were contacted to ensure the incorporation of the majority of pertinent studies.

Two reviewers independently assessed the quality of all included studies using Hoy's risk of bias assessment, a tool that evaluates the internal and external validity of prevalence or incidence studies (Hoy *et al.*, 2012). This 10-item assessment tool features items 1-4, concentrating on the external validity of the study, and items 5-10, focusing on internal validity. Each item was rated with one for low risk and zero for high risk. The score was then classified as low (9-10), moderate (7-8), or high (0-6) risk of bias (Lundorff *et al.*, 2017). In the event of any data discrepancies, a third expert reviewer was consulted. Inter-rater agreement between the two reviewers was assessed using Cohen's Kappa test. Cohen proposed that the Kappa result be interpreted as

Figure 1. PRISMA flow diagram



follows: Values ≤ 0 indicate no agreement, 0.01-0.20 as none to slight, 0.21-0.40 as fair, 0.41-0.60 as moderate, 0.61-0.80 as substantial, and 0.81-1.00 as almost perfect agreement (McHugh, 2012).

Statistical analysis and assessment of publication bias

Data were analyzed using a random-effects model with Comprehensive Meta-Analysis (CMA) software version 3.0 to calculate the pooled prevalence rates. The primary results were reported in proportion format, accompanied by a 95% confidence interval (95% CI) and 95% prediction interval (95% PrI). The prediction interval signifies the range of prevalence in future studies akin to those included in the meta-analysis (IntHout *et al.*, 2016). Heterogeneity was evaluated using I^2 and Cochrane's Q-statistics, with p-values < 0.10 denoting significant statistical heterogeneity. I^2 values of 25%, 25%-75%, and 75% were categorized as minimal, moderate, and high heterogeneity, respectively (Higgins *et al.*, 2003).

When heterogeneity was present, subgroup and meta-regression analyses were employed to pinpoint moderator variables, with a p-value <0.05 indicating a significant moderator variable among groups. Additionally, sensitivity analysis was performed using sample sizes of less than 30 and a one-study-removal technique. To ensure the robustness of the study findings, the results of the sensitivity analysis were compared to those from the initial pooled prevalence analysis and scrutinized for consistency.

To evaluate the potential presence of publication bias, we depicted prevalence estimates on a funnel plot and employed Egger's regression intercept, Begg and Mazumdar rank correlation, and Kendall's tau without continuity correction. The presence of an asymmetric funnel plot with no points on one side would suggest the existence of publication bias (Ahn and Kang, 2018), while a p-value < 0.1 indicates publication bias (Peters *et al.*, 2006). In the event of detecting publication bias, the Duval and Tweedie trim and fill methods were applied for correction (Peters *et al.*, 2006).

Results

Characteristics of included studies

A thorough exploration of the literature was carried out across six electronic databases, resulting in the identification of 652 studies. Following the removal of duplicates, the remaining 352 studies underwent screening based on title and abstract, applying the previously outlined eligibility criteria. Subsequently, 85 studies met the criteria for full-text review, but seven were excluded due to reasons such as duplicate publication, absence of outcome interest measurement, or insufficient data. A manual search through the website and reference list of relevant studies revealed 18 studies from previous meta-analyses (Lin *et al.*, 2016) and one study from Google Scholar (Muzasti and Harahap, 2019) meeting the inclusion criteria and eligible for analysis. Figure 1 provides an overview of the literature identified at each stage of the procedure.

Finally, 97 studies were included in this meta-analysis with 315,875 participants in total. These studies were conducted in Asia (43 studies), Australia (1 study), Africa (5 studies), Europe (28 studies), North America (15 studies), and South America (5 studies) (Appendix 2). The percentage of females was higher than males (55.21% vs. 44.59%), the mean age was 53.22 (12.97) years, the mean BMI was 24.77 (4.61) kg/m^2, and the duration of dialysis was 51.82 (44.35) months. The study identified hyperparathyroidism (77.39%), peripheral neuropathy (69.63%), hypertension (50.09%), and diabetes mellitus (50.75%) as the most prevalent medical comorbidities. Additionally, psychological issues were observed, with anxiety and depression affecting 61.40% and 22.68% of the participants in the study, respectively. Moreover, other sleep problems experienced by CKD patients besides RLS in this study were poor sleep quality, sleepiness, insomnia, and obstructive sleep apnea (Table 1, Appendix 3).

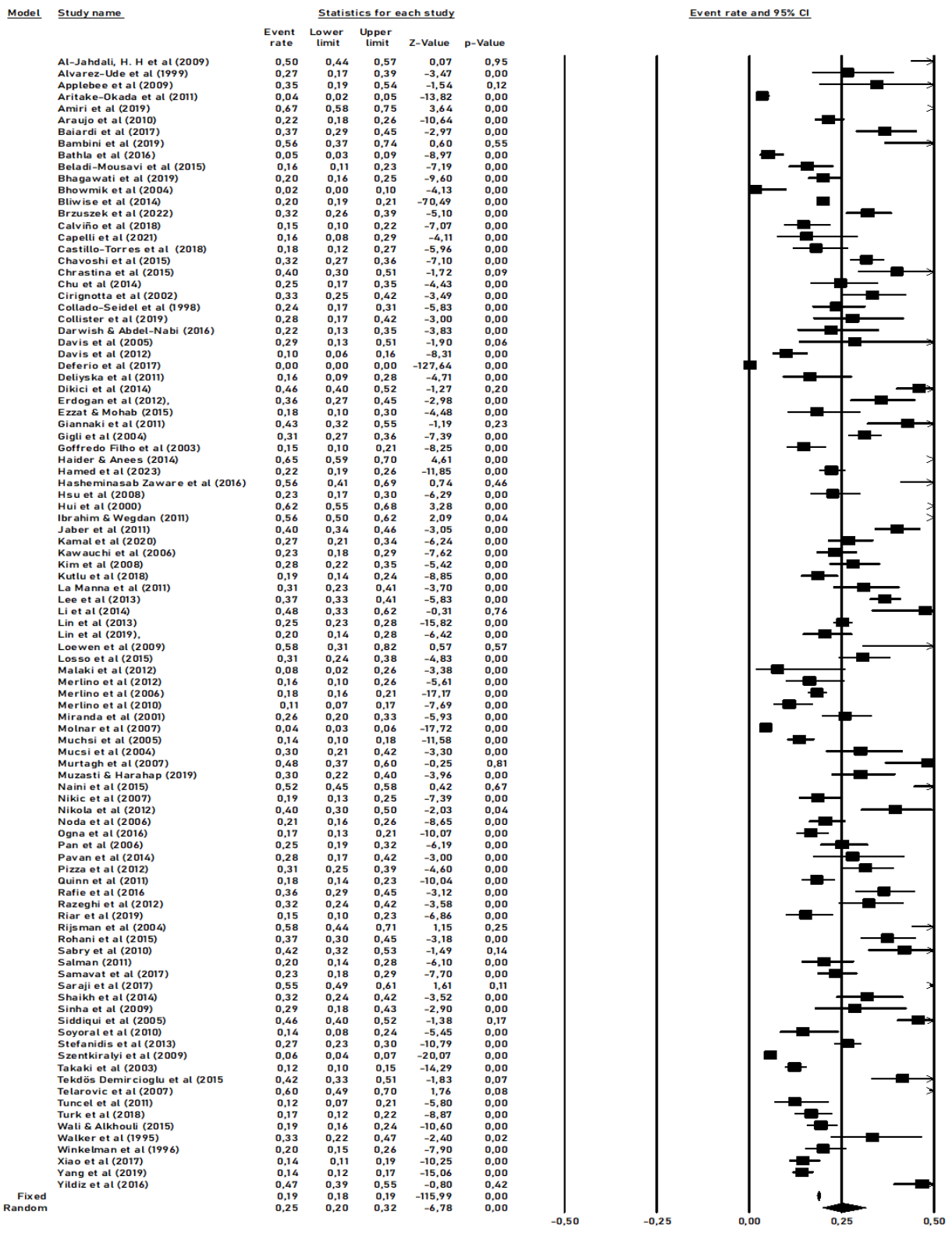
Quality assessments and sensitivity analysis

We assessed the study quality of all included studies using Hoy's risk of bias, and two raters performed the evaluation independently. We found 24 studies with low risk of bias and 73 studies with moderate risk. The Cohen's Kappa coefficient test showed almost perfect agreement between the two raters (κ = 0.85, p-value = <0.001) (Appendix 3).

Sensitivity analysis was performed based on the study sample size < 30 and the one-study removed technique. First, we independently analyzed studies with a sample size of <30. After excluding five studies with a sample size < 30, the RLS prevalence changed from 25% (95%CI: 20% to 32%) to 25% (95%CI: 19% to 31%), indicating a minor difference in the prevalence. Second, we performed a sensitivity analysis using the one-study-removed technique. Similarly, when one study was excluded, the RLS prevalence changed from 25% (95%CI: 20% to 32%) to 27% (95%CI: 24% to 29%), indicating a minor difference. Thus, the results of the current meta-analysis could be considered robust.

Meta-analysis prevalence of RLS

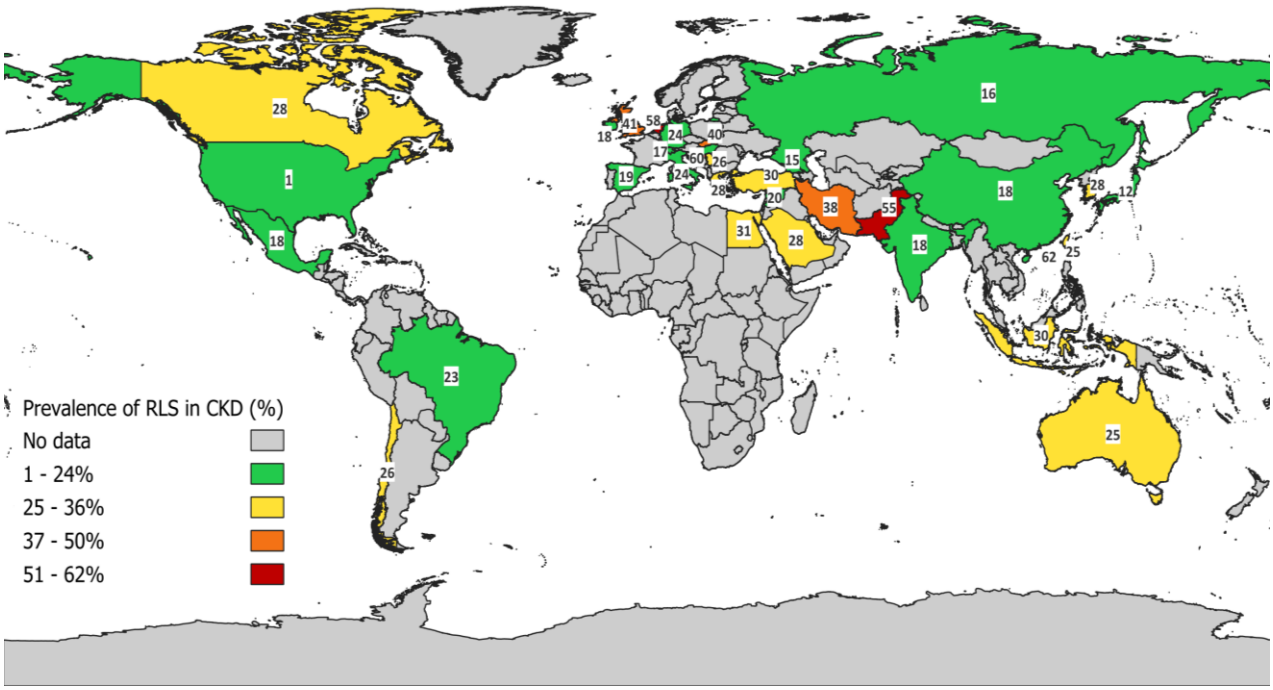
Figure 2. Forest plot of RLS prevalence among people with chronic kidney disease



Total studies: k= 97 (315,875)
Heterogeneity: Q= 12605.35; p-value= < 0.001; I^2= 99.24%; Tau^2= 2.44
Overall effect (random effect, 95%CI)= 0.25 (0.20 to 0.32), p-value= < 0.001
Prediction Interval: 0.01 to 0.88

The pooled prevalence of RLS among CKD patients is shown in Figure 2, with a total prevalence rate of 25% (95% CI: 20% to 32%). According to the prediction interval, the future prevalence of RLS was expected to vary from 1% to 88%. Figure 3 depicts a global map of the prevalence of RLS among chronic kidney disease patients in various geographical regions. We detected statistical heterogeneity with a p-value of < 0.001 and a Q= 12605.35, I^2 = 99.24% and τ^2= 2.44. We assessed

Figure 3. The world map depicts the pooled prevalence of RLS among people with chronic kidney disease in various geographical regions. This map was created with QGIS 3.30



publication bias, and the result of Egger's regression intercept and Begg and Mazumdar rank correlation Kendall's tau without continuity correction was p-value < 0.1, which indicated a publication bias (p-value=0.03, 95% CI 0.28 to 7.14, t-value 2.15; and p-value= 0.002, Tau= - 0.21, respectively) (Appendix 4). After conducting the Duval trim and fill method, by adding 28 studies, the point estimate changed to 18.11% (95%CI 14.45% to 22.46%) (Appendix 4).

Sub-group and meta-regression analysis

Table 2 displays the results of a moderator analysis using subgroup and meta-regression analyses. Moderator analysis revealed that levels of serum iron and phosphorus were significant moderators, while other moderators were not significant. An increased iron level (-0.01, 95%CI: - 0.02 to -0.00) will decrease the prevalence of RLS, while an increasing phosphorus level (0.20, 95%CI: 0.06 to 0.34) will increase RLS (Table 2).

Discussions

We estimated the pooled prevalence of RLS to be 25% (95% CI: 20% to 32%) among patients with CKD. The current findings are consistent with the previous meta-analyses that found RLS prevalence in CKD was 24.2% (95%CI: 20.1–28.7) (Lin et al., 2016), and the pooled prevalence of RLS among patients undergoing hemodialysis was 24% (95 %CI: 21.0%–26.0 %). A systematic review by Saparfour et al. (2023) found that RLS prevalence is two to three times more common in patients with CKD compared to the general population, and a meta-analysis found that CKD patients have a sixfold increase in the likelihood of RLS when compared to the general population (Aini *et al.*, 2024). Regarding the population, RLS prevalence in adults and children-adolescents in this study was almost similar (25% vs. 21%, respectively). Previous meta-analyses also found that RLS prevalence in children and adolescents was 21% (Kang et al., 2022).

RLS is a neurological sensorimotor disorder characterized by distressing sensations in the limbs, particularly the legs, that appear or worsen during periods of inactivity. The sensations worsen during the evening and nighttime hours (Shi et al., 2015). The exact cause of RLS is unknown, and it is referred to as primary (idiopathic) RLS; however, secondary RLS is linked to various systemic disorders, particularly iron deficiency and chronic renal insufficiency (Saparfour et al., 2023). While the prevalence of RLS is generally low in CKD patients, it can exacerbate the burden and cause significant inconvenience in those undergoing dialysis. Notably, the presence of restless legs syndrome in dialysis patients may also suggest potential issues with the adequacy of the dialysis treatment (Mao et al., 2014).

Prior meta-analysis revealed that age, female gender, dialysis duration, Kt/V or index of dialysis adequacy (dialyzer clearance of urea * dialysis time/volume of distribution of urea), serum phosphate, serum calcium, hemoglobin, diabetes, and hypertension

acted as significant moderators (Lin et al., 2016). However, in our meta-analysis, we only found iron and phosphorus as significant moderators. A higher iron level will decrease RLS prevalence or, vice versa, lower iron level will increase RLS prevalence. Previous meta-analyses found an association between phosphorus and RLS (Mansourian et al., 2020), and between iron and RLS (Mao et al., 2014). Iron deficiency in ESRD patients may cause RLS due to various underlying mechanisms, including anemia and changes in dopamine metabolism in the central nervous system (Beladi-Mousavi et al., 2015). Furthermore, brain iron deficiency and dopaminergic neurotransmission abnormalities play a central role in the pathogenesis of RLS, along with other nondopaminergic systems, though the exact mechanisms are still unknown (Safarpour et al., 2023).

High phosphorus levels, or hyperphosphatemia, in CKD patients, can often be asymptomatic. However, in some cases, it can lead to low calcium levels in the blood, causing symptoms such as muscle cramps or spasms (National Kidney Foundation, 2024). Because dopamine is involved in the regulation of phosphate excretion in the kidney, some situations that disrupt the functions of dopaminergic neurons may result in hyperphosphatemia, which plays an important role in diffuse vascular calcification in patients with end-stage renal failure. This condition may deteriorate vasculature functions, leading to the development of RLS (Mansourian et al., 2020). High phosphate levels are harmful to the cardiovascular system, and phosphate may be classified as a uremic toxin because of its effects on sleep disorders (Santos et al., 2016).

Our meta-analysis exhibits several strengths: (1) A thorough exploration was conducted using seven databases, complemented by manual searches of reference lists and Google Scholar, without restrictions on time and language; (2) In moderator analysis, a comprehensive examination of variables or risk factors was undertaken; (3) Stringent methodological procedures, including independent screening, meticulous data extraction, rigorous quality assessment, and adherence to PRISMA guidelines for reporting, were employed; and (4) Sensitivity analyses were performed to affirm the robustness of the study findings. However, the study has certain limitations: (1) Significant heterogeneity was observed in the results, prompting a subgroup analysis and meta-regression to identify potential sources of heterogeneity; (2) The outcomes of moderator analysis in both the current meta-analysis and previous studies remain debated, highlighting the need for larger longitudinal studies to establish causal relationships of restless legs syndrome (RLS) risk factors in CKD patients; and (3) Evidence of publication bias was detected, necessitating the implementation of the Duval and Tweedie trim and fill method for correction.

Conclusion

Approximately one-fourth of CKD patients experience RLS. Regarding the population, RLS prevalence in adults and children-adolescents was almost similar. The significant moderators in this meta-analysis were the level of serum iron and phosphorus. However, many studies' findings remain debatable. Further longitudinal research is needed to determine the associated risk factors of RLS in CKD patients, and future studies should focus on developing interventions to reduce RLS symptoms. Moreover, encouraging collaboration among healthcare professionals to develop a comprehensive approach and early assessment of RLS is crucial to improving the quality of life for CKD patients.

Acknowledgments

The authors are responsible for the contents of this document, which includes their findings and conclusions.

Funding Source

This research did not receive any specific grant from public, commercial, or non-profit funding agencies.

Conflict of Interest

The authors declare that there is no known competing conflict of interest that could have influenced the work described in this paper.

Reference

Ahn, E. & Kang, H. (2018). Introduction to systematic review and meta-analysis. Korean J Anesthesiol, 71.2, 103-112.doi: 10.4097/kjae.2018.71.2.103

Aini, N., *et al.* (2024). *Association between chronic kidney disease and restless leg syndrome (RLS): A systematic review and meta-analysis*. *Sleep Biol Rhythms,* 22.2, 227-237.doi: 10.1007/s41105-024-00513-4

Beladi-Mousavi, S. S., *et al.* (2015). *Restless legs syndrome: Associated risk factors in hemodialysis patients*. *Nephro-Urology Monthly,* 7.6.doi: 10.5812/numonthly.31967

Chen, J.-J., *et al.* (2022). Pharmacological and non-pharmacological treatments for restless legs syndrome in end-stage kidney disease: a systematic review and component network meta-analysis. Nephrology Dialysis Transplantation, 37.10, 1982-1992.doi: 10.1093/ndt/gfab290

Ghanei Gheshlagh, R., *et al.* (2017). *The prevalence of restless legs syndrome in patients undergoing hemodialysis: A systematic review and meta-analysis study*. *Basic Clin Neurosci,* 8.2, 105-112.doi: 10.18869/nirp.bcn.8.2.105

Giannaki, C. D., *et al.* (2017). *Restless legs syndrome is contributing to fatigue and low quality of life levels in hemodialysis patients*. *World J Nephrol,* 6.5, 221-242.doi: 10.5527/wjn.v6.i5.236

Higgins, J. P., *et al.* (2003). *Measuring inconsistency in meta-analyses*. *Bmj,* 327.7414, 557-60.doi: 10.1136/bmj.327.7414.557

Hoy, D., *et al.* (2012). *Assessing risk of bias in prevalence studies: Modification of an existing tool and evidence of interrater agreement*. *J Clin Epidemiol,* 65.9, 934-9.doi: 10.1016/j.jclinepi.2011.11.014

Inthout, J., *et al.* (2016). *Plea for routinely presenting prediction intervals in meta-analysis*. *BMJ Open,* 6.7, e010247.doi: 10.1136/bmjopen-2015-010247

Kang, K.-T., *et al.* (2022). *Prevalence of sleep disorders in children with chronic kidney disease: a meta-analysis*. *Pediatric Nephrology,* 37.11, 2571-2582.doi: 10.1007/s00467-022-05536-y

Kubo, K., *et al.* (2016). *Relationship between quality of life and restless legs syndrome among a community-dwelling population in Japan*. *Neuropsychiatr Dis Treat,* 12. 809-15.doi: 10.2147/NDT.S102089

Lin, X. W., *et al.* (2019). *Restless legs syndrome in end stage renal disease patients undergoing hemodialysis*. *BMC Neurol,* 19.1, 47.doi: 10.1186/s12883-019-1265-y

Lin, Z., *et al.* (2016). *Prevalence of restless legs syndrome in chronic kidney disease: A systematic review and meta-analysis of observational studies*. *Renal Failure,* 38.9, 1335-1346.doi: 10.1080/0886022X.2016.1227564

Liu, Y., *et al.* (2024). *Prevalence of restless legs syndrome in maintenance hemodialysis patients: A systematic review and meta-analysis*. *Sleep Med,* 114. 15-23.doi: 10.1016/j.sleep.2023.11.1138

Lundorff, M., *et al.* (2017). *Prevalence of prolonged grief disorder in adult bereavement: A systematic review and meta-analysis*. *J Affect Disord,* 212. 138-149.doi: 10.1016/j.jad.2017.01.030

Mansourian, M., *et al.* (2020). *Are serum vitamin D, calcium and phosphorous associated with restless leg syndrome? A systematic review and meta-analysis*. *Sleep Med,* 75. 326-334.doi: 10.1016/j.sleep.2020.08.022

Mao, S., *et al.* (2014). *Restless legs syndrome in dialysis patients: A meta-analysis*. *Sleep Med,* 15.12, 1532-8.doi: 10.1016/j.sleep.2014.07.017

Maung, S. C., *et al.* (2016). *Sleep disorders and chronic kidney disease*. *World J Nephrol,* 5.3, 224-32.doi: 10.5527/wjn.v5.i3.224

Mchugh, M. L. (2012). *Interrater reliability: The kappa statistic*. *Biochem Med (Zagreb),* 22.3, 276-82.doi:

Muzasti, R. A. & Harahap, R. H. 2019. The role of anemia to restless legs syndrome in regular hemodialysis patients in Haji Adam Malik Medan general hospital. *Proceedings of the 2nd International Conference on Tropical Medicine and Infectious Disease.*

National Kidney Foundation. 2024. *Kidney failure risk factor: Serum phosphorus* [Online]. Available: https://www.kidney.org/content/kidney-failure-risk-factor-serum-phosphorus [Accessed January 14 2024].

Nigam, G., *et al.* (2018). *Exploring sleep disorders in patients with chronic kidney disease*. *Nat Sci Sleep,* 10. 35-43.doi: 10.2147/NSS.S125839

Novak, M., *et al.* (2015). *Restless legs syndrome in patients with chronic kidney disease*. *Semin Nephrol,* 35.4, 347-58.doi: 10.1016/j.semnephrol.2015.06.006

Page, M. J., *et al.* (2021). *The PRISMA 2020 statement: An updated guideline for reporting systematic reviews*. *BMJ,* 372. n71.doi: 10.1136/bmj.n71

Peters, J. L., *et al.* (2006). *Comparison of two methods to detect publication bias in meta-analysis*. *JAMA,* 295.6.doi:

Safarpour, Y., *et al.* (2023). *Restless Legs Syndrome in Chronic Kidney Disease- a Systematic Review*. *Tremor and other hyperkinetic movements (New York, N.Y.),* 13. 10.doi: https://dx.doi.org/10.5334/tohm.752

Santos, R. S., *et al.* (2016). *Parathyroidectomy improves restless leg syndrome in patients on hemodialysis*. *PLoS One,* 11.5, e0155835.doi: 10.1371/journal.pone.0155835

Saparfour, Y., *et al.* (2023). *Restless legs syndrome in chronic kidney disease: A systematic review*. *Tremor Other Hyperkinet Mov (N Y),* 13. 10.doi: 10.5334/tohm.752

Shi, Y., *et al.* (2015). *Prevalence and risk factors of restless legs syndrome among Chinese adults in a rural community of Shanghai in China*. *PLoS One,* 10.3, e0121215.doi: 10.1371/journal.pone.0121215

Tan, L. H., *et al.* (2022). *Insomnia and poor sleep in CKD: A systematic review and meta-analysis*. *Kidney Med,* 4.5, 100458.doi: 10.1016/j.xkme.2022.100458

How to cite this article: Aini, N., Janistra, F. E., Putri, A. R., Fauk, N. K., and Arifin, H. (2024) 'Meta-analysis of the prevalence of restless leg syndrome and associated risk factors in chronic kidney disease patients', *Jurnal Ners*, 19(2), pp. 240-272. doi: http://dx.doi.org/10.20473/jn.v19i2.54993

Table 1. Demographics of included studies

	Number of studies	Number of participants (%)	Mean	SD
Sample size	97	315,875		
Age (years)	82	313,570	53.22	12.97
Duration of dialysis (months)	49	11,579	51.82	44.35
BMI (kg/m²)	32	286,887	24.77	4.61
Sex				
Male	82	140,327 (44.59%)		
Female	82	174,391 (55.21%)		
Population				
Children and Adolescent	6	433 (0.14%)		
Adult	91	315,442 (99.86%)		
Country geographical area				
Asia	43	9,256 (2.93%)		
Australia	1	85 (0.03%)		
Africa	5	1,098 (0.35%)		
Europe	28	6,568 (2.08%)		
North America	15	297,935 (94.32%)		
South America	5	933 (0.29%)		
Study design				
Cross-sectional	82	18,004 (5.69%)		
Cohort	5	1,036 (0.33%)		
Case-control	10	296,835 (93.98%)		
Laboratory parameters				
Albumin (g/dL)	29	287,797	3.76	0.48
Bilirubin (mg/dL)	1	65	0.69	0.21
BUN (mg/dL)	20	4,895	61.79	18.10
Calcium (mg/dL)	31	6,976	7.39	1.04
Creatinine (mg/dL)	31	285,587	43.12	12.18
Cholesterol (gr/dL)	2	170	175.94	46.85
Chloride (mmol/L)	2	243	103.40	34.15
Ferritin (ng/mL)	40	7,914	443.51	335.92
Folate (ng/mL)	1	129	7.0	2.44
GFR (ml/min/1.73 m2)	11	2,815	30.90	12.46
Hemoglobin (g/dL)	53	27,433	10.98	1.61
Hematocrit (%)	3	393	13.96	2.38
Iron (ng/dL)	21	4,284	63.37	32
Kt/V (index of dialysis adequacy)	20	4,078	1.37	0.27
Magnesium (mg/dL)	4	1,032	2.67	0.86
Phosphate (mg/dL)	14	3,416	3.86	1.13
Phosphorus (mg/dL)	20	3,846	4.22	1.83
Potassium (mmol/L)	9	2,006	5.04	0.71
PTH (pg/mL)	26	6,568	295.61	306.27
Sodium (mmol/L)	3	725	137.43	3.25
Transferrin (mg/dL)	6	1,205	218.94	47.19
Uric Acid (mg/dL)	2	504	6.80	3.67
Vitamin D (ng/mL)	3	389	189.4	62.47
Vitamin B12 (ng/mL)	1	129	25.0	8.60
Life style				
Alcohol use	4	38 (11.66%)		
Smoking	14	228 (15.77%)		
Medical comorbidities				
Anemia	5	230 (33.57%)		
Cancer	1	5 (15.63%)		
Cardiovascular disease	9	220 (26.99%)		
Cerebrovascular disease	5	76 (11.13%)		
Congestive heart failure	5	180 (24.86%)		
COPD	4	65 (18.47%)		
Diabetes Mellitus	43	2884 (44.88%)		
Hepatitis	1	2 (4.35%)		
Hypertension	28	1,267 (50.09%)		
Hyperparathyroidism	2	154 (77.39%)		
Hyperkalemia	1	40 (34.48%)		
Hyperuricemia	1	50 (43.11%)		
Osteoarthritis	1	11 (20%)		
Peripheral Neuropathy	2	94 (69.63%)		

Polyneuropathy	1	13 (27%)		
Peripheral vascular disease	5	58 (9.97%)		
Rheumatoid arthritis	1	2 (3.60%)		
Urologic disease	2	20 (27.28%)		
Psychological problem				
Anxiety	2	105 (61.40%)		
Depression	8	188 (22.68%)		
Other sleep problems				
ESS score	13	488	7.02	4.29
PSQI score	7	313	8.94	4.29
ISI score	2	189	15.29	1.82
Poor sleep quality	3	126 (75%)		
Daytime sleepiness	4	43 (25%)		
Insomnia	12	418 (61.20%)		
Obstructive sleep apnea	11	219 (21.14%)		

Note: ESS= Epworth Sleepiness Scale; ISI= Insomnia Severity Index, PSQI= The Pittsburgh Sleep Quality Index, COPD= Chronic obstructive pulmonary disease, Kt/V= dialyzer clearance of urea * dialysis time/volume of distribution of urea.

Table 2. Moderator analysis of RLS among people with chronic kidney disease

Variables	n	df	Prevalence % (95%CI)	p-value
Subgroup analysis				
Sex				
Male	82 (140,327)	81	0.13 (0.10 to 0.17)	0.13
Female	82 (174,391)	81	0.10 (0.07 to 0.13)	
Population				
Children and Adolescent	6 (433)	5	0.21 (0.14 to 0.30)	0.40
Adult	91 (315,442)	92	0.25 (0.20 to 0.32)	
County geographical area				
Asia	43 (9,256)	42	0.27 (0.23 to 0.32)	0.97
Africa	5 (1,098)	4	0.28 (0.16 to 0.45)	
Australia	1 (85)	0	0.25 (0.17 to 0.35)	
Europe	28 (6,568)	27	0.25 (0.20 to 0.30)	
North America	15 (297,935)	14	0.21 (0.06 to 0.52)	
South America	5 (933)	4	0.26 (0.19 to 0.35)	
Study design				
Cross-sectional	82 (18,004)	81	0.27 (0.24 to 0.30)	0.75
Cohort	5 (1,036)	4	0.26 (0.15 to 0.41)	
Case-control	10 (296,835)	9	0.14 (0.02 to 0.57)	

Meta-regression analysis	n		Scale	Coefficient (95%CI)	p-value
Age	82 (313,570)	81	Per 1-year increase	0.00 (-0.02 to 0.02)	0.87
Duration of dialysis (months)	49 (11,579)	48	Per 1-month increase	0.00 (-0.01 to 0.01)	0.43
BMI	32 (286,887)	31	Per 1 increase	-0.06 (-0.22 to 0.10)	0.44
Albumin (g/dL)	29 (287,797)	28	Per 1 increase	0.31 (-1.11 to 1.74)	0.67
BUN (mg/dL)	20 (4,895)	19	Per 1 increase	0.00 (-0.00 to 0.01)	0.41
Calcium (mg/dL)	31 (6,976)	30	Per 1 increase	-0.02 (-0.09 to 0.06)	0.68
Creatinine (mg/dL)	31 (285,111)	30	Per 1 increase	0.00 (-0.00 to 0.00)	0.85
Ferritin (ng/mL)	40 (7,914)	39	Per 1 increase	0.00 (-0.00 to 0.00)	0.20
GFR (ml/min/1.73 m2)	11 (2,815)	10	Per 1 increase	-0.01 (-0.04 to 0.01)	0.33
Hemoglobin (g/dL)	53 (27,433)	52	Per 1 increase	0.04 (-0.12 to 0.20)	0.61
Iron (ng/dL)	21 (4,284)	20	Per 1 increase	-0.01 (-0.02 to -0.00)	0.02
Kt/V (index of dialysis adequacy)	20 (4,078)	19	Per 1 increase	-0.21 (-1.77 to 1.35)	0.79
Magnesium (mg/dL)	4 (1,032)	3	Per 1 increase	-0.13 (-0.50 to 0.24)	0.50
Phosphate (mg/dL)	14 (3,416)	13	Per 1 increase	-0.09 (-0.25 to 0.08)	0.31
Phosphorus (mg/dL)	20 (3,846)	19	Per 1 increase	0.20 (0.06 to 0.34)	0.01
Potassium (mmol/L)	9 (2,006)	8	Per 1 increase	0.36 (-0.57 to 1.29)	0.44
PTH (pg/mL)	26 (6,568)	25	Per 1 increase	0.00 (-0.00 to 0.00)	0.20
Transferrin (mg/dL)	6 (1,205)	6	Per 1 increase	-0.01 (-0.02 to 0.00)	0.09
ESS score	13 (488)	12	Per 1 increase	0.11 (-0.08 to 0.29)	0.25
Proportion of OSA	11 (219)	10	Per 1% increase	0.00 (-0.00 to 0.00)	0.29
Proportion of insomnia	12 (418)	11	Per 1% increase	-0.00 (-0.02 to 0.01)	0.76
Proportion of smoking	14 (228)	13	Per 1% increase	-0.02 (-0.04 to 0.00)	0.10
Proportion of alcohol use	4 (38)	3	Per 1% increase	0.05 (-0.07 to 0.02)	0.15
Proportion of anemia	5 (230)	4	Per 1% increase	0.07 (-0.02 to 0.16)	0.11
Proportion of cardiovascular disease	9 (220)	8	Per 1% increase	0.07 (-0.02 to 0.17)	0.12
Proportion of cerebrovascular disease	5 (76)	4	Per 1% increase	0.18 (-0.40 to 0.76)	0.54
Proportion of congestive heart failure	5 (180)	4	Per 1% increase	-0.08 (-0.40 to 0.24)	0.63
Proportion of COPD	4 (65)	3	Per 1% increase	-0.04 (-0.15 to 0.08)	0.52

Proportion of diabetes mellitus	43 (2,884)	42	Per 1% increase	0.00 (-0.02 to 0.02)	0.81
Proportion of hypertension	28 (1,267)	27	Per 1% increase	-0.02 (-0.03 to 0.00)	0.07
Proportion of peripheral vascular disease	5 (58)	4	Per 1% increase	0.00 (-0.83 to 0.83)	1.00
Proportion of depression	8 (188)	7	Per 1% increase	0.04 (-0.01 to 0.09)	0.09

Note: BMI= body mass index, BUN= blood urea nitrogen, GFR= glomerular filtration rate, PTH= Parathyroid hormone, Excessive daytime Sleepiness, PSQI= The Pittsburgh Sleep Quality Index, OSA= obstructive sleep apnea, COPD= Chronic obstructive pulmonary disease, Kt/V= dialyzer clearance of urea * dialysis time/volume of distribution of urea.

Appendix 1. Search String

Database	Result	String
CINAHL	46	S1= AB prevalence OR prevalence OR prevalence study OR incidence OR incidence OR incidence rate OR rate, incidence S2= AB restless legs syndrome OR ekbom syndrome OR ekbom`s syndrome OR rls/wed OR willis ekbom disease OR willis ekbom disorder OR willis-ekbom disease OR willis-ekbom`s disease OR wittmaack-ekbom syndrome OR anxietas tibiarum OR leg, restless OR restless arm OR restless arm syndrome OR restless arms OR restless arms syndrome OR restless leg OR restless leg syndrome OR restless legs OR restless legs syndrome OR syndrome of restless legs OR syndrome, restless legs S3= AB kidney disease OR disease, kidney OR kidney disease OR kidney diseases OR kidney disorder OR kidney pathology OR nephropathy OR perinephritis OR perirenal infection OR renal disease OR renal disorder OR unilateral kidney disease OR chronic kidney failure OR chronic kidney disease OR chronic kidney disorder OR chronic kidney failure OR chronic kidney insufficiency OR chronic nephropathy OR chronic renal disease OR chronic renal failure OR chronic renal insufficiency OR kidney chronic failure OR kidney disease, chronic OR kidney failure, chronic OR kidney function, chronic disease OR renal insufficiency, chronic S1 AND S2 AND S3 Augmented Words - apply equivalent theme Search Mode - find all search terms
Cochrane	15	#1 (Prevalence OR prevalence study OR incidence):ti,ab,kw #2 (restless legs syndrome OR ekbom syndrome willis OR willis-ekbom disease OR wittmaack-ekbom syndrome OR anxietas tibiarum):ti,ab,kw #3 (kidney diseases OR kidney disorder OR kidney pathology OR nephropathy OR perinephritis OR perirenal infection OR renal disease OR renal disorder OR chronic kidney failure OR chronic kidney disease OR chronic kidney disorder OR chronic kidney failure OR chronic kidney insufficiency OR chronic nephropathy OR chronic renal disease OR chronic renal failure OR chronic renal insufficiency OR kidney chronic failure OR kidney function, chronic disease OR renal insufficiency, chronic):ti,ab,kw #1 AND #2 AND #3
Embase	295	#1 'prevalence'/exp OR 'prevalence' OR 'prevalence study' OR 'incidence'/exp OR 'incidence' OR 'incidence rate' OR 'rate, incidence' #2 'restless legs syndrome'/exp OR 'ekbom syndrome' OR 'ekbom`s syndrome' OR 'rls/wed' OR 'willis ekbom disease' OR 'willis ekbom disorder' OR 'willis-ekbom disease' OR 'willis-ekbom`s disease' OR 'wittmaack-ekbom syndrome' OR 'anxietas tibiarum' OR 'leg, restless' OR 'restless arm' OR 'restless arm syndrome' OR 'restless arms' OR 'restless arms syndrome' OR 'restless leg' OR 'restless leg syndrome' OR 'restless legs' OR 'restless legs syndrome' OR 'syndrome of restless legs' OR 'syndrome, restless legs' #3 'kidney disease'/exp OR 'disease, kidney' OR 'kidney disease' OR 'kidney diseases' OR 'kidney disorder' OR 'kidney pathology' OR 'nephropathy' OR 'perinephritis' OR 'perirenal infection' OR 'renal disease' OR 'renal disorder' OR 'unilateral kidney disease' OR 'chronic kidney failure'/exp OR 'chronic kidney disease' OR 'chronic kidney disorder' OR 'chronic kidney failure' OR 'chronic kidney insufficiency' OR 'chronic nephropathy' OR 'chronic renal disease' OR 'chronic renal failure' OR 'chronic renal insufficiency' OR 'kidney chronic failure' OR 'kidney disease, chronic' OR 'kidney failure, chronic' OR 'kidney function, chronic disease' OR 'renal insufficiency, chronic' #4 #1 AND #2 AND #3 #5 #4 AND ('article'/it OR 'review'/it)
Pubmed	34	(("Prevalence"[Mesh]) AND "Restless Legs Syndrome"[Mesh]) AND "Kidney Failure, Chronic"[Mesh]
SCOPUS	159	(TITLE-ABS-KEY (prevalence OR "Point Prevalence" OR "period prevalence" OR incidence)) AND (TITLE-ABS-KEY ("Restless Legs" OR "Willis Ekbom Disease" OR "Disease, Willis Ekbom" OR "Wittmaack-Ekbom Syndrome" OR "Restless Leg Syndrome")) AND (TITLE-ABS-KEY ("End-Stage Kidney Disease" OR "Kidney Disease, End-Stage" OR "Chronic Kidney Failure" OR "End-Stage Renal Failure" OR "Renal Failure, Chronic" OR "Chronic Renal Failure" OR esrd))
WOS	47	AB=(prevalence OR Point Prevalence OR period prevalence OR incidence) AND AB=(Restless Legs OR Willis Ekbom Disease OR Disease, Willis Ekbom OR Wittmaack-Ekbom Syndrome OR Restless Leg Syndrome) AND AB=(End-Stage Kidney Disease OR Kidney Disease, End-Stage OR Chronic Kidney Failure OR End-Stage Renal Failure OR Renal Failure, Chronic OR Chronic Renal Failure OR ESRD)

MEDLINE-OVID		((period prevalence.mp OR period prevalences.mp OR point prevalence.mp OR point prevalences.mp OR prevalence.mp OR prevalence, period.mp OR prevalence, point.mp OR prevalences.mp) AND (disease, willis ekbom.mp OR restless leg syndrome.mp OR restless legs.mp OR restless legs syndrome.mp OR syndrome, restless leg.mp OR syndrome, willis ekbom.mp OR syndrome, wittmaack ekbom.mp OR willis ekbom disease.mp OR willis ekbom syndrome.mp OR wittmaack ekbom syndrome.mp)) AND (chronic kidney disease.mp OR chronic kidney diseases.mp OR chronic kidney insufficiencies.mp OR chronic kidney insufficiency.mp OR chronic renal disease.mp OR chronic renal diseases.mp OR chronic renal insufficiencies.mp OR disease, chronic kidney.mp OR disease, chronic renal.mp OR diseases, chronic kidney.mp OR diseases, chronic renal.mp OR kidney disease, chronic.mp OR kidney diseases, chronic.mp OR kidney insufficiencies, chronic.mp OR kidney insufficiency, chronic.mp OR renal disease, chronic.mp OR renal diseases, chronic.mp OR renal insufficiencies, chronic.mp OR renal insufficiency, chronic.mp)

Appendix 2. Reference of Included Studies

No.	Study	Reference
1	Al-Jahdali, H. H et al (2009)	Al-Jahdali, H. H., Al-Qadhi, W. A., Khogeer, H. A., Al-Hejaili, F. F., Al-Ghamdi, S. M., & Al Sayyari, A. A. (2009). Restless legs syndrome in patients on dialysis. *Saudi J Kidney Dis Transpl.* 20(3), 378-385.
2	Alvarez-Ude et al (1999)	Alvarez-Ude, F., Alamo, C., Fernandez-Reyes, M. J., Bravo, B., Vicente, E., Ferrer, M., Alonso, J., & Badia, X. (1999). Sleep complaints and perceived health status in patients in long-term hemodialysis. *Nefrologia.* 19(2), 168-176.
3	Applebee et al (2009)	Applebee, G. A., Guillot, A. P., Schuman, C. C., Teddy, S., & Attarian, H. P. (2009). Restless legs syndrome in pediatric patients with chronic kidney disease. *Pediatric Nephrology.* 24(3), 545-548. https://doi.org/https://dx.doi.org/10.1007/s00467-008-1057-x
4	Aritake-Okada et al (2011)	Aritake-Okada, S., Nakao, T., Komada, Y., Asaoka, S., Sakuta, K., Esaki, S., Nomura, T., Nakashima, K., Matsuura, M., & Inoue, Y. (2011). Prevalence and clinical characteristics of restless legs syndrome in chronic kidney disease patients. *Sleep Medicine.* 12(10), 1031-1033. https://doi.org/10.1016/j.sleep.2011.06.014
5	Amiri et al (2019)	Amiri, M., Bidaki, R., Avazbakhsh, M., Mirhosseini, H., & Yamola, M. (2019). Prevalence and correlates of restless legs syndrome in chronic renal failure patients undergoing hemodialysis. *Koomesh.* 21(3), 493-497
6	Araujo et al (2010)	Araujo, S. M., de Bruin, V. M., Nepomuceno, L. A., Maximo, M. L., Daher Ede, F., Correia Ferrer, D. P., & de Bruin, P. F. (2010). Restless legs syndrome in end-stage renal disease: Clinical characteristics and associated comorbidities. *Sleep Medicine.*11(8), 785-790. https://doi.org/10.1016/j.sleep.2010.02.011
7	Baiardi et al (2017)	Baiardi, S., Mondini, S., Baldi antognini, a., Santoro, a., & Cirignotta, F. (2017). Survival of Dialysis Patients with Restless Legs Syndrome: A 15-Year Follow-Up Study. *American Journal of Nephrology.* 46(3), 224-230. https://doi.org/10.1159/000479938
8	Bambini et al (2019)	Bambini, B. B. M., Moyses, R. M. A., Batista, L. C. D., Coelho, B., Tufik, S., Elias, R. M., & Coelho, F. M. (2019). Restless legs syndrome in patients on hemodialysis: Polysomnography findings. *Hemodialysis International.* 23(4), 445-448. https://doi.org/10.1111/hdi.12781
9	Bathla et al (2016)	Bathla, N., Ahmad, S., Gupta, R., & Ahmad, S. (2016). Prevalence and correlates of Willis-Ekbom's disease/restless legs syndrome in patients undergoing hemodialysis. *Saudi journal of kidney diseases and transplantation : An Official Publication of The Saudi Center for Organ Transplantation, Saudi Arabia.* 27(4), 685-691. https://doi.org/10.4103/1319-2442.185224
10	Beladi-Mousavi et al (2015)	Beladi-Mousavi, S. S., Jafarizade, M., Shayanpour, S., Bahadoram, M., Moosavian, S. M., & Houshmand, G. (2015). Restless legs syndrome: Associated risk factors in hemodialysis patients. *Nephro-Urology Monthly.* 7(6), Article e31967. https://doi.org/10.5812/numonthly.31967
11	Bhagawati et al (2019)	Bhagawati, J., Kumar, S., Agrawal, A. K., Acharya, S., Wanjari, A. K., & Kamble, T. K. (2019). Impact of different stages of chronic kidney disease on the severity of Willis-Ekbom disease. *Journal of Family Medicine and Primary Care.* 8(2), 432-436. https://doi.org/https://dx.doi.org/10.4103/jfmpc.jfmpc_418_18
12	Bhowmik et al (2004)	Bhowmik, D., Bhatia, M., Tiwari, S., Mahajan, S., Gupta, S., Agarwal, S. K., & Dash, S. C. (2004). Low prevalence of restless legs syndrome in patients with advanced chronic renal failure in the indian population: A case controlled study. *Renal Failure.* 26(1), 69-72. https://doi.org/10.1081/JDI-120028557
13	Bliwise et al (2014)	Bliwise, D. L., Zhang, R. H., & Kutner, N. G. (2014). Medications associated with restless legs syndrome: A case-control study in the US Renal Data System (USRDS). *Sleep Medicine.* 15(10), 1241-1245. https://doi.org/10.1016/j.sleep.2014.05.011
14	Brzuszek et al (2022)	Brzuszek, A., Hazara, A. M., & Bhandari, S. (2022). The prevalence and potential aetiological factors associated with restless legs syndrome in patients with chronic kidney disease: A cross-sectional study. *Int Urol Nephrol.* 54(10), 2599-2607. https://doi.org/10.1007/s11255-022-03166-9
15	Calviño et al (2018)	Calviño, J., Cigarrán, S., Gonzalez-Tabares, L., Guijarro, M., Millán, B., Cobelo, C., Cillero, S., & Sobrido, M. J. (2018). Restless legs syndrome: An unresolved uremic disorder after renal transplantation. *Nephron.* 139(1), 23-29. https://doi.org/10.1159/000486401
16	Capelli et al (2021)	Capelli, I., Pizza, F., Ruggeri, M., Gasperoni, L., Carretta, E., Donati, G., Cianciolo, G., Plazzi, G., & La Manna, G. (2021). Time evolution of restless legs syndrome in haemodialysis patients. *Clinical Kidney Journal.* 14(1), 341-347. https://doi.org/10.1093/ckj/sfz148
17	Castillo-Torres et al (2018)	Castillo-Torres, S. A., Ibarra-Sifuentes, H. R., Sánchez-Terán, H., Sánchez-Martínez, C., Chávez-Luévanos, B., & Estrada-Bellmann, I. (2018). Restless legs syndrome in end-stage renal disease patients undergoing hemodialysis. *Arq Neuropsiquiatr.* 76(12), 827-830. https://doi.org/10.1590/0004-282x20180133
18	Chavoshi et al (2015)	Chavoshi, F., Einollahi, B., Haghighi, K. S., Saraei, M., & Izadianmehr, N. (2015). Prevalence and sleep related disorders of restless leg syndrome in hemodialysis patients. *Nephro-Urology Monthly.* 7(2), Article e24611. https://doi.org/10.5812/numonthly.24611
19	Chrastina et al (2015)	Chrastina, M., Martinkova, J., Minar, M., Zilinska, Z., Valkovic, P., & Breza, J. (2015). Impact of kidney transplantation on restless legs syndrome. *Bratisl Lek Listy.* 116(7), 404-407. https://doi.org/10.4149/bll_2015_077

20	Chu et al (2014)	Chu, L., Chu, E., Dogra, G., & Chakera, A. (2014). Restless legs syndrome: An underappreciated and distressing problem for haemodialysis patients. *Internal Medicine Journal.* 44(10), 1030-1033. https://doi.org/10.1111/imj.12559
21	Cirignotta et al (2002)	Cirignotta, F., Mondini, S., Santoro, A., Ferrari, G., Gerardi, R., & Buzzi, G. (2002). Reliability of a questionnaire screening restless legs syndrome in patients on chronic dialysis. *Am J Kidney Dis.* 40(2), 302-306. https://doi.org/10.1053/ajkd.2002.34508
22	Collado-Seidel et al (1998)	Collado-Seidel, V., Kohnen, R., Samtleben, W., Hillebrand, G. F., Oertel, W. H., & Trenkwalder, C. (1998). Clinical and biochemical findings in uremic patients with and without restless legs syndrome. *American Journal of Kidney Diseases*, 31(2), 324-328.
23	Collister et al (2019)	Collister, D., Rodrigues, J. C., Mazzetti, A., Salisbury, K., Morosin, L., Rabbat, C., Brimble, K. S., & Walsh, M. (2019). Screening questions for the diagnosis of restless legs syndrome in hemodialysis. *Clinical Kidney Journal.* 12(4), 559-563. https://doi.org/10.1093/ckj/sfy129
24	Darwish & Abdel-Nabi (2016)	Darwish, A. H., & Abdel-Nabi, H. (2016). Sleep disorders in children with chronic kidney disease. *International Journal of Pediatrics and Adolescent Medicine.* 3(3), 112-118. https://doi.org/10.1016/j.ijpam.2016.06.001
25	Davis et al (2005)	Davis, I. D., Baron, J., O'Riordan, M. A., & Rosen, C. L. (2005). Sleep disturbances in pediatric dialysis patients. *Pediatric Nephrology.* 20(1), 69-75. https://doi.org/10.1007/s00467-004-1700-0
26	Davis et al (2012)	Davis, I. D., Greenbaum, L. A., Gipson, D., Wu, L. L., Sinha, R., Matsuda-Abedini, M., Emancipator, J. L., Lane, J. C., Hodgkins, K., Nailescu, C., Barletta, G. M., Arora, S., Mahan, J. D., & Rosen, C. L. (2012). Prevalence of sleep disturbances in children and adolescents with chronic kidney disease. *Pediatric nephrology.* 27(3), 451-459. https://doi.org/https://dx.doi.org/10.1007/s00467-011-2010-y
27	Deferio et al (2017)	Deferio, J. J., Govindarajulu, U., Brar, A., Cukor, D., Lee, K. G., & Salifu, M. O. (2017). Association of restless legs syndrome and mortality in end-stage renal disease: An analysis of the United States Renal Data System (USRDS). *BMC Nephrology.* 18(1), Article 258. https://doi.org/10.1186/s12882-017-0660-0
28	Deliyska et al (2011)	Deliyska, B., Shivarov, H., Nenchev, N., Shurliev, V., Vasilev, V., Kaludina, I., Lazarov, V., Trifonova, D., Sredkov, I., Milanova, M., & Spasova, S. (2011). Comparative study on restless legs syndrome in predialysis and dialysis patients. *Nephrology, Dialysis and Transplantation.* 17(1), 26-30.
29	Dikici et al (2014)	Dikici, S., Bahadir, A., Baltaci, D., Ankarali, H., Eroglu, M., Ercan, N., & Sav, T. (2014). Association of anxiety, sleepiness, and sexual dysfunction with restless legs syndrome in hemodialysis patients. *Hemodial Int.* 18(4), 809-818. https://doi.org/10.1111/hdi.12175
30	Erdogan et al (2012)	Erdogan, A., Dervisoglu, E., & Kutlu, A. (2012). Sleep quality and its correlates in patients on continuous ambulatory peritoneal dialysis. *Scand J Urol Nephrol.* 46(6), 441-447. https://doi.org/10.3109/00365599.2012.693134
31	Ezzat & Mohab (2015)	Ezzat, H., & Mohab, A. (2015). Prevelance of sleep disorders among ESRD patients. *Nephrology Dialysis Transplantation.* 30, iii621. https://doi.org/10.1093/ndt/gfv200.57
32	Giannaki et al (2011)	Giannaki, C. D., Sakkas, G. K., Karatzaferi, C., Hadjigeorgiou, G. M., Lavdas, E., Liakopoulos, V., Tsianas, N., Koukoulis, G. N., Koutedakis, Y., & Stefanidis, I. (2011). Evidence of increased muscle atrophy and impaired quality of life parameters in patients with uremic restless legs syndrome. *PLoS One. 6*(10), e25180. https://doi.org/10.1371/journal.pone.0025180
33	Gigli et al (2004)	Gigli, G. L., Adorati, M., Dolso, P., Piani, A., Valente, M., Brotini, S., & Budai, R. (2004). Restless legs syndrome in end-stage renal disease. *Sleep Medicine.* 5(3), 309-315. https://doi.org/10.1016/j.sleep.2004.01.014
34	Goffredo Filho et al (2003)	Goffredo Filho, G. S., Gorini, C. C., Purysko, A. S., Silva, H. C., & Elias, I. E. (2003). Restless legs syndrome in patients on chronic hemodialysis in a Brazilian city: Frequency, biochemical findings and comorbidities. *Arq Neuropsiquiatr.* 61(3b), 723-727. https://doi.org/10.1590/s0004-282x2003000500004
35	Haider & Anees (2014)	Haider, I., & Anees, M. (2014). Restless legs syndrome in end stage renal disease patients on haemodialysis. *Pakistan Journal of Medical Sciences.* 30(6). https://doi.org/10.12669/pjms.306.5691
36	Hamed et al (2023)	Hamed, S. A., Abdulhamid, S. K., El-Hadad, A. F., Fawzy, M., & Abd-Elhamed, M. A. (2023). Restless leg syndrome in patients with chronic kidney disease: A hospital-based study from Upper Egypt. *International Journal of Neuroscience.* 133(3), 257-268. https://doi.org/10.1080/00207454.2021.1910256
37	Hasheminasab Zaware et al (2016)	Hasheminasab Zaware, R., Mahmoodi Meymand, M. H., Rezaeian, M., Mohammadi Kamalabadi, N., Mostafavi, S. A., Abdolkarimi Dawarani, M. A., Jome Yazdian, R., & Bidaki, R. (2016). Insomnia and restless leg syndrome in patients undergoing chronic hemodialysis in Rafsanjan Ali Ibn Abitaleb Hospital. *Nephro-Urology Monthly.* 8(1), e29527. https://doi.org/10.5812/numonthly.29527
38	Hsu et al (2008)	Hsu, C. Y., Lee, C. T., Lee, Y. J., Huang, T. L., Yu, C. Y., Lee, L. C., Lam, K. K., Chien, Y. S., Chuang, F. R., & Hsu, K. T. (2008). Better sleep quality and less daytime symptoms in patients on evening hemodialysis: A questionnaire-based study. *Artificial Organs.* 32(9), 711-716. https://doi.org/10.1111/j.1525-1594.2008.00593.x
39	Hui et al (2000)	Hui, D. S. C., Wong, T. Y. H., Ko, F. W. S., Li, T. S. T., Choy, D. K. L., Wong, K. K., Szeto, C. C., Lui, S. F., & Li, P. K. T. (2000). Prevalence of sleep disturbances in Chinese patients with end-stage renal failure on continuous ambulatory peritoneal dialysis. *American Journal of Kidney Diseases.* 36(4), 783-788. https://doi.org/10.1053/ajkd.2000.17664
40	Ibrahim & Wegdan (2011)	Ibrahim, J. M., & Wegdan, O. M. (2011). Epidemiology of sleep disorders in patients with chronic renal disease in Cairo, Egypt. *J Egypt Public Health Assoc.* 86(3-4), 68-72. https://doi.org/10.1097/01.EPX.0000399136.00486.4e
41	Jaber et al (2011)	Jaber, B. L., Schiller, B., Burkart, J. M., Daoui, R., Kraus, M. A., Lee, Y., Miller, B. W., Teitelbaum, I., Williams, A. W., & Finkelstein, F. O. (2011). Impact of short daily hemodialysis on restless legs symptoms and sleep disturbances. *Clin J Am Soc Nephrol.* 6(5), 1049-1056. https://doi.org/10.2215/cjn.10451110
42	Kamal et al (2020)	Kamal, M., Zaki, N. F. W., Yousef, E. A., Eltoraby, E., Manzar, M. D., & Pandi-Perumal, S. R. (2020). An egyptian study of sleep disorders and its correlates in end-stage renal disease patients receiving hemodialysis. *Sleep and Vigilance.* 4(2), 213-220. https://doi.org/10.1007/s41782-020-00095-4
43	Kawauchi et al (2006)	Kawauchi, A., Inoue, Y., Hashimoto, T., Tachibana, N., Shirakawa, S., Mizutani, Y., Ono, T., & Miki, T. (2006). Restless legs syndrome in hemodialysis patients: Health-related quality of life and laboratory data analysis. *Clin Nephrol. 66*(6), 440-446. https://doi.org/10.5414/cnp66440

44	Kim et al (2008)	Kim, J.-M., Kwon, H.-M., Lim, C. S., Kim, Y. S., Lee, S.-J., & Nam, H. (2008). Restless legs syndrome in patients on hemodialysis: Symptom severity and risk factors. *J Clin Neurol.* 4, 153-157. https://doi.org/10.3988/jcn.2008.4.4.153
45	Kutlu et al (2018)	Kutlu, R., Selcuk, N. Y., Sayin, S., & Kal, O. (2018). Restless legs syndrome and quality of life in chronic hemodialysis patients. *Nigerian Journal of Clinical Practice.* 21(5), 573-577. https://doi.org/10.4103/njcp.njcp_84_17
46	La Manna et al (2011)	La Manna, G., Pizza, F., Persici, E., Baraldi, O., Comai, G., Cappuccilli, M. L., Centofanti, F., Carretta, E., Plazzi, G., Coli, L., Montagna, P., & Stefoni, S. (2011). Restless legs syndrome enhances cardiovascular risk and mortality in patients with end-stage kidney disease undergoing long-term haemodialysis treatment. *Nephrology Dialysis Transplantation.* 26(6), 1976-1983. https://doi.org/10.1093/ndt/gfq681
47	Lee et al (2013)	Lee, J., Nicholl, D. D. M., Ahmed, S. B., Loewen, A. H. S., Hemmelgarn, B. R., Beecroft, J. M., Turin, T. C., & Hanly, P. J. (2013). The prevalence of restless legs syndrome across the full spectrum of kidney disease. *Journal of clinical sleep medicine: JCSM: Official publication of the American Academy of Sleep Medicine*. 9(5), 455-459. https://doi.org/https://dx.doi.org/10.5664/jcsm.2664
48	Li et al (2014)	Li, H., Li, X. B., Feng, S. J., Zhang, G. Z., Wang, W., & Wang, S. X. (2014). Sleep disorders and its related risk factors in patients undergoing chronic peritoneal dialysis. *Chinese Medical Journal*. 127(7), 1289-1293. https://doi.org/10.3760/cma.j.issn.0366-6999.20132428
49	Lin et al (2013)	Lin, C. H., Wu, V. C., Li, W. Y., Sy, H. N., Wu, S. L., Chang, C. C., Chiu, P. F., Lion, H. H., Lin, C. Y., Chang, H. W., Lin, S. Y., Wu, K. D., Chen, Y. M., & Wu, R. M. (2013). Restless legs syndrome in end-stage renal disease: A multicenter study in Taiwan. *European Journal of Neurology.* 20(7), 1025-1031. https://doi.org/10.1111/ene.12095
50	Lin et al (2019)	Lin, X. W., Zhang, J. F., Qiu, M. Y., Ni, L. Y., Yu, H. L., Kuo, S. H., Ondo, W. G., Yu, Q., & Wu, Y. C. (2019). Restless legs syndrome in end stage renal disease patients undergoing hemodialysis. *BMC Neurol.* 19(1), 47. https://doi.org/10.1186/s12883-019-1265-y
51	Loewen et al (2009)	Loewen, A., Siemens, A., & Hanly, P. (2009). Sleep disruption in patients with sleep apnea and end-stage renal disease. *Journal of Clinical Sleep Medicine.* 5(4). 324-329.
52	Losso et al (2015)	Losso, R. L. M., Minhoto, G. R., & Riella, M. C. (2015). Sleep disorders in patients with end-stage renal disease undergoing dialysis: comparison between hemodialysis, continuous ambulatory peritoneal dialysis and automated peritoneal dialysis. *International Urology and Nephrology.* 47(2), 369-375. https://doi.org/10.1007/s11255-014-0860-5
53	Malaki et al (2012)	Malaki, M., Mortazavi, F. S., Moazemi, S., & Shoaran, M. (2012). Insomnia and limb pain in hemodialysis patients: what is the share of restless leg syndrome? *Saudi journal of kidney diseases and transplantation*: An official publication of the Saudi Center for Organ Transplantation, Saudi Arabia, 23(1), 15-20. https://www.scopus.com/inward/record.uri?eid=2-s2.0-84857182480&partnerID=40&md5=0fb784b1be861f4d49f96698ab12a03f
54	Merlino et al (2012)	Merlino, G., Lorenzut, S., Romano, G., Sommaro, M., Fontana, A., Montanaro, D., Valente, M., Gigli, G. L., Merlino, G., Lorenzut, S., Romano, G., Sommaro, M., Fontana, A., Montanaro, D., Valente, M., & Gigli, G. L. (2012). Restless legs syndrome in dialysis patients: A comparison between hemodialysis and continuous ambulatory peritoneal dialysis. *Neurological Sciences*. 33(6), 1311-1318. https://doi.org/10.1007/s10072-012-0953-9
55	Merlino et al (2006)	Merlino, G., Piani, A., Dolso, P., Adorati, M., Cancelli, I., Valente, M., & Gigli, G. L. (2006). Sleep disorders in patients with end-stage renal disease undergoing dialysis therapy. *Nephrology Dialysis Transplantation.* 21(1), 184-190. https://doi.org/10.1093/ndt/gfi144
56	Merlino et al (2010)	Merlino, G., Lorenzut, S., Gigli, G. L., Romano, G., Montanaro, D., Moro, A., & Valente, M. (2010). A case-control study on restless legs syndrome in nondialyzed patients with chronic renal failure. *Mov Disord.* 25(8), 1019-1025. https://doi.org/10.1002/mds.23010
57	Miranda et al (2001)	Miranda, M., Araya, F., Castillo, J. L., Durán, C., González, F., & Arís, L. (2001). Restless legs syndrome: A clinical study in adult general population and in uremic patients. *Revista médica de Chile.* 129(2), 179-186.
58	Molnar et al (2007)	Molnar, M. Z., Novak, M., Szeifert, L., Ambrus, C., Keszei, A., Koczy, A., Lindner, A., Barotfi, S., Szentkiralyi, A., Remport, A., & Mucsi, I. (2007). Restless legs syndrome, insomnia, and quality of life after renal transplantation. *Journal of Psychosomatic Research.* 63(6), 591-597. https://doi.org/10.1016/j.jpsychores.2007.06.007
59	Mucsi et al (2005)	Mucsi, I., Molnar, M. Z., Ambrus, C., Szeifert, L., Kovacs, A. Z., Zoller, R., Barótfi, S., Remport, A., & Novak, M. (2005). Restless legs syndrome, insomnia and quality of life in patients on maintenance dialysis. *Nephrol Dial Transplant.* 20(3), 571-577. https://doi.org/10.1093/ndt/gfh654
60	Mucsi et al (2004)	Mucsi, I., Molnar, M. Z., Rethelyi, J., Vamos, E., Csepanyi, G., Tompa, G., Baroffi, S., Marton, A., & Novak, M. (2004). Sleep disorders and illness intrusiveness in patients on chronic dialysis. *Nephrology Dialysis Transplantation.* 19(7), 1815-1822. https://doi.org/10.1093/ndt/gfh130
61	Murtagh et al (2007)	Murtagh, F. E. M., Addington-Hall, J. M., Edmonds, P. M., Donohoe, P., Carey, I., Jenkins, K., & Higginson, I. J. (2007). Symptoms in advanced renal disease: A cross-sectional survey of symptom prevalence in stage 5 chronic kidney disease managed without dialysis . *Journal of Palliative Medicine.* 10(6), 1266-1276. https://doi.org/10.1089/jpm.2007.0017
62	Muzasti & Harahap (2019)	Muzasti, R. A., & Harahap, R. H. (2019). The role of anemia to restless legs syndrome in regular hemodialysis patients in Haji Adam Malik Medan general hospital Proceedings of the 2nd International Conference on Tropical Medicine and Infectious Disease.
63	Naini et al (2015)	Naini, A. E., Amra, B., Mahmoodnia, L., & Taheri, S. (2015). Sleep apnea syndrome and restless legs syndrome in kidney transplant recipients. *Advanced biomedical research.* 4, 206. https://doi.org/https://dx.doi.org/10.4103/2277-9175.166142
64	Nikić et al (2007)	Nikić, P. M., Andrić, B. R., Stojanović-Stanojević, M., Dordević, V., Petrović, D., & Stojimirović, B. B. (2007). Restless legs syndrome prevalence in patients on chronic hemodialysis in central Serbia. *Vojnosanitetski pregled. Military-medical and pharmaceutical review.* 64(2), 129-134. https://doi.org/10.2298/VSP0702129N

65	Nikola et al (2012)	Nikola, S., Marinela, K., Jelena, J., & Vidojko, D. (2012). Restless legs syndrome in patients on hemodialysis: Frequency, severity and risk factors. *Medicinski Casopis.* 46(3), 138-144. https://doi.org/10.5937/mckg46-2330
66	Noda et al (2006)	Noda, A., Nakai, S., Soga, T., Sugiura, T., Iwayama, N., Maeda, K., Atarashi, M., Yasuma, F., Ozaki, N., Yokota, M., & Koike, Y. (2006). Factors contributing to sleep disturbance and hypnotic drug use in hemodialysis patients. *Intern Med.* 45(22), 1273-1278. https://doi.org/10.2169/internalmedicine.45.1826
67	Ogna et al (2016)	Ogna, A., Forni Ogna, V., Haba Rubio, J., Tobback, N., Andries, D., Preisig, M., Tafti, M., Vollenweider, P., Waeber, G., Marques-Vidal, P., & Heinzer, R. (2016). Sleep Characteristics in Early Stages of Chronic Kidney Disease in the HypnoLaus Cohort. *Sleep.* 39(4), 945-953. https://doi.org/https://dx.doi.org/10.5665/sleep.5660
68	Pan et al (2006)	Pan, J. Y., Zhang, J. H., Ma, P., Liang, H. J., & Huang, Z. T. (2006). Effect of restless legs syndrome on the sleep quality of hemodialysis patients. *Chinese Journal of Clinical Rehabilitation.* 10(10), 19-21. https://www.scopus.com/inward/record.uri?eid=2-s2.0-33646036172&partnerID=40&md5=ccdf937a9bb10bf6c98f764d0c1ae8ad
69	Pavan et al (2014)	Pavan, M., & Sathish, J. (2014). Restless legs syndrome in patients on chronic hemodialysis. *Dial Traspl.* 35, 3-6. https://doi.org/http://dx.doi.org/10.1016/j.dialisis.2013.05.002
70	Pizza et al (2012)	Pizza, F., Persici, E., La Manna, G., Campieri, C., Plazzi, G., Carretta, E., Cappuccilli, M. L., Ferri, B., Stefoni, S., & Montagna, P. (2012). Family recurrence and oligo-anuria predict uremic restless legs syndrome. *Acta Neurol Scand.* 125(6), 403-409. https://doi.org/10.1111/j.1600-0404.2011.01581.x
71	Quinn et al (2011)	Quinn, C., Uzbeck, M., Saleem, I., Cotter, P., Ali, J., O'Malley, G., Gilmartin, J. J., & O'Keeffe, S. T. (2011). Iron status and chronic kidney disease predict restless legs syndrome in an older hospital population. *Sleep Medicine.* 12(3), 295-301. https://doi.org/10.1016/j.sleep.2010.08.014
72	Rafie et al (2016)	Rafie, S., Jafari, M., Azizi, M., Bahadoram, M., & Jafari, S. (2016). Restless legs syndrome in hemodialysis patients. *Saudi journal of kidney diseases and transplantation*: An official publication of the Saudi Center for Organ Transplantation, Saudi Arabia, 27(2), 326-330. https://doi.org/10.4103/1319-2442.178553
73	Razeghi et al (2012)	Razeghi, E., Sahraian, M. A., Heidari, R., & Bagherzadeh, M. (2012). Association of inflammatory biomarkers with sleep disorders in hemodialysis patients. *Acta Neurol Belg.* 112(1), 45-49. https://doi.org/10.1007/s13760-012-0003-7
74	Riar et al (2019)	Riar, S. K., Greenbaum, L. A., Bliwise, D. L., & Leu, R. M. (2019). Restless Legs Syndrome in Chronic Kidney Disease: Is Iron or Inflammatory Status To Blame? *Journal of clinical sleep medicine*: JCSM: Official publication of the American Academy of Sleep Medicine. 15(11), 1629-1634. https://doi.org/https://dx.doi.org/10.5664/jcsm.8028
75	Rijsman et al (2004)	Rijsman, R. M., Weerd, A. W. D., Stam, C., Kerkhof, G. A., & Rosman, J. B. (2004). Periodic limb movement disorder and restless legs syndrome in dialysis patients. *NEPHROLOGY. 9*, 353–361.
76	Rohani et al (2015)	Rohani, M., Aghaei, M., Jenabi, A., Yazdanfar, S., Mousavi, D., & Miri, S. (2015). Restless legs syndrome in hemodialysis patients in Iran. *Neurological Sciences.* 36(5), 723-727. https://doi.org/10.1007/s10072-014-2026-8
77	Sabry et al (2010)	Sabry, A. A., Abo-Zenah, H., Wafa, E., Mahmoud, K., El-Dahshan, K., Hassan, A., Abbas, T. M., Saleh, A. B., & Okasha, K. (2010). Sleep disorders in hemodialysis patients. *Saudi journal of kidney diseases and transplantation*: An official publication of the Saudi Center for Organ Transplantation, Saudi Arabia, 21(2), 300-305.
78	Salman (2011)	Salman, S. M. (2011). Restless legs syndrome in patients on hemodialysis. *Saudi journal of kidney diseases and transplantation*: An official publication of the Saudi Center for Organ Transplantation, Saudi Arabia, 22(2), 368-372.
79	Samavat et al (2017)	Samavat, S., Fatemizadeh, S., Fasihi, H., & Farrokhy, M. (2017). Restless leg syndrome, insomnia, and depression in hemodialysis patients: Three sides of a triangle? *Nephro-Urology Monthly.* 9(3), Article e45076. https://doi.org/10.5812/numonthly.45076
80	Saraji et al (2017)	Saraji, N. Z., Hami, M., Boostani, R., & Mojahedi, M. J. (2017). Restless leg syndrome in chronic hemodialysis patients in Mashhad hemodialysis centers. *Journal of Renal Injury Prevention.* 6(2), 137-141. https://doi.org/10.15171/jrip.2017.27
81	Shaikh et al (2014)	Shaikh, R. A., Solangi, S., Rathi, S. K., & Shaikh, Q. H. (2014). Prevalence of restless legs syndrome in Haemodialysis patients. *Journal of the Liaquat University of Medical and Health Sciences.* 13(1), 18-21. https://www.scopus.com/inward/record.uri?eid=2-s2.0-84904560040&partnerID=40&md5=217b069534a3d800862f7d920789879b
82	Sinha et al (2009)	Sinha, R., Davis, I. D., & Matsuda-Abedini, M. (2009). Sleep disturbances in children and adolescents with non-dialysis-dependent chronic kidney disease. *Archives of Pediatrics and Adolescent Medicine.* 163(9), 850-855. https://doi.org/10.1001/archpediatrics.2009.149
83	Siddiqui et al (2005)	Siddiqui, S., Kavanagh, D., Traynor, J., Mak, M., Deighan, C., & Geddes, C. (2005). Risk factors for restless legs syndrome in dialysis patients. *Nephron Clin Pract.* 101(3), c155-160. https://doi.org/10.1159/000087073
84	Soyoral et al (2010)	Soyoral, Y., Sayarlioğlu, H., Tuncel, D., Şahin, M., Doğan, E., & Erkoç, R. (2010). Prevalence and risk factors of restless leg syndrome in a single hemodialysis unit. *Turkish Journal of Medical Sciences.* 40(3), 443-446. https://doi.org/10.3906/sag-0903-10
85	Stefanidis et al (2013)	Stefanidis, I., Vainas, A., Dardiotis, E., Giannaki, C. D., Gourli, P., Papadopoulou, D., Vakianis, P., Patsidis, E., Eleftheriadis, T., Liakopoulos, V., Pournaras, S., Sakkas, G. K., Zintzaras, E., & Hadjigeorgiou, G. M. (2013). Restless legs syndrome in hemodialysis patients: An epidemiologic survey in greece. *Sleep Medicine.* 14(12), 1381-1386. https://doi.org/10.1016/j.sleep.2013.05.022
86	Szentkiralyi et al (2009)	Szentkiralyi, A., Molnar, M. Z., Czira, M. E., Deak, G., Lindner, A. V., Szeifert, L., Torzsa, P., Vamos, E. P., Zoller, R., Mucsi, I., & Novak, M. (2009). Association between restless legs syndrome and depression in patients with chronic kidney disease. *Journal of Psychosomatic Research.* 67(2), 173-180. https://doi.org/10.1016/j.jpsychores.2009.05.004
87	Takaki et al (2003)	Takaki, J., Nishi, T., Nangaku, M., Shimoyama, H., Inada, T., Matsuyama, N., Kumano, H., & Kuboki, T. (2003). Clinical and psychological aspects of restless legs syndrome in uremic patients on hemodialysis. *American Journal ofKidney Diseases.* 41, 833-839.

88	Tekdöş Demircioğlu et al (2015)	Tekdöş Demircioğlu, D., Kavadar, G., Esen Öre, Ö., Emre, T. Y., & Yaka, U. (2015). Relationship between restless leg syndrome and quality of life in uremic patients. *Agri: Agri (Algoloji) Dernegi'nin Yayin organidir, The journal of the Turkish Society of Algology.* 27(2), 73-78. https://doi.org/10.5505/agri.2015.19327
89	Telarović et al (2007)	Telarović, S., Relja, M., & Trkulja, V. (2007). Restless legs syndrome in hemodialysis patients: Association with calcium antagonists - A preliminary report. *European Neurology.* 58(3), 166-169. https://doi.org/10.1159/000104718
90	Tuncel et al (2011)	Tuncel, D., Orhan, F. O., Sayarlioglu, H., Isik, I. O., Utku, U., & Dinc, A. (2011). Restless legs syndrome in hemodialysis patients: Association with depression and quality of life. *Sleep Breath.* 15(3), 311-315. https://doi.org/10.1007/s11325-010-0382-z
91	Turk et al (2018)	Turk, A. C., Ozkurt, S., Turgal, E., & Sahin, F. (2018). The association between the prevalence of restless leg syndrome, fatigue, and sleep quality in patients undergoing hemodialysis. *Saudi Med J.* 39(8), 792-798. https://doi.org/10.15537/smj.2018.8.22398
92	Wali & Alkhouli (2015)	Wali, S. O., & Alkhouli, A. F. (2015). Restless legs syndrome among Saudi end-stage renal disease patients on hemodialysis. *Saudi Medical Journal.* 36(2), 204-210. https://doi.org/10.15537/smj.2015.2.10036
93	Walker et al (1995)	Walker, S., Fine, A., & Kryger, M. H. (1995). Sleep complaints are common in a dialysis unit. *American Journal of Kidney Diseases*. 26(5), 751-756.
94	Winkelman et al (1996)	Winkelman, J. W., Chertow, G. M., & Lazarus, J. M. (1996). Restless legs syndrome in end-stage renal disease. *American Journal of Kidney Diseases.* 28(3), 372-378. https://doi.org/10.1016/S0272-6386(96)90494-1
95	Xiao et al (2017)	Xiao, J.-P., Zhang, G.-X., Chen, L., Sun, B.-G., Zhang, H.-X., Chen, L.-H., Yuan, L., Hao, L., & Wang, D.-G. (2017). Restless legs syndrome in maintenance hemodialysis patients: an epidemiologic survey in Hefei. *International Urology and Nephrology.* 49(7), 1267-1272. https://doi.org/https://dx.doi.org/10.1007/s11255-017-1573-3
96	Yang et al (2019)	Yang, Y., Ye, H., He, Q., Zhang, X., Yu, B., Yang, J., & Chen, J. (2019). Association between predialysis hypermagnesaemia and morbidity of uraemic restless legs syndrome in maintenance haemodialysis patients: A retrospective observational study in Zhejiang, China. *BMJ Open*. 9(7). https://doi.org/10.1136/bmjopen-2018-027970
97	Yildiz et al (2016)	Yildiz, D., Kahveciołlu, S., Buyukkoyuncu, N., Kilic, A. K., Yildiz, A., Gul, C. B., Seferoglu, M., & Tufan, F. (2016). Restless-legs syndrome and insomnia in hemodialysis patients. *Renal Failure*. 38(2), 194-197. https://doi.org/10.3109/0886022X.2015.1111118

Appendix 3. Characteristics Included Studies of the Prevalence of RLS Among Chronic Kidney Disease

No	Author (year), Country, Study design	Population characteristics (m + SD); (n, %)	RLS prevalence (n, %), Diagnostic tool	Comorbidities, Life style & other sleep problems (m ± SD); (n, %)	Laboratory parameters (m ± SD)	Risk of bias
1	Al-Jahdali, H. H et al (2009), Saudi Arabia, Cross-sectional	Sample size: 227 Population: Adult Mean Age (years): 55.70 + 17.02 Sex: NI Duration of dialysis (months): 40.40 + 37.80	Prevalence: 114 (50.22) Diagnostic tool: IRLSSG	NI	NI	8-M
2	Alvarez-Ude et al (1999), Spain, Cross-sectional	Sample size: 60 Population: Adult NI	Prevalence: 16 (26.67) Diagnostic tool: the Spanish versions of the Medical Outcome Study Sleep Scale	NI	NI	8-M
3	Applebee et al (2009), USA, Cross-sectional	Sample size: 26 Participants: Children and Adolescent Mean Age (years): 13.70 ± 0.50 Sex: M: 13 (50) F: 13 (50) BMI, kg/m2: 21.30 ± 6.70	Prevalence: 9 (34.62) Diagnostic tool: RLS for Children	NI	Creatinine (mg/dl): 1.50 ± 0.60 Ferritin (ng/mL): 151 ± 169 Hemoglobin (g/dL): 12.60 ± 1.40 Iron (ng/dL): 70.50 ± 45.80	9-L
4	Aritake-Okada et al (2011), Japan, Cross-sectional	Sample size: 514 Population: Adult Mean Age (years): 66.31 + 14.78 Sex: M: 353 (68.68) F: 151 (31.32)	Prevalence: 18 (3.50) Diagnostic tool: IRLSSG		BUN (mg/dL): 38.60 ± 21.50 Creatinine (mg/dL): 3.90 ± 3.80 GFR (ml/min/1.73 m2): 24.40 ± 17.30	9-L
5	Amiri et al (2019), Iran, Cross-sectional	Sample size: 116 Population: Adult Mean Age (years): 60.10 + 14.40 Sex: M: 68 (58.62) F: 48 (41.38)	Prevalence: 78 (67.24) Diagnostic tool: IRLSSG	NI	NI	8-M
6	Araujo et al (2010), Brazil, Cross-sectional	Sample size: 400 Population: Adult Mean Age (years): 51.52 ± 15.68 Sex: M: 236 (59) F: 164 (41) BMI, kg/m2: 23.19 ± 3.97 Dialysis duration (months): 70.92 ± 66.24	Prevalence: 86 (21.5) Diagnostic tool: IRLSSG	Diabetes mellitus: 12 (13.95) Hypertension: 16 (18.60) ESS score: 8.37 ± 4.67 Sleep quality: 10.07 ± 6.90	Albumin (g/dL): 4.03 ± 0.32 Calcium (mg/dL): 8.68 ± 0.75 Ferritin (ng/mL): 435.70 ± 342.07 Hemoglobin (g/dL): 11.28 ± 1.87 PTH (pg/mL): 418.58 ± 507.72	9-L
7	Baiardi et al (2017), Italy, Cohort Prospective	Sample size: 128 Population: Adult Mean Age (years): 61.27 + 13.47 Sex: M: 80 (62.50) F: 48 (37.50) Duration of dialysis (months): 83.10 + 79.60	Prevalence: 47 (36.72) Diagnostic tool: IRLSSG	Diabetes mellitus: 6 (12.70) Peripheral vascular disease: 7 (14.90)	NI	8-M

8	Bambini et al (2019), Brazil, Case-control	Sample size: 25 Population: Adult Mean Age (years): 50 + 10 Sex: M: 7 (28) F: 18 (72) BMI, kg/m2: 25.70 + 4.80	Prevalence: 14 (56) Diagnostic tool: PSG	Hypertension: 14 (100) Smoking: 2 (14.30) ESS score: 7.70 ± 4.50	Albumin (g/dL): 4.0 ± 0.6 Calcium (mg/ dL): 9.80 ± 0.8 Creatinine (mg/dl): 8.40 ± 2.30 Hemoglobin (mg/dL): 11.20 ± 2.30 Iron (ng/dL): 57 ± 15 Vitamin D (ng/mL): 22.80 ± 7.80	9-L
9	Bathla et al (2016), Saudi Arabia, Cross-sectional	Sample size: 194 Population: Adult Mean Age (years): 54.40 ± 15 Sex: M: 113 (58.25) F: 81 (41.75) Duration of dialysis (months): 36.60 + 19.30	Prevalence: 10 (5.2) Diagnostic tool: IRLSSG	NI	NI	7-M
10	Beladi-Mousavi et al (2015), Iran, Cross-sectional	Sample size: 139 Population: Adult Mean Age (years): 51.82 ± 13.32 Sex: M: 60 (43.17) F: 79 (56.83) Duration of dialysis (months): 31.56 + 30.14	Prevalence: 22 (15.83) Diagnostic tool: IRLSSG	NI	Calcium (mg/dL): 8.54 ± 1.18 Ferritin (ng/mL): 713 ± 211.81 Hemoglobin (g/dL): 10.32 ± 1.59 Kt/V: 1.25 ± 0.03 Phosphate (mg/dL): 5.57 ± 1.59	8-M
11	Bhagawati et al (2019), India, Cross-sectional	Sample size: 300 Population: Adult Mean Age (years): 47.58 ± 15.04 Sex: M: 223 (74.33) F: 77 (25.67)	Prevalence: 60 (20) Diagnostic tool: IRLSSG	Diabetes mellitus: 14 (23.33) Hypertension: 29 (48.33) Smoking: 28 (46.67)	NI	8-M
12	Bhowmik et al (2004), India, Case-control	Sample size: 65 Population: Adult Mean Age (years): 42.40 ± 14.90 Sex: M: 50 (76.92) F: 15 (23.08) BMI, kg/m2: 21.50 ± 3.50	Prevalence: 1 (1.54) Diagnostic tool: IRLSSG	NI	Albumin (g/dL): 3.60 ± 0.7 Bilirubin (mg/dL): 0.69 ± 0.21 BUN (mg/dL): 134.80 ± 51.60 Calcium (mg/dL): 8.70 ± 1.08 Cholesterol (gr/dL): 179.20 ± 56.90 Creatinine (mg/dL): 6.60 ± 2.20 Ferritin (ng/mL): 157.60 ± 109.90 GFR (ml/min/1.73 m2): 10.40 ± 2.90 Hemoglobin (g/dL): 8.54 ± 2.17 Phosphate (mg/dL): 5.16 ± 1.05	7-M
13	Bliwise et al (2014), USA, Case-control	Sample size: 16,165 Population: Adult Mean Age (years): 61.40 ± 14.90 Sex: M: 7,856 (48.59) F: 8,309 (51.41) Medication: antidepressants, antiemetics with significant dopamine blockade, neuroleptic, antihistamines, erythropoietin.	Prevalence: 3,234 (20) Diagnostic tool: IRLSSG	Diabetes mellitus: 1,753 (54.20)	Hemoglobin (g/dL): 10.07 ± 1.58	9-L

14	Brzuszek et al (2022), United Kingdom, Cross-sectional	Sample size: 212 Population: Adult Mean Age (years): 64.30 ± 15.50 Sex: M: 124 (58.49) F: 88 (41.51)	Prevalence: 68 (32.08) Diagnostic tool: IRLSSG	Cardiovascular disease: 17 (25) Diabetes mellitus: 24 (35.29) Smoking: 6 (8.82)	Albumin (g/dL): 3.44 ± 0.48 Ferritin (ng/mL): 310 ± 218.5 Hemoglobin (g/dL): 11.27 ± 1.57 Phosphate (mmol/L): 1.40 ± 0.4 Potassium (mmol/L): 4.80 ± 0.6	9-L
15	Calviño et al (2018), Spain, Cross-sectional	Sample size: 129 Population: Adult Mean Age (years): 57 ± 12.80 Sex: M: 82 (63.57) F: 47 (36.43) BMI, kg/m2: 29.90 ± 7.72	Prevalence: 19 (14.73) Diagnostic tool: IRLSSG	COPD: 3 (15.80) Diabetes mellitus: 8 (42.10) Depression: 5 (26.30) Congestive heart failure: 10 (5.20)	Calcium (mg/dL): 9.4 ± 0.45 Creatinine (mg/dL): 1.6 ± 0.67 Ferritin (ng/mL): 222 ± 176.0 Folate (ng/mL): 7.0 ± 2.44 Hemoglobin (g/dL): 12.80 ± 1.69 Iron (ng/dL): 86 ± 28.40 Phosphate (mg/dL): 3.6 ± 0.76 Transferrin (mg/dL): 239 ± 38.5 Vitamin B12 (ng/mL): 515 ± 149.9 Vitamin D (ng/mL): 25 ± 8.6	8-M
16	Capelli et al (2021), Italy, Cohort Prospective	Sample size: 45 Population: Adult Mean Age (years): 59.76 + 13.38 Sex: M: 26 (44.58) F: 19 (55.42) BMI, kg/m2: 25.41 + 4.45	Prevalence: 7 (15.56) Diagnostic tool: IRLSSG	Diabetes mellitus: 1 (14) Cholesterol (mg/dL): 172.67 ± 36.80 ESS score: 10.71 ± 3.09 Insomnia: 6 (86)	Albumin (g/dL): 3.88 ± 0.42 BUN (mg/dl): 7.24 ± 1.68 Creatinine (mg/dL): 7.51 ± 3.72 Ferritin (ng/mL): 561.16 ± 820.88 Hemoglobin (g/dL): 10.28 ± 0.77 Iron (ng/dL): 41.3 ±18.80 PTH (pg/mL): 411.40 ± 220.24	8-M
17	Castillo-Torres et al (2018), Mexico, Cross-sectional	Sample size: 105 Population: Adult Mean Age (years): 49.35 + 16.31 Sex: M: 47 (44.76) F: 58 (55.24) Duration of dialysis (months): 47.52 + NI	Prevalence: 19 (18.09) Diagnostic tool: IRLSSG	Anemia: 12 (63.20) Cerebrovascular disease: 2 (10.50) Diabetes mellitus: 11 (57.90) Hypertension: 18 (97.40) Peripheral Neuropathy: 2 (10.50)	BUN (mg/dL): 53.60 ± 27.30 Calcium (mg/dL): 8.20 ± 0.9 Chloride (mmol/L): 101.90 ± 4.80 Creatinine (mg/dL): 9.70 ± 3.60 GFR (mL/min/1.73m2): 7.30 ± 3.20 Hemoglobin (g/dL): 7.91 ± 1.38 Hematocrit (%): 24.80 ± 4.30 Magnesium (mg/dL): 2.70 ± 0.4 Phosphorus (mg/dL): 5.10 ± 1.50 Potassium (mmol/L): 5.0 ± 0.9 Sodium (mmol/L): 137.10 ± 2.90	7-M
18	Chavoshi et al (2015), Iran, Cross-sectional	Sample size: 397 Population: Adult Mean Age (years): 57.60 ± 15.40 Sex: M: 209 (52.64) F: 188 (47.36) BMI, kg/m2: 24.21 + NI Medication: anti-hypertension, diabetes, corticosteroid.	Prevalence: 126 (31.70) Diagnostic tool: IRLSSG	Anemia: 16 (27.60) Cardiovascular disease: 26 (27.10) Diabetes mellitus: 50 (35.20) Hypertension: 45 (30) Smoking: 13 (18.80) Poor sleep quality: 96 (76.20)	NI	9-L
19	Chrastina et al (2015), Slovakia, Cross-sectional	Sample size: 75 Population: Adult Mean Age (years): 51.14 ± 11.12 Sex: M: 39 (52%) F: 36 (48%)	Prevalence: 30 (40.54) Diagnostic tool: IRLSSG	NI	Calcium (mg/dL): 2.53 ± 0.23 Creatinine (mg/dL): 119.81 ± 44.77 Ferritin (ng/mL): 551.23 ± 431.87 GFR (mL/min/1.73m2): 59.30 ± 18.75 Hemoglobin (g/dL): 12.82 ± 1.24 Iron (ng/dL): 13.38 ± 3.94	9-L

		Dialysis duration (months): 40.84 ± 30.74			Phosphorus (mg/dL): 4.45 ± 15.43	
20	Chu et al (2014), Australia, Cross-sectional	Sample size: 85 Population: Adult Mean Age (years): 63.68 ± 14.38 Sex: M: 54 (63.53) F: 31 (36.47) Duration of dialysis (months): 27.69 ± 32.55 Medication: Benzodiazepine	Prevalence: 21 (30.88) Diagnostic tool: IRLSSG	Diabetes mellitus: 8 (38.10)	BUN (mg/dL): 19.69 ± 4.89 Ferritin (ng/mL): 763.07± 570.78 Hemoglobin (g/dL): 10.54 ± 0.77 Kt/V: 1.55 ± 0.41	7-M
21	Cirignotta et al (2002), Italy, Cross-sectional	Sample size: 114 Population: Adult Mean Age (years): 63.60 ± 12.70 Sex: M: 70 (61.40) F: 40 (35.09) Dialysis duration (months): 74.10 ± 71.10	Prevalence: 38 (33.30) Diagnostic tool: RLSQ	NI	NI	8-M
22	Collado-Seidel et al (1998), Germany, Cross-sectional	Sample size: 136 Population: Adult Mean Age (years): 59 ± NI Sex: M: 84 (61.76) F: 52 (38.24) Dialysis duration (months): 54 ± NI	Prevalence: 32 (23) Diagnostic tool: IRLSSG	NI	Calcium (mg/dL): 10.0 ± 2.40 Creatinine (mg/dL): 10.90 ± 2.30 Ferritin (ng/mL): 278 ± 269 Hemoglobin (g/dL): 10.0 ± 1.0 Iron (ng/dL): 52 ± 26 Phosphate (mg/dL): 5.50 ± 1.70 PTH (pg⁄mL): 75 ± 66 Transferrin (mg/dL): 228 ± 49	8-M
23	Collister et al (2019), Canada, Cohort	Sample size: 50 Population: Adult Mean Age (years): 64 ± 12.40 Sex: M: 26 (52) F: 24 (48) Medication: Dopamine	Prevalence: 14 (28) Diagnostic tool: IRLSSG	Diabetes mellitus: 7 (50) Cardiovascular disease: 2 (14.30) Cerebrovascular disease: 1 (7.10) Peripheral vascular disease: 1 (7.10) Obstructive sleep apnea: 3 (21.40)	Albumin (g/dL): 3.2 ± 0.23 Hemoglobin (g/dL): 10.4 ± 1.0 PTH (pg/mL): 72.1 ± 51.7	8-M
24	Darwish & Abdel-Nabi (2016), Egypt, Case-control	Sample size: 54 Participants: Children and Adolescent Mean Age (years): 9.88 ± 2.85 Sex: M: 31 (57.41) F: 23 (42.59) BMI, kg/m2: 17.93 ± 3.31 Dialysis duration (months): 26.77 ± 25.87	Prevalence: 12 (22.22) Diagnostic tool: RLSQ	ESS score: 9.07 ± 3.74	Calcium (mg/dL): 9.96 ± 0.76 Creatinine (mg/dL): 2.98 ± 2.55 GFR (mL/min/1.73m2): 10.69 ± 2.33 Hemoglobin (g/dL): 10.93 ± 1.20 Kt⁄V: 1.13 ± 0.08 Phosphorus (mg/dL): 4.72 ± 0.79	8-M
25	Davis et al (2005), USA, Cross-sectional	Sample size: 21 Participants: Children and Adolescent Mean Age (years): 14.30 ± 4.50	Prevalence: 6 (28.57) Diagnostic tool: RLSQ	ESS score: 9.0 ± 3.10	Hemoglobin (g/dL): 11.0 ± 2.0	8-M

		Sex: M: 11 (52.38) F: 10 (47.62)				
26	Davis et al (2012), USA, Cross-sectional	Sample size: 159 Participants: Children and Adolescent Mean Age (years): 13.80 ± 3.60 Sex: M: 81 (50.94) F: 78 (49.06) Medication: Antihypertensives, Corticosteroids, Erythropoiesis-stimulating agents, CNS-stimulating agents, Antidepressants, Antihistamines	Prevalence: 16 (10.06) Diagnostic tool: Standard criteria for the diagnosis of RLS in children and adolescents	Daytime Sleepiness: 7 (43.75) ESS score: 6.30 ± 4.70 Obstructive sleep apnea: 4 (25%)	GFR (mL/min/1.73m2): 67.30 ± 42.30	9-L
27	Deferio et al (2017), USA, Case-control	Sample size: 279,956 Population: Adult Mean Age (years): 62.05 ± 15.39 Sex: M: 122,400 (43.72) F: 157,556 (56.28) BMI, kg/m2: 28.98 ± 7.57	Prevalence: 372 (0.13) Diagnostic tool: IRLSSG	Anemia: 44 (11.83) Cardiovascular disease: 64 (17.20) Congestive heart failure: 98 (26.34) Cerebrovascular disease: 30 (8.06) Diabetes mellitus: 145 (38.98) Depression: 15 (4.03) Hypertension: 311 (83.6) Peripheral vascular disease: 38 (10.22) Obstructive sleep apnea: 17 (4.57)	Albumin (g/dL): 3.32 ± 0.64 Creatinine: 6.64 ± 3.74	8-M
28	Deliyska et al (2011), Russia, Cross-sectional	Sample size: 61 Population: Adult Dialysis duration (months): 58.33 ± 14.06	Prevalence: 10 (16.39) Diagnostic tool: IRLSSG	NI	Creatinine (mg/dl): 3.21 ± 1.06 Hemoglobin (g/dL): 10.68 ± 1.69 Phosphate (mmol/L): 4.72 ± 1.29	8-M
29	Dikici et al (2014), Turkey, Cross-sectional	Sample size: 246 Population: Adult Mean Age (years): 59.70 ± 14.0 Sex: M: 124 (50.20) F: 122 (49.80) Dialysis duration (months): 58.80 ± 50.40	Prevalence: 113 (45.9) Diagnostic tool: IRLSSG	NI	Albumin (g/dL): 3.80 ± 0.4 Ferritin (ng/mL): 754.70 ± 440.5 Hemoglobin (g/dL): 11.10 ± 1.30 PTH (pg/mL): 417.50 ± 391.20	8-M
30	Erdogan et al (2012), Turkey, Cross-sectional	Sample size: 112 Population: Adult Mean Age (years): 51 ± 15 Sex: M: 60 (53.57) F: 52 (46.43) Dialysis duration (months): 41 ± 29 BMI, kg/m2: 27.50 ± 5.70	Prevalence: 40 (35.71) Diagnostic tool: IRLSSG	NI	Albumin (g/dL): 3.40 ± 0.5 BUN (mg/dL): 108 ± 34 Calcium (mg/dL): 8.89 ± 0.98 Creatinine (mg/dL): 7.70 ± 2.80 Ferritin (ng/mL): 632.16 ± 710.54 GFR (mL/min/1.73m2): 5.0 ± 3.70 Hemoglobin (g/dL): 10.50 ± 1.90 Kt/V: 1.61 ± 0.48 Phosphate (mg/dL): 4.45 ± 1.21	8-M

					PTH (pg/mL): 299.58 ± 292.03	
31	Ezzat & Mohab (2015), Egypt, Case-control	Sample size: 60 Population: Adult	Prevalence: 11 (18.33) Diagnostic tool: PSG	NI	NI	7-M
32	Giannaki et al (2011), Greece, Cross-sectional	Sample size: 70 Population: Adult Mean Age (years): 54.10 ± 16.90 Sex: M: 51 (72.86%) F: 19 (27.14%) Dialysis duration (months): 36 ± 31.20 BMI, kg/m2: 25.50 ± 4.20	Prevalence: 30 (42.86%) Diagnostic tool: IRLSSG	ESS Score: 7.1 ± 4.4	Ferritin (ng/mL): 241.10 ± 206.60 Hemoglobin (g/dL): 12.20 ± 1.50 Kt/V: 1.22 ± 0.4	9-L
33	Gigli et al (2004), Italy, Cross-sectional	Sample size: 407 Population: Adult Mean Age (years): 64.62 ± 13.17 Sex: M: 252 (61.92) F: 155 (38.08) BMI, kg/m2: 25 ± 5.50 Medication: antihypertensive, antidiabetics, benzodiazepines, clonidine, calcitriol, erythropoietin.	Prevalence: 127 (31.20) Diagnostic tool: IRLSSG	Alcohol use: 20 (15.50) Smoking: 15 (11.80) ESS score: 4.70 ± 3.70	NI	7-M
34	Goffredo Filho et al (2003), Brazil, Cross-sectional	Sample size: 176 Population: Adult Mean Age (years): 52 ± 13.90 Sex: M: 107 (60.80) F: 69 (39.20)	Prevalence: 26 (14.77) Diagnostic tool: IRLSSG	Diabetes mellitus: 6 (27.27) Hypertension: 22 (84.62)	Calcium (mg/dL): 2.19 ± 0.09 Creatinine (mg/dL): 8.39 ± 2.99 Hemoglobin (g/dL): 6.57 ± 0.93 Phosphorus (mg/dL): 1.51 ± 0.12 PTH (pg/mL): 181.90 ± 124.60	9-L
35	Haider & Anees (2014), Pakistan, Cross-sectional	Sample size: 250 Population: Adult Mean Age (years): 45.27 ± NI Sex: M: 153 (61.20) F: 97 (38.80) Duration of dialysis (months): 26.10 ± NI	Prevalence: 162 (64.80) Diagnostic tool: IRLSSG	NI	NI	8-M
36	Hamed et al (2023), Egypt, Cross-sectional	Sample size: 520 Population: Adult Mean Age (years): 50.45 ± 3.63 Sex: M: 200 (38.46) F: 320 (61.54) BMI, kg/m2: 30.46 ± 2.23	Prevalence: 116 (22.31) Diagnostic tool: IRLSSG	Anxiety: 100 (86.21) Diabetes mellitus: 56 (48.28) Depression: 92 (79.31) Hypertension: 36 (31.03) Hyperuricemia: 50 (43.10) Peripheral neuropathy: 92 (79.31) Hyperkalemia: 40 (34.48) Hyperparathyroidism: 84 (72.41) ESS score: 14.66 ± 1.08 Insomnia (ISI score): 18.66 ± 1.8	Albumin (g/dL): 2.60 ± 0.48 BUN (mg/dL): 15.36 ± 2.58 Calcium (mg/dL): 6.54 ± 0.30 Creatinine (mg/dL): 5.98 ± 1.17 Ferritin (ng/mL): 110.26 ± 6.35 Hemoglobin (g/dL): 8.82 ± 1.36 Iron (ng/dL): 88.29 ± 3.06 Magnesium (mg/dL): 2.35 ± 0.8 Phosphate (mg/dL): 5.42 ± 1.52 Potassium (mmol/L): 4.20 ± 0.6 Sodium (mmol/L): 136.0 ± 2.64	7-M

37	Hasheminasab Zaware et al (2016), Iran, Cross-sectional	Sample size: 45 Population: Adult Mean Age (years): NI Sex: M:21 (46.67) F: 23 (53.33)	Prevalence: 25 (55) Diagnostic tool: RLSQ	NI	NI	8-M
38	Hsu et al (2008), Taiwan, Cross-sectional	Sample size: 150 Population: Adult Mean Age (years): 55.28 + 11.09 Sex: M: 67 (44.67) F: 83 (55.33) BMI, kg/m2: 22.31 + 3.30 Duration of dialysis (months): 60.14 + 43.80	Prevalence:34 (22.7) Diagnostic tool: The sleep questionnaire	ESS score: 2.37 ± 2.77 Sleep quality: 5.92 ± 4.30	Albumin (g/dL): 3.92 ± 2.73 BUN (mg/dL): 68.60 ± 17.56 Creatinine (mg/dL): 11.89 ± 2.64 Hemoglobin (g/dL): 11.52 ± 8.54 Kt/V: 1.39 ± 0.24 PTH (pg/mL): 210.29 ± 295.07	7-M
39	Hui et al (2000), Hongkong, Cross-sectional	Sample size: 201 Population: Adult Mean Age (years): 56.70 + 12 Sex: M: 103 (51.24) F: 98 (48.76) BMI, kg/m2: 23.60 + 3.50 Duration of dialysis (months): 36 + 27.60	Prevalence: 124 (62) Diagnostic tool: the Sleep and Health Questionnaire (SHQ).	Alcohol use: 4 (3.23) Diabetes mellitus: 48 (23.90) Hypertension: 6 (4.84) Smoking: 9 (4.50)	NI	7-M
40	Ibrahim & Wegdan (2011), Egypt, Cross-sectional	Sample size: 264 Population: Adult Mean Age (years): 50.83 ± 14.48 Sex: M: 147 (55.68) F: 117 (44.32) Duration of dialysis (months): 25.41 + 16.21	Prevalence: 149 (56.44) Diagnostic tool: IRLSSG	Anemia: 145 (59.20) Diabetes mellitus: 107 (66.50) Hypertension: 74 (61.70) Insomnia: 86 (57.72) Obstructive sleep apnea: 56 (21.20)	NI	9-L
41	Jaber et al (2011), USA, Cohort Prospective	Sample size: 235 Population: Adult Mean Age (years): 52 ± 15 Sex: M: 150 (63.83) F: 85 (36.17) BMI, kg/m2: 29 + 7 Duration of dialysis (months): 43.20 + 49.20	Prevalence: 94 (40) Diagnostic tool: IRLSSG	COPD: 8 (8.51) Diabetes mellitus: 45 (47.87) Congestive heart failure: 24 (25.53) Cerebrovascular disease: 8 (8.51) Hypertension: 83 (88.29) Peripheral vascular disease: 9 (9.57) Smoking: 15 (15.96)	Albumin (g/dL): 3.80 ± 0.5 BUN (mg/dL): 60 ± 18 Calcium (mg/dL): 8.90 ± 0.8 Creatinine (mg/dL): 9.30 ± 3.40 Ferritin (ng/mL): 490 ± 253 Hemoglobin (g/dL): 11.60 ± 1.40 Phosphorus (mg/dL): 5.90 ± 1.50 Potassium (mmol/L): 4.90 ± 0.7	8-M
42	Kamal et al (2020), Egypt, Cross-sectional	Sample size: 200 Population: Adult Mean Age (years): 51.70 ± 6 Sex: M: 133 (66.50%) F: 67 (33.50%) BMI, kg/m2: 26.70 + 1.90	Prevalence: 54 (26.90) Diagnostic tool: IRLSSG	ESS score: 7.50 ± 3.40 Sleep quality: 6.10 ± 3.90	Albumin (g/dL): 4.0 ± 0.66 Calcium (mg/dL): 8.67 ± 0.35 Creatinine (mg/dL): 4.70 ± 0.7 Hemoglobin (g/dL): 10.30 ± 0.8 Iron (ng/dL): 77.20 ± 8.60 Kt/V: 1.12 ± 0.06 Phosphorus (mg/dL): 4.40 ± 0.6	7-M

		Duration of dialysis (months): 43.20 + 22.80				
43	Kawauchi et al (2006), Japan, Cross-sectional	Sample size: 228 Population: Adult	Prevalence: 53 (23) Diagnostic tool: IRLSSG	NI	NI	8-M
44	Kim et al (2008), South Korea, Cross-sectional	Sample size: 164 Population: Adult Mean Age (years): 62.20 ± 12.70 Population: Adult Sex: M: 92 (56.09) F: 72 (43.91) BMI, kg/m2: 22.50 ± 3.80 Dialysis duration (months): 61.32 ± 57.96	Prevalence: 46 (28.05) Diagnostic tool: IRLSSG	Diabetes mellitus: 33 (71.74) Hepatitis: 2 (4.35) ESS Score: 5.70 ± 3.84	BUN (mg/dl): 58.70 ± 22.78 Creatinine (mg/dL): 8.94 ± 2.63 Ferritin (ng/mL): 291.89 ± 264.53 Hemoglobin (g/dL): 10.98 ± 1.46 Iron (ng/dL): 70.44 ± 24.92 Phosphate (mmol/L): 4.57 ± 1.77 PTH (pg⁄mL): 177.34 ± 162.60	7-M
45	Kutlu et al (2018), Turkey, Cross-sectional	Sample size: 237 Population: Adult	Prevalence: 44 (18.6) Diagnostic tool: IRLSSG	NI	NI	8-M
46	La Manna et al (2011), Italy, Cross-sectional	Sample size: 100 Population: Adult Mean Age (years): 65.0 ± 14.20 Sex: M: 63 (63%) F: 37 (37%) BMI, kg/m2: 24.70 ± 4.60 Duration of dialysis (months): 61.80 ± 86	Prevalence: 31 (31) Diagnostic tool: IRLSSG	NI	Albumin (g/dL): 3.60 ± 0.4 Ferritin (ng/mL): 158.40 ± 325.30 Creatinine (mg/dL): 9.10 ± 2.60 Hemoglobin (g/dL): 10.20 ± 1.20 Iron (ng/dL): 40.8 ± 21 Kt/V: 1.30 ± 0.4 Phosphorus (mg/dL): 4.90 ± 1.50 Potassium (mmol/L): 5.50 ± 0.6 PTH (pg/mL): 295.30 ± 254.60 Sodium (mmol/L): 139.20 ± 4.20	8-M
47	Lee et al (2013), Canada, Cross-sectional	Sample size: 500 Population: Adult Mean Age (years): 59.97 + 16.25 Sex: M: 299 (59.80) F: 201 (40.20) BMI, kg/m2: 29.13 + 7.29 Medication: anti-depressant	Prevalence: 184 (36.80) Diagnostic tool: IRLSSG	Congestive heart failure: 35 (19.02) Cerebrovascular disease: 36 (19.56) COPD: 40 (21.73) Diabetes mellitus: 66 (35.87) Hypertension: 138 (75)	Hemoglobin (g/dL): 12.94 ± 1.92	7-M
48	Li et al (2014), China, Cross-sectional	Sample size: 42 Population: Adult	Prevalence: 20 (47.62) Diagnostic tool: IRLSSG	NI	NI	7-M
49	Lin et al (2013), Taiwan, Cross-sectional	Sample size: 1,130 Population: Adult Mean Age (years): 61.90 + 12.60 Sex: M: 641 (56.73) F: 489 (43.27) Duration of dialysis (months): 76.80 ± 73.20	Prevalence: 286 (25.31) Diagnostic tool: IRLSSG	Diabetes mellitus: 128 (45.40) Hypertension: 147 (52.10)	Albumin (g/dL): 3.90 ± 0.4 BUN (mg/dL): 71.70 ± 18.0 Calcium (mg/dL): 8.70 ± 2.40 Creatinine (mg/dl): 10.2 ± 2.40 Ferritin (ng/mL): 403.0 ± 293.1 Hemoglobin (g/dL): 10.60 ± 1.30 Iron (ng/dL): 63.50 ± 31.20 Phosphate (mg/dL): 5.0 ± 1.40 PTH (pg/mL): 323.0 ± 376.90	8-M
50	Lin et al (2019), China, Cross-sectional	Sample size: 137 Population: Adult Mean Age (years): 55.47 ± 12.76	Prevalence: 28 (20.44) Diagnostic tool: IRLSSG	Alcohol use: 5 (17.90) Depression: 5 (17.90) Diabetes mellitus: 9 (32.10)	Albumin (g/dL): 3.97 ± 0.63 BUN (mg/dL): 30.34 ± 5.39 Calcium (mg/dL): 2.32 ± 0.26	8-M

		Sex: M: 74 (54) F: 63 (46) Duration of dialysis (months): 98.35 ± 71.66		Hypertension: 24 (86.0) Smoking: 9 (32.10) Sleep quality: 9.67 ± 6.05	Ferritin (ng/mL): 137.42 ± 139.98 Hemoglobin (g/dL): 10.54 ± 2.21 Iron (ng/dL): 15.29 ± 4.29 Kt/V: 1.49 ± 0.34 Phosphorus (mg/dL): 2.11 ± 0.70 Transferrin (mg/dL): 212 ± 52	
51	Loewen et al (2009), Canada, Case-control	Sample size: 12 Population: Adult Mean Age (years): 58 ± 11 Sex: M: 12 (75) F: 3 (25) BMI, kg/m2: 28 ± 6	Prevalence: 7 (58.33%) Diagnostic tool: IRLSSG	ESS Score: 10.80 ± 3.80 Poor sleep quality: 5 (71.43)	NI	7-M
52	Losso et al (2015), Brazil, Cross-sectional	Sample size: 166 Population: Adult Mean Age (years): 51.95 ± 15.27 Sex: M: 89 (53.61) F: 77 (46.39)	Prevalence: 51 (30.72) Diagnostic tool: IRLSSG	Diabetes mellitus: 15 (29.41) Hypertension: 22 (43.14)	Albumin (g/dL): 3.74 ± 0.54 Hemoglobin (g/dL): 11.92 ± 2.74 Kt/V: 1.59 ± 0.55	9-L
53	Malaki et al (2012), Iran, Cross-sectional	Sample size: 26 Population: Adult Mean Age (years): 35.7 ± 21.9 Sex: M: 6 (23.08%) F: 20 (76.92%) Duration of dialysis (months): 34.80 ± 18	Prevalence: 2 (7.69) Diagnostic tool: IRLSSG	NI	Creatinine (mg/dL): 8.02 ± 2.34 Ferritin (ng/mL): 506.77 ± 282.59 Hemoglobin (g/dL): 10.86 ± 1.52 Iron (ng/dL): 133.95 ± 160.25 Kt/V: 1.44 ± 0.47 Phosphorus (mg/dL): 6.18 ± 1.67	7-M
54	Merlino et al (2012), Italy, Cross-sectional	Sample size: 86 Population: Adult Mean Age (years): 62.68 ± 15.72 Sex: M: 57 (66.28) F: 29 (33.72) Duration of dialysis (months): 43.80 ± 56.60	Prevalence: 14 (16.28) Diagnostic tool: IRLSSG	ESS score: 4.81 ± 3.75 Insomnia: 13 (92.86) Sleep quality: 6.74 ± 3.52	Albumin (g/dL): 3.40 ± 1.45 BUN (mg/dL): 67.83 ± 24.16 Calcium (mg/dL): 6.98 ± 3.27 Creatinine (mg/dL): 8.69 ± 3.23 Ferritin (ng/mL): 408.56 ± 447.18 Hemoglobin (g/dL): 11.23 ± 2.80 Iron (ng/dL): 64.9 ± 28.47 Phosphorus (mg/dL): 3.92 ± 2.15 Potassium (mmol/L): 4.86 ± 0.86 PTH (pg/mL): 278.83 ± 249.73 Transferrin (mg/dL): 171.92 ± 41.54	7-M
55	Merlino et al (2006), Italy, Cross-sectional	Sample size: 883 Population: Adult Mean Age (years): 64.95 ± 12.85 Sex: M: 540 (61.16) F: 343 (38.84) BMI, kg/m2: 24.06 ± 4.12 Duration of dialysis (months): 68.73 ± 74.80	Prevalence: 162 (18.40) Diagnostic tool: IRLSSG	Insomnia: 112 (69.14) Obstructive sleep apnea: 25 (14.19)	NI	9-L
56	Merlino et al (2010), Italy, Case-control	Sample size: 138 Population: Adult Mean Age (years): 69.80 ± 11.70	Prevalence: 15 (10.87) Diagnostic tool: IRLSSG	NI	Albumin (g/dL): 3.99 ± 0.52 BUN (mg/dL): 55.90 ± 32.10 Calcium (mg/dL): 8.81 ± 1.60	8-M

		Sex: M: 85 (61.59) F: 53 (38.40)			Chloride (mmol/L): 104.90 ± 63.50 Creatinine (mg/dL): 2.20 ± 1.10 Ferritin (ng/mL): 115.30 ± 133.0 Hemoglobin (g/dL): 12.70 ± 1.60 Iron (ng/dL): 71.90 ± 22.30 Magnesium (mg/dL): 4.40 ± 2.0 Phosphorus (mg/dL): 1.60 ± 1.0 PTH (pg/mL): 122.10 ± 144.90 Transferrin (mg/dL): 272.7 ± 59.1	
57	Miranda et al (2001), Chile, Cross-sectional	Sample size: 166 Population: Adult	Prevalence: 43 (25.90) Diagnostic tool: IRLSSG	NI	NI	8-M
58	Molnar et al (2007), Hungary, Cross-sectional	Sample size: 785 Population: Adult Mean Age (years): 49 ± 12 Sex: M: 463 (58.98) F: 322 (41.02) Duration of dialysis (months): 21 ± 21.48	Prevalence: 35 (4.5) Diagnostic tool: RLSQ	Diabetes mellitus: 6 (17.14)	Albumin (g/dL): 4.20± 0.3 GFR (mL/min/1.73m2): 50 ± 19 Hemoglobin (g/dL): 13.3 ± 1.90	9-L
59	Mucsi et al (2005), Canada, Cross-sectional	Sample size: 333 Population: Adult Mean Age (years): 54 ± 15 Sex: M: 193 (57.96) F: 140 (42.4) Duration of dialysis (months): 36.34 ± 40.71	Prevalence: 45 (13.51) Diagnostic tool: RLSQ	Diabetes mellitus: 11 (24) Insomnia: 16 (35.56)	Ferritin (ng/mL): 379 ± 236.50 Kt/V: 1.3 ± 0.29 Phosphorus (mg/dL): 1.95 ± 0.56 PTH (pg/mL): 32 ± NI	8-M
60	Mucsi et al (2004), Hungary, Cross-sectional	Sample size: 73 Population: Adult Mean Age (years): 58.69 ± 14 Sex: M: 31 (42.47) F: 42 (57.53)	Prevalence: 22 (30.14) Diagnostic tool: RLSQ	Diabetes mellitus: 18 (81.82)	Albumin (g/dL): 3.83 ± 0.40 Hemoglobin (g/dL): 10.74 ± 1.23 Kt/V: 1.23 ± 0.25	7-M
61	Murtagh et al (2007), United Kingdom, Cross-sectional	Sample size: 66 Population: Adult Mean Age (years): 82 ± 6.60 Sex: M: 32 (48.50) F: 34 (51.50)	Prevalence: 32 (48) Diagnostic tool: MSAS-SF	Cancer: 5 (15.63) Cardiovascular disease: 11 (34.38) Diabetes mellitus: 8 (25) Hypertension: 1 (3.13)	GFR (mL/min/1.73m2): 11.20 ± 2.80	7-M
62	Muzasti & Harahap (2019), Indonesia, Cross-sectional	Sample size: 106 Population: Adult Mean Age (years): 48.4 ± 13.29 Sex: M: 70 (66%) F: 36 (34%) Dialysis duration (months): 24.20 ± 12.45	Prevalence: 32 (30.20%) Diagnostic tool: IRLSSG	NI	Calcium (mg/dL): 8.1 ±1.01 Ferritin (ng/mL): 1193 ± 862.75 Hemoglobin (g/dL): 9.0 ± 1.47 Iron (ng/dL): 66.30 ± 31.10 Phosphate (mg/dL): 5.50 ± 2.09	8-M
63	Naini et al (2015), Iran, Cross-sectional	Sample size: 200 Population: Adult	Prevalence: 103 (51.5) Diagnostic tool: RLSQ	Diabetes mellitus: 21 (20.4) Hypertension: 9 (8.7)	Creatinine (mg/dL): 1.32 ± 0.51	8-M

		Mean Age (years): 45.86 ± 10.24 Sex: M: 100 (50) F: 100 (50)		Obstructive sleep apnea: 43 (41.7)		
64	Nikić et al (2007), Serbia, Cross-sectional	Sample size: 166 Population: Adult Mean Age (years): 56.12 ± 13.42 Sex: M: 112 (67.47) F: 54 (32.53) BMI, kg/m2: 23.34 ± 3.56	Prevalence: 31 (22.96) Diagnostic tool: IRLSSG	NI	BUN (mg/dL): 27.85 ± 6.68 Calcium (mg/dL): 2.26 ± 0.19 Creatinine (mg/dL): 928.59 ± 249.78 Hemoglobin (g/dL): 9.82 ± 5.23 Kt/V: 1.15 ± 0.19 Phosphorus (mg/dL): 1.67 ± 0.49	8-M
65	Nikola et al (2012), Serbia, Cross-sectional	Sample size: 96 Population: Adult Mean Age (years): 56.3 ± 11.4 Sex: M: 59 (61.46%) F: 37 (38.54%) Dialysis duration (months): 68.10 ± 54.10	Prevalence: 38 (39.58%) Diagnostic tool: IRLSSG	Cardiovascular Disease: 23 (60.50) Depression: 23 (60.50) Diabetes mellitus: 6 (5) Hypertension: 18 (47.40) Insomnia: 18 (47.40)	Albumin (g/dL): 3.45 ± 0.21 BUN (mg/dL): 23.80 ± 4.90 Calcium (mg/dL): 2.40 ± 0.2 Creatinine (mg/dL): 93.17 ± 16.67 Ferritin (ng/mL): 490.0 ± 490.4 Hemoglobin (g/dL): 11.39 ± 1.91 Phosphate (mg/dL): 1.5 ± 0.4 Potassium (mmol/L): 5.40 ± 0.9 PTH (pg/mL): 249.0 ± 283.90	8-M
66	Noda et al (2006), Japan, Cross-sectional	Sample size: 252 Population: Adult Mean Age (years): 59.30 ± 10.80 Sex: M: 160 (63.74) F: 92 (36.26) BMI, kg/m2: 20.60 ± 2.80	Prevalence: 52 (20.63) Diagnostic tool: two questions about RLS	Insomnia: 31 (59.62)	NI	8-M
67	Ogna et al (2016), Switzerland, Cross-sectional	Sample size: 282 Population: Adult Mean Age (years): 63.36 ± 10.65 Sex: M: 156 (55.32) F: 126 (44.68) BMI, kg/m2: 26.6 ± 4.61	Prevalence: 47 (16.67) Diagnostic tool: IRLSSG	Alcohol use: 9 (19.15) Depression: 6 (12.77) Diabetes mellitus: 11 (23.40) Hypertension: 32 (68.08) Smoking: 10 (21.28) Obstructive sleep apnea: 23 (48.94)	GFR (mL/min/1.73m2): 68.53 ± 18.94	9-L
68	Pan et al (2006), China, Cross-sectional	Sample size: 171 Population: Adult	Prevalence: 43 (25.15) Diagnostic tool: IRLSSG	NI	NI	8-M
69	Pavan et al (2014), India, Cross-sectional	Sample size: 50 Population: Adult Mean Age (years): 64.30 ± 14 Sex: M: 37 (74) F: 13 (26) BMI, kg/m2: 21.30 ± 2.60 Dialysis duration (months): 16 ± 3.40	Prevalence: 14 (28) Diagnostic tool: IRLSSG	NI	BUN (mg/dL): 68.70 ± 3.90 Calcium (mg/dL): 9.70 ± 3.84 Creatinine (mg/dL): 7.57 ± 2.36 Ferritin (ng/mL): 137.0 ± NI Hemoglobin (g/dL): 9.60 ± 0.78 Phosphorus (mg/dL): 4.50 ± 1.18	7-M
70	Pizza et al (2012), Italy, Cross-sectional	Sample size: 162 Population: Adult Mean Age (years): 66.5 ± 14.3 Sex:	Prevalence: 51 (31.48) Diagnostic tool: IRLSSG	Diabetes mellitus: 16 (31.37) ESS score: 6.98 ± 4.21 Insomnia: 34 (66.67)	Albumin (g/dL): 3.76 ± 0.42 Calcium (mg/dL): 8.83 ± 0.87 Creatinine (mg/dL): 9.58 ± 2.66	8-M

		M: 105 (64.81) F: 57 (35.19) BMI, kg/m2: 24.80 ± 4.40			Ferritin (ng/mL): 256.61 ± 343.32 Hemoglobin (g/dL): 10.72 ± 1.42 Iron (ng/dL): 46.51 ± 22.82 Kt/V: 1.35 ± 0.35 Phosphorus (mg/dL): 5.25 ± 1.51 Potassium (mmol/L): 5.57 ± 0.69 PTH (pg/mL): 331.43 ± 234.01	
71	Quinn et al (2011), Ireland, Cross-sectional	Sample size: 301 Population: Adult Mean Age (years): 71.21 ± 31.95 Sex: M: 140 (46.51) F: 161 (53.49) BMI, kg/m2: 23.66 ± 10.79 Medication: Antipsychotic, Lithium Antihistamine, Beta blockers	Prevalence: 55 (18.3) Diagnostic tool: IRLSSG	Anxiety: 5 (9.10) Cardiovascular disease: 16 (29.10) Congestive heart failure: 13 (23.60) COPD: 14 (25.50) Depression: 11 (20.0) Diabetes mellitus: 12 (21.80) Hypertension: 21 (38.20) Osteoarthritis: 11 (20.0) Peripheral vascular disease: 3 (5.50) Rheumatoid arthritis: 2 (3.60) Smoking: 9 (16.40)	NI	8-M
72	Rafie et al (2016), Saudi Arabia, Cross-sectional	Sample size: 137 Population: Adult	Prevalence: 50 (36.49) Diagnostic tool: IRLSSG	NI	NI	8-M
73	Razeghi et al (2012), Iran, Cross-sectional	Sample size: 108 Population: Adult Mean Age (years): 56 ± 15 Sex: M: 62 (57.41) F: 46 (42.59) Dialysis duration (months): 75 ± NI	Prevalence: 35 (32.41) Diagnostic tool: IRLSSG	Insomnia: 18 (51.43%) Poor sleep quality: 25 (71.43) Obstructive sleep apnea: 3 (8.57)	Albumin (g/dL): 3.8 ± 0.5 Ferritin (ng/mL): 626 ± 583 Hemoglobin (g/dL): 10.80 ± 2.10 Phosphorus (mg/dL): 5.60 ± 1.60 PTH (pg/mL): 518 ± 628	8-M
74	Riar et al (2019), Georgia Cross-sectional	Sample size: 124 Population: Children & Adolescent Mean Age (years): 13.40 ± 3.10 Sex: M: 80 (64.50) F: 44 (35.50)	Prevalence: 19 (15.30) Diagnostic tool: IRLSSG	Anemia: 13 (68.40)	Ferritin (ng/mL): 51.2 ± 191.56 Hemoglobin (g/dL): 11.70 ± 1.60	8-M
75	Rijsman et al (2004), Netherlands, Cross-sectional	Sample size: 48 Population: Adult Mean Age (years): 55 ± 12 Sex: M: 41 (85.42) F: 7 (14.58) Dialysis duration (months): 87.24 ± 166.68	Prevalence: 28 (58.33) Diagnostic tool: IRLSSG	Diabetes: 4 (14.29) Hypertension: 7 (25)	NI	7-M
76	Rohani et al (2015), Iran, Cross-sectional	Sample size: 163 Population: Adult Mean Age (years): 61.30 ± 13.30 Sex: M: 103 (63.20) F: 60 (36.80)	Prevalence: 61 (37.40) Diagnostic tool: IRLSSG	Cardiovascular diseases: 20 (32.80) Diabetes mellitus: 34 (55.70) Hypertension: 34 (55.70) Smoking: 29 (47.50)	BUN (mg/dL): 47.20 ± 12.40 Ferritin (ng/mL): 1281 ± 556 GFR (mL/min/1.73m2): 9.20 ± 3.10 Hemoglobin (g/dL): 12.70 ± 2.0 Kt/V: 1.50 ± 0.2	8-M

		BMI, kg/m2: 23.60 ± 1.50 Dialysis duration (months): 22.80 ± 16.80		Insomnia: 54 (88.50)		
77	Sabry et al (2010), Saudi Arabia, Cross-sectional	Sample size: 88 Population: Adult Mean Age (years): 41.59 ± 16.30	Prevalence: 37 (42.05) Diagnostic tool: IRLSSG	NI	NI	7-M
78	Salman (2011), Syria, Cross-sectional	Sample size: 123 Population: Adult Mean Age (years): 41.95 ± 15.11 Sex: M: 70 (56.91) F: 53 (43.09)	Prevalence: 25 (20.30) Diagnostic tool: IRLSSG	NI	NI	8-M
79	Samavat et al (2017), Iran, Cross-sectional	Sample size: 235 Population: Adult Mean Age (years): 57.30 ± 15.90 Sex: M: 133 (56.59) F: 102 (43.41) BMI, kg/m2: 25.90 ± 5.50 Dialysis duration (months): 54.60 ± 76.30	Prevalence: 55 (23.4) Diagnostic tool: IRLSSG	Diabetes mellitus: 30 (54.50) Hypertension: 10 (18.20) Urologic disease: 3 (5.50) Insomnia: 29 (52.73) Sleep quality: 6.70 ± 4.30	Albumin (g/dL): 4.06 ± 0.75 Calcium (mg/dL): 8.50 ± 0.8 Hemoglobin (g/dL): 10.60 ± 1.80 Phosphorus (mg/dL): 5.10 ± 1.40 PTH (pg/mL): 242 ± 413 Uric Acid (mg/dL): 6.90 ± 5.20 Vitamin D (ng/mL): 30.40 ± 29.70	8-M
80	Saraji et al (2017), Iran, Cross-sectional	Sample size: 260 Population: Adult Mean Age (years): 48.99 ± 15.72 Sex: M: 154 (59.40) F: 106 (40.60) Dialysis duration (months): 47.88 ± 40.44 BMI, kg/m2: 23.48 ± 4.34 Medication: Anti-histaminic, Benzodiazepines, Anticonvulsant, Gabapentin	Prevalence: 143 (55) Diagnostic tool: IRLSSG	Diabetes mellitus: 26 (81.20) Hypertension: 46 (59.10) Urologic disease: 17 (36.20)	BUN (mg/dL): 126.78 ± 34.95 Calcium (mg/dL): 8.43 ± 0.86 Ferritin (ng/mL): 1107 ± NI Hemoglobin (g/dL): 11.04 ± 1.98 Kt/V: 1.36 ± 0.33 Phosphorus (mg/dL): 5.79 ± 1.37 PTH (pg/mL): 485.28 ± 451.85	8-M
81	Shaikh et al (2014), Pakistan, Cross-sectional	Sample size: 100 Population: Adult	Prevalence: 32 (32) Diagnostic tool: IRLSSG	NI	NI	8-M
82	Sinha et al (2009), Canada, Cross-sectional	Sample size: 49 Participants: Children & Adolescence Mean Age (years): 13.86 ± 3.49 Sex: M: 35 (71.43) F: 14 (28.57) Medication: antidepressant, iron supplement, asthma	Prevalence: 14 (28.57) Diagnostic tool: Pediatric sleep questionnaire	Daytime sleepiness: 2 (14.28) Insomnia: 1 (7.14) Obstructive sleep apnea: 1 (7.14)	Hemoglobin (g/dL): 12.53 ± 1.55	7-M
83	Siddiqui et al (2005), United Kingdom, Cross-sectional	Sample size: 277 Population: Adult Mean Age (years): 61.79 ± 15.33 Sex: M: 144 (51.98) F: 133 (48.02	Prevalence: 127 (45.80) Diagnostic tool: IRLSSG	Diabetes mellitus: 12 (9.45) Smoking: 27 (21.26)	Albumin (g/dL): 3.98 ± 0.45 Calcium (mg/dL): 2.30 ± 0.2 Ferritin (ng/mL): 341.16 ± 251.21 Hemoglobin (g/dL): 11.40 ± 1.60 Phosphate (mg/dL): 1.50 ± 0.6 PTH (pg/mL): 30.57 ± 32.24	9-L

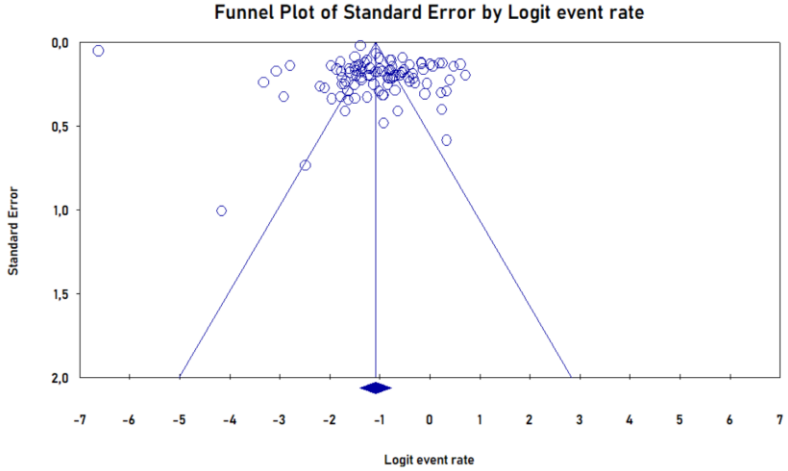
		Medication: betalockers, erythropoietin				
84	Soyoral et al (2010), Turkey, Cross-sectional	Sample size: 76 Population: Adult Mean Age (years): 52.28 ± 18.13 Sex: M: 42 (44.74) F: 34 (55.76) Dialysis duration (months): 45.61 ± 32.54	Prevalence: 11 (14.47) Diagnostic tool: IRLSSG	Diabetes mellitus: 9 (81.82)	Creatinine (mg/dL): 7.2 ± 2.5 Ferritin (ng/mL): 739.3 ± 345.3 Hemoglobin (g/dL): 10.60 ± 1.70 Iron (ng/dL): 116.60 ± 118.10 Kt/V: 1.60 ± 0.2 PTH (pg/mL): 301.80 ± 464.40	7-M
85	Stefanidis et al (2013), Greece, Cross-sectional	Sample size: 579 Population: Adult Mean Age (years): 65 ± 13 Sex: M: 343 (59.24) F: 236 (40.76) Dialysis duration (months): 45.61 ± 32.54	Prevalence: 154 (26.6) Diagnostic tool: IRLSSG	NI	Albumin (g/dL): 4.13 ± 0.32 BUN (mg/dL): 155 ± 33 Calcium (mg/dL): 8.80 ± 0.8 Ferritin (ng/mL): 254 ± 286 Hemoglobin (g/dL): 11.20 ± 1.30 Iron (ng/dL): 45.20 ± 25.50 Kt/V: 1.10 ± 0.2 Phosphorus (mg/dL): 5.80 ± 1.70 PTH (pg/mL): 356 ± 298 Transferrin (mg/dL): 190 ± 43	9-L
86	Szentkiralyi et al (2009), Hungary, Cross-sectional	Sample size: 949 Population: Adult Mean Age (years): 48 ± 13 Sex: M: 525 (55.32) F: 424 (44.68) Dialysis duration (months): 30 ± 32.59	Prevalence: 55 (5.79) Diagnostic tool: RLSQ	Depression: 31 (56.36) Diabetes mellitus: 6 (10.91)	Albumin (g/dL): 4.10 ± 0.4 GFR (mL/min/1.73m2): 41 ± 20 Hemoglobin (g/dL): 12 ± 2.20	8-M
87	Takaki et al (2003), Japan, Cross-sectional	Sample size: 490 Population: Adult Mean Age (years): 60.18 ± 11.64 Sex: M: 285 (58.16) F: 205 (41.84) Dialysis duration (months): 82.90 ± 69.20 Medication: Vitamin D, Benzodiazepines, Antidepressants	Prevalence: 60 (12.24) Diagnostic tool: RLSSG	Diabetes mellitus: 14 (23.33) Smoking: 16 (26.67)	Albumin (g/dL): 3.80 ± 0.3 BUN (mg/dL): 78.20 ± 12.1 Calcium (mg/dL): 9.40 ± 0.8 Creatinine (mg/dL): 11.90 ± 2.40 Hemoglobin (g/dL): 9.80 ± 1.10 Kt/V: 1.36 ± 0.23 Phosphorus (mg/dL): 6.20 ± 1.20 Potassium (mmol/L): 5.10 ± 0.5 PTH (pg/mL): 198.70 ± 216.60	9-L
88	Tekdöş Demircioğlu et al (2015), Turkey, Cross-sectional	Sample size: 118 Population: Adult Mean Age (years): 61.35 ± 13.17 Sex: (authors only provided data for RLS) M: 23 (46.94) F: 26 (53.06) Dialysis duration (months): 114.24 ± 83.65	Prevalence: 49 (41.53) Diagnostic tool: IRLSSG	NI	Ferritin (ng/mL): 873.36 ± 748.26 PTH (pg/mL): 580.34 ± 588.10	9-L
89	Telarović et al (2007), Croatia, Cross-sectional	Sample size: 82 Population: Adult Mean Age (years): 64.21 ± 18.22	Prevalence: 49 (59.76) Diagnostic tool: IRLSSG	Cardiovascular disease: 41 (84) Diabetes mellitus: 16 (33) Polyneuropathy: 13 (27)	NI	7-M

		Sex: M: 53 (64.63) F: 29 (35.37) Dialysis duration (months): 68.16 ± 6.56 Medication: Erythropoietin, Calcitriol, ACE inhibitors, β-Blockers. Ca2+ antagonists, Benzodiazepines				
90	Tuncel et al (2011), Turkey, Cross-sectional	Sample size: 81 Population: Adult Mean Age (years): 52.49 ± 16.03 Sex: M: 41 (51.62) F: 40 (48.38) Dialysis duration (months): 21.29 ± 33	Prevalence: 10 (12.35) Diagnostic tool: IRLSSG	ESS score: 2.5 ± 1.8	Ferritin (ng/mL): 1,236 ± 651 Hemoglobin (g/dL): 11.90 ± 2.10 Kt/V: 1.40 ± 0.3	7-M
91	Turk et al (2018), Turkey, Cross-sectional	Sample size: 220 Population: Adult Mean Age (years): 59.67 ± 1.38 Sex: M: 112 (50.91) F: 108 (49.09) Dialysis duration (months): 91.08 ± 8.64	Prevalence: 37 (16.82) Diagnostic tool: IRLSSG	Diabetes mellitus: 21 (56.80) Hypertension: 13 (35.10) Smoking: 28 (75.70) Sleep quality: 11.41 ± 0.65	Albumin (g/dL): 4.12 ± 0.02 Calcium (mg/dL): 11.39 ± 2.55 Ferritin (ng/mL): 644.97 ± 50.24 Hemoglobin (g/dL): 14.48 ± 2.93 Iron (ng/dL): 54.89 ± 3.06 Kt/V: 1.74 ± 0.05	9-L
92	Wali & Alkhouli (2015), Saudi Arabia, Cross-sectional	Sample size: 355 Population: Adult Mean Age (years): 48.50 ± 15.40 Sex: M: 217 (61.13) F: 138 (38.87) BMI, kg/m2: 25.18 ± 6.80 Dialysis duration (months): 79.20 ± 72	Prevalence: 69 (19.44) Diagnostic tool: IRLSSG	Daytime sleepiness: 28 (40.58) Obstructive sleep apnea: 41 (59.42)	NI	9-L
93	Walker et al (1995), Canada, Cross-sectional	Sample size: 54 Population: Adult	Prevalence: 18 (33.33) Diagnostic tool: IRLSSG	NI	NI	7-M
94	Winkelman et al (1996), USA, Case-control	Sample size: 204 Population: Adult Mean Age (years): 56.80 ± 15.80 Sex: M: 96 (47.06) F: 108 (52.94) Dialysis duration (months): 55.20 ± 56.40	Prevalence: 41 (20.09) Diagnostic tool: IRLSSG	NI	Calcium (mg/dL): 9.0 ± 1.30 Hemoglobin (g/dL): 9.80 ± 1.40 Iron (ng/dL): 54.90 ± 29.30 PTH (pg/mL): 462.30 ± 516.50	8-M
95	Xiao et al (2017), China, Cross-sectional	Sample size: 269 Population: Adult Mean Age (years): 51.80 ± 14.30 Sex:	Prevalence: 39 (14.49) Diagnostic tool: IRLSSG	Diabetes mellitus: 11 (28.2) Hypertension: 35 (89.7) Sleep quality: 11.86 ± 4.72	BUN (mg/dL): 25.11 ± 11.63 Calcium (mg/dL): 2.22 ± 0.23 Creatinine (mg/dL): 11.46 ± 3.85	8-M

		M: 188 (69.89) F: 81 (30.11) Dialysis duration (months): 45.46 ± 46.95			Ferritin (ng/mL): 310.95 ± 329.41 Hemoglobin (g/dL): 9.87 ± 1.35 Magnesium (mmol/L): 1.23 ± 0.25 Phosphate (mg/dL): 0.15 ± 0.09 Phosphorus (mg/dL): 2.07 ± 0.47 PTH (pg/mL): 394.66 ± 351.81 Uric Acid (mg/dL): 6.69 ± 2.14	
96	Yang et al (2019), China, Cohort	Sample size: 578 Population: Adult Mean Age (years): 59.45 ± 14.06 Sex: M: 363 (62.80) F: 215 (37.20) BMI, kg/m2: 21.98 ± 3.44 Dialysis duration (months): 42.60 ± 38.88	Prevalence: 83 (14.36) Diagnostic tool: IRLSSG	Diabetes mellitus: 27 (32.50) Hypertension: 35 (42.20) Hyperparathyroidism: 70 (84.30)	Ferritin (ng/mL): 217.68 ± 225.27 Hemoglobin (g/dL): 9.81 ± 1.33 PTH (pg/ml): 431.03 ± 336.11 Kt/V: 1.29 ± 0.22	9-L
97	Yildiz et al (2016), Turkey, Case-control	Sample size: 156 Population: Adult Mean Age (years): 50.60 ± 14.10 Sex: M: 88 (56.41) F: 68 (43.59)	Prevalence: 73 (46.79) Diagnostic tool: IRLSSG	Diabetes mellitus: 13 (17.81) Hypertension: 24 (32.88) Smoking: 21 (28.77) Daytime Sleepiness: 6 (8.22) ESS score: 6.16 ± 11.22 Insomnia (ISI score): 11.92 ± 20.95	NI	9-L

Note: Note: BMI= body mass index, BUN= blood urea nitrogen, GFR= glomerular filtration rate, PTH= Parathyroid hormone, International restless legs syndrome study group (IRLSSG), Restless legs syndrome questionnaire (RLSQ), Polysomnography (PSG), The Memorial Symptom Assessment Scale Short Form (MSAS-SF), , ESS= Excessive daytime Sleepiness=, PSQI= The Pittsburgh Sleep Quality Index, OSA= obstructive sleep apnea, COPD= Chronic obstructive pulmonary disease, Kt/V= dialyzer clearance of urea * dialysis time/volume of distribution of urea.

Appendix 4. Publication bias



Begg and Mazumdar rank correlation

Kendall's S statistic (P-Q)	-975,00000

Kendall's tau without continuity correction

Tau	-0,20945
z-value for tau	3,03874
P-value (1-tailed)	0,00119
P-value (2-tailed)	0,00238

Kendall's tau with continuity correction

Tau	-0,20924
z-value for tau	3,03562
P-value (1-tailed)	0,00120
P-value (2-tailed)	0,00240

Egger's regression intercept

Intercept	3,71122
Standard error	1,72947
95% lower limit (2-tailed)	0,27779
95% upper limit (2-tailed)	7,14465
t-value	2,14587
df	95,00000
P-value (1-tailed)	0,01722
P-value (2-tailed)	0,03443

Duval and Tweedie's trim and fill

		Fixed Effects			Random Effects			Q Value
	Studies Trimmed	Point Estimate	Lower Limit	Upper Limit	Point Estimate	Lower Limit	Upper Limit	
Observed values		0,18737	0,18363	0,19118	0,25176	0,19716	0,31555	12605,3501
Adjusted values	28	0,15821	0,15518	0,16130	0,18114	0,14453	0,22458	14615,5282