УДК 616.8-009.836:616-07:615.2

https://doi.org/10.47526/YJoHS-2025.1-04

RESTLESS LEGS SYNDROME: CLINICAL AND BIOCHEMICAL ASPECTS AND OPTIMIZATION OF DIAGNOSIS AND THERAPY

Raimova M.[1], Yodgarova U.[1], Sadykova K.[2]
Tashkent State Dental Institute, Tashkent, Uzbekistan[1]
Khoja Akhmet Yassawi International Kazakh-Turkish University, Turkistan, Kazakhstan[2]

Abstract. Restless legs syndrome is a prevalent neuropsychiatric disorder that has a considerable impact on patients' quality of life, characterised by an irresistible urge to move the lower extremities, particularly during restful periods and at night. This condition is associated with unpleasant sensations in the legs, which often result in chronic sleep disturbances, such as difficulty in falling asleep and staying asleep. Consequently, individuals suffering from this disorder frequently experience daytime fatigue, cognitive impairments, and an increased risk of developing anxiety and depressive disorders. Despite its high prevalence, the disorder remains underdiagnosed, leading to delays in the initiation of appropriate treatment and the management of symptoms.According to epidemiological studies, the prevalence of restless legs syndrome ranges from 5-10% among the adult population, with a higher prevalence observed among women and elderly individuals.The etiology of restless legs syndrome is multifactorial, involving genetic predisposition, neurochemical imbalances, iron deficiency, and hormonal dysfunctions, such as hypothyroidism. Adequate diagnosis and effective therapeutic management are contingent on a comprehensive understanding of these mechanisms. This necessitates the exploration of biochemical markers that may facilitate restless legs syndrome diagnosis and optimize treatment strategies. Among these, thyroid-stimulating hormone and interleukin-6 have been identified as potential indicators of pathological processes associated with the disorder.The evaluation of these biochemical markers may contribute to a more individualized approach to treatment, enabling better disease management. The current treatment options for restless legs syndrome include pharmacological and non-pharmacological interventions. A range of pharmaceuticals, including dopamine agonists, anticonvulsants, and iron supplements, are frequently prescribed with the aim of alleviating symptoms. In addition to drug therapy, non-drug interventions, such as regular physical activity and lifestyle modifications, have been shown to be of significant benefit to patients. A multidisciplinary approach that takes into account neurochemical, biochemical, and hormonal disturbances is essential for achieving better control of symptoms, improving sleep quality, and reducing the psychological burden associated with this disorder. The importance of early diagnosis and the development of personalised treatment strategies cannot be overstated in this context, as they have the potential to significantly enhance the quality of life for individuals affected by restless legs syndrome.

Keywords: restless legs syndrome, neuropsychiatric disorder, sleep disturbances, daytime fatigue, cognitive impairments, iron deficiency, thyroid-stimulating hormone, interleukin-6, dopamine agonists, quality of life.

Мазасыз аяқтар синдромы: клиникалық және биохимиялық аспектілері және диагностика мен терапияны оңтайландыру

Раимова М.[1], Едгарова У.[1], Садыкова К.[2]
Ташкент Мемлекеттік стоматология институты, Ташкент, Өзбекстан[1]
Қожа Ахмет Ясауи атындағы Халықаралық қазақ-түрік университеті, Түркістан қ., Қазақстан[2]

Аңдатпа. Мазасыз аяқ синдромы - пациенттердің өмір сүру сапасына айтарлықтай әсер ететін жалпы жүйке-психикалық бұзылыс, әсіресе тыныштық кезеңінде және түнде төменгі аяқтарын қозғалтуға деген ұмтылыспен сипатталады. Бұл жағдай аяқтардағы жағымсыз сезімдермен байланысты, бұл көбінесе ұйқының созылмалы бұзылуына әкеледі, мысалы, ұйқышылдық және ұзақ ұйықтау қиындықтары. Демек, бұл бұзылудан зардап шегетін адамдарда күндізгі шаршау, когнитивті бұзылулар және мазасыздық пен депрессиялық бұзылулардың даму қаупі артады. Жоғары таралуына қарамастан, көп жағдайда диагностикаланбайды, бұл емдеудің кешігуіне және оның тиімділігінің төмендеуіне әкеледі. Эпидемиологиялық зерттеулерге сәйкес, ересектер арасында мазасыз аяқ синдромының таралуы 5-10% аралығында, әйелдер мен егде жастағы адамдарда жоғары таралу байқалады. Мазасыз аяқ синдромының этиологиясы көп факторлы және генетикалық бейімділікті, нейрохимиялық теңгерімсіздікті, темір тапшылығын және гипотиреоз сияқты гормоналды бұзылуларды қамтиды. Тиісті диагностика және тиімді терапевтік емдеу осы механизмдерді жан-жақты түсінуге байланысты. Бұл мазасыз аяқ синдромын диагностикалауды жеңілдететін және емдеу стратегияларын оңтайландыратын биохимиялық маркерлерді зерттеуді қажет етеді. Олардың ішінде қалқанша безді ынталандыратын гормон мен интерлейкин-6 аурумен байланысты патологиялық процестердің ықтимал көрсеткіштері ретінде анықталды. Осы биохимиялық маркерлерді бағалау аурудың ағымын жақсы бақылауға мүмкіндік беретін емдеудің жеке тәсіліне ықпал етуі мүмкін. Мазасыз аяқ синдромын емдеудің заманауи әдістеріне фармакологиялық және дәрілік емес араласулар жатады. Симптомдарды жеңілдету үшін көптеген дәрі-дәрмектер тағайындалады, соның ішінде допамин агонистері, құрысуға қарсы препараттар және темір препараттары. Дәрілік терапиядан басқа, тұрақты физикалық белсенділік және өмір салтын өзгерту сияқты дәрілік емес араласулар пациенттерге айтарлықтай пайда әкелетіні дәлелденді. Нейрохимиялық, биохимиялық және гормоналды бұзылуларды ескеретін пәнаралық тәсіл симптомдарды жақсырақ бақылауға қол жеткізеді, ұйқы сапасын жақсарту және осы бұзылумен байланысты психологиялық жүктемені азайту үшін қажет. Бұл тұрғыда ерте диагностиканың және жеке емдеу стратегияларын әзірлеудің маңыздылығын асыра бағалау қиын, өйткені олар мазасыз аяқ синдромынан зардап шегетін адамдардың өмір сүру сапасын айтарлықтай жақсарта алады.

Түйін сөздер: мазасыз аяқ синдромы, жүйке-психикалық бұзылулар, ұйқының бұзылуы, күндізгі шаршау, когнитивті бұзылулар, темір тапшылығы, қалқанша безді ынталандыратын гормон, интерлейкин-6, допамин агонистері, өмір сапасы.

Синдром беспокойных ног: клинические и биохимические аспекты, оптимизация диагностики и терапии

Раимова М.[1], Едгарова У.[1], Садыкова К.[2]
Ташкентский Государственный стоматологический институт, Ташкент, Узбекистан[1]
Международный казахско-турецкий университет имени Ходжа Ахмеда Ясави, г.Туркестан, Казахстан[2]

Аннотация. Синдром беспокойных ног - распространенное нервно-психическое расстройство, оказывающее значительное влияние на качество жизни пациентов, характеризующееся непреодолимым желанием двигать нижними конечностями, особенно в периоды покоя и ночью. Это состояние связано с неприятными ощущениями в ногах, которые часто приводят к хроническим нарушениям сна, таким как трудности с засыпанием и продолжительным пребыванием во сне. Следовательно, люди, страдающие этим расстройством, часто испытывают дневную усталость, когнитивные нарушения и повышенный риск развития тревожных и депрессивных расстройств. Несмотря на свою высокую распространенность, это заболевание по-прежнему недостаточно диагностируется, что приводит к задержке лечения и снижению его эффективности. Согласно эпидемиологическим исследованиям, распространенность синдрома беспокойных ног среди взрослого населения колеблется в пределах 5-10%, причем более высокая распространенность наблюдается среди женщин и пожилых людей. Этиология синдрома беспокойных ног многофакторна и включает генетическую предрасположенность, нейрохимический дисбаланс, дефицит железа и гормональные нарушения, такие как гипотиреоз. Адекватная диагностика и эффективное терапевтическое лечение зависят от всестороннего понимания этих механизмов. Это требует изучения биохимических маркеров, которые могут облегчить диагностику синдрома беспокойных ног и оптимизировать стратегии лечения. Среди них тиреотропный гормон и интерлейкин-6 были определены как потенциальные индикаторы патологических процессов, связанных с этим заболеванием. Оценка этих биохимических маркеров может способствовать более индивидуальному подходу к лечению, что позволит лучше контролировать течение заболевания. Современные методы лечения синдрома беспокойных ног включают фармакологические и немедикаментозные вмешательства. Для облегчения симптомов часто назначают целый ряд лекарственных препаратов, включая агонисты дофамина, противосудорожные препараты и препараты железа. В дополнение к медикаментозной терапии было доказано, что немедикаментозные вмешательства, такие как регулярная физическая активность и изменение образа жизни, приносят значительную пользу пациентам. Междисциплинарный подход, учитывающий нейрохимические, биохимические и гормональные нарушения, необходим для достижения лучшего контроля над симптомами, улучшения качества сна и снижения психологической нагрузки, связанной с этим расстройством. В этом контексте важность ранней диагностики и разработки индивидуальных стратегий лечения трудно переоценить, поскольку они могут значительно улучшить качество жизни людей, страдающих синдромом беспокойных ног.

Ключевые слова: синдром беспокойных ног, нервно-психическое расстройство, нарушения сна, дневная утомляемость, когнитивные нарушения, дефицит железа, тиреотропный гормон, интерлейкин-6, агонисты дофамина, качество жизни.

Introduction

Restless legs syndrome (RLS) is a neurological disorder characterized by unpleasant sensations in the legs and an irresistible urge to move them, especially at rest and at night. The symptoms of this syndrome can significantly reduce the quality of life of patients by disrupting sleep and causing daytime fatigue. In recent decades, the biochemical and neuropathophysiological mechanisms underlying RLS have been elucidated, opening up new possibilities for diagnosis and

therapy. This article reviews the clinical manifestations, diagnostic criteria, differential diagnosis and biochemical aspects of the disease, as well as methods for optimizing diagnosis and treatment, including the role of hormones such as thyroid stimulating hormone (TSH), hypoxia inducible factor-1 (HIF-1) and interleukin-6 (IL-6) [1-3].

Restless legs syndrome is a common disorder. According to various studies, its prevalence in the population ranges from 5% to 10%, with the disease occurring more often in women than in men [4]. The prevalence of RLS increases significantly with age, especially in people over 40 years of age, and reaches its peak in the elderly. There is also a high incidence of RLS in patients with chronic diseases such as diabetes, kidney disease, neuropathy, as well as in people with iron deficiency and thyroid insufficiency [5]. Studies have shown that about 2-3% of the population experiences RLS symptoms, but only 1-2% seek medical attention, indicating a high proportion of undetected and untreated cases [6]. Restless legs syndrome also has a genetic predisposition, and having a history of RLS in close relatives increases the likelihood of developing the disease [7].

The purpose of this literature review is to analyze current data on the clinical and biochemical aspects of restless legs syndrome (RLS) with an emphasis on identifying effective strategies for optimizing its diagnosis and therapeutic treatment.

Search strategy. The literature review analyzed articles published from the scientific databases PubMed, Medline, Google Scholar, Embase, and Web of Science from 2019 to 2025.

Etiopathogenesis

The etiology and pathogenesis of restless legs syndrome remain unclear, but several main factors influencing the development of the disease are currently identified.

1.Genetic factors. Numerous studies indicate a genetic predisposition to RLS. Certain mutations have been identified in genes encoding proteins involved in neurotransmitter systems, such as the dopamine system. Genetic factors can influence functional changes in brain structures that regulate motor activity, leading to impaired control of limb movement at rest [8].

2. Neurochemical changes. One of the main pathogenetic mechanisms of RLS is dysfunction of the dopamine system. Recent studies have shown that patients with RLS have changes in the activity of dopamine receptors and dopamine transport, which may explain the worsening of symptoms at night and at rest [9].

3. Iron deficiency. Low iron levels, especially in the central nervous system, also play an important role in the pathogenesis of RLS. Iron is necessary for the normal functioning of enzymes involved in the synthesis of neurotransmitters such as dopamine. Recent studies suggest that iron deficiency may impair the function of dopaminergic neurons, which contributes to the development of RLS symptoms [10].

4. Inflammatory processes. Exposure to chronic inflammation may also be an important mechanism in the development of RLS. Elevated levels of proinflammatory cytokines such as interleukin-6 (IL-6) may affect the central nervous system, impairing neuroplasticity and exacerbating disease symptoms [11].

5. Hormonal imbalances. Recent studies have revealed a link between RLS and hormonal disorders such as hypothyroidism. Elevated levels of thyroid stimulating hormone (TSH) may be associated with the development of restless legs syndrome, especially in elderly patients, indicating an important role of thyroid function in the pathogenesis of the disease [12].

Clinical manifestations of restless legs syndrome

Restless legs syndrome is characterized by a complex of symptoms that include unpleasant sensations in the lower extremities, such as crawling, tickling, heaviness, or pain. These symptoms often occur at rest, especially in the evening and at night, and may be relieved by movement. Patients often report that they need to constantly move their legs to relieve these sensations, which can lead to insomnia and impaired quality of life. RLS symptoms may also be associated with other conditions, such as depression, anxiety disorders, and chronic fatigue [13]. Symptoms can vary in

intensity and duration, making diagnosis and treatment challenging. It is important to consider that RLS can be primary or secondary. Primary RLS has a genetic predisposition and develops without apparent external causes, while secondary RLS is often associated with other diseases such as diabetic neuropathy, iron deficiency anemia, chronic renal failure and thyroid disease [14].

Diagnostic criteria. To diagnose RLS, a number of criteria are used, as proposed by the International Society for the Study of RLS. According to these criteria, all of the following features must be present to diagnose RLS:

1. Unexplained sensations in the legs: Patients describe them as crawling, tickling, burning, pain, or a feeling of heaviness that occurs or intensifies at rest.

2. Exacerbation of symptoms in the evening and at night: Symptoms usually worsen or begin to appear in the evening hours or at night.

3. Exacerbation of symptoms with no leg movements: Symptoms are relieved or disappear when moving the legs, such as walking or stretching.

4. Sleep disturbance: Symptoms lead to insomnia and disruption of the normal sleep-wake cycle [15].

An additional criterion is the exclusion of other diseases that may cause similar symptoms [16].

Differential diagnostics. Differential diagnosis of RLS includes a number of diseases that may have similar symptoms. Among them:

- Neurological diseases: peripheral neuropathy, diabetic neuropathy, Parkinson's disease.
- Muscle disorders: muscle spasms, myofascial pain.
- Venous insufficiency: thrombophlebitis, varicose veins.
- Osteoarthritis and other joint diseases: diseases of the joints of the lower extremities that cause pain when moving.
- Psychiatric disorders: anxiety disorders, depression, hypochondria, which can mask the symptoms of RLS.

Differential diagnosis requires a thorough examination, including neurophysiological and biochemical tests, as well as exclusion of other diseases with similar clinical manifestations [17].

Optimization of diagnostics and therapy. Optimization of RLS diagnostics and therapy involves a comprehensive approach that includes diagnostic criteria, biochemical markers, and personalized treatment methods. This approach helps to more accurately identify the disease, assess its severity, and adjust treatment.

Diagnostics. In order to diagnose RLS, it is important not only to use clinical criteria, but also a biochemical examination, including tests for TSH, HIF-1, and IL-6. For example, a TSH test helps to exclude hypothyroidism as a cause of symptoms, and a study of IL-6 levels can show whether there is inflammation that affects the development of RLS. Using the IRLSSG Rating Scale helps to objectively assess the severity of the disease and its impact on the patient's daily life [18].

Treatment

Treatment of restless legs syndrome (RLS) should be multifaceted and take into account all possible factors influencing the development and severity of symptoms of the disease. Complex therapy includes drug treatment, non-drug correction methods and elimination of biochemical disorders that contribute to the progression of the disease.

Drug treatment. The main goal of drug therapy is to reduce motor symptoms, improve sleep quality and eliminate possible neurochemical dysfunctions.

Dopaminergic drugs: Dopamine receptor agonists such as pramipexole and rotigotine are first-line drugs for RLS, as they help normalize dopaminergic activity in the central nervous system. These drugs effectively reduce motor symptoms, especially at night, and help patients better control the urge to move. However, long-term use may lead to an increase in symptoms (augmentation), which requires careful titration of the dosage and periodic review of the treatment regimen [19].

Anticonvulsants: Drugs such as gabapentin and pregabalin are used in RLS accompanied by severe pain or sensory disturbances. They have the ability to reduce the hyperexcitability of the

nervous system and reduce nocturnal paresthesia. These drugs are especially useful in patients suffering from chronic pain and sleep disorders [20].

Iron supplements: Studies show that patients with RLS often have iron deficiency or low ferritin levels, which leads to impaired dopamine synthesis and worsening of symptoms. In such cases, iron supplementation is recommended, especially when ferritin levels are below 50 ng/mL. Parenteral iron may be more effective than oral iron, especially in patients with impaired absorption [21].

Opioid drugs: In rare, severe cases, when standard therapy is ineffective, weak opioid receptor agonists (e.g. tramadol or oxycodone) can be used. They have a central analgesic effect and help to cope with severe movement disorders. However, their use requires caution due to the risk of addiction and side effects [22].

Non-drug treatment methods. Complementary therapeutic approaches can significantly enhance the effectiveness of drug treatment and reduce the severity of symptoms.

Physical activity: Regular moderate exercise such as walking, stretching, and yoga can improve circulation and muscle tone, reducing nighttime symptoms of RLS. However, excessive exercise, especially before bedtime, can worsen symptoms [12].

Optimizing sleep: Maintaining good sleep hygiene is key to managing symptoms. It is recommended to maintain a regular sleep schedule, avoid caffeine and alcohol before bed, create a comfortable bedroom environment (darkness, quiet, moderate temperature), and avoid prolonged periods of inactivity [15].

Correction of biochemical disorders. Modern research emphasizes the importance of identifying and correcting biochemical factors that contribute to the development of RLS.

Hormonal balance: Elevated levels of thyroid stimulating hormone (TSH) may indicate hypothyroidism, which is often associated with RLS. Correction of hypothyroidism with thyroid hormones helps stabilize metabolic processes and may improve the course of the disease [16].

Inflammatory markers: Patients with elevated levels of interleukin-6 (IL-6), which indicates systemic inflammation, may experience more severe RLS symptoms. In such cases, the use of anti-inflammatory drugs and lifestyle modifications to reduce the body's inflammatory response are recommended [17].

Hypoxia and oxygen metabolism: Elevated levels of hypoxia inducible factor-1 (HIF-1) indicate possible decreased tissue oxygen supply, which may worsen RLS symptoms. Improving microcirculation and using drugs that promote tissue oxygenation may be beneficial in such patients [20].

Personalized approach to treatment. The modern approach to the treatment of restless legs syndrome requires individualization of therapy taking into account biochemical and hormonal indicators. Including the assessment of TSH, IL-6 and HIF-1 levels in standard diagnostic algorithms allows not only to identify possible mechanisms of disease development, but also to select the most effective treatment methods.

Complex therapy, combining drug and non-drug strategies, helps reduce the severity of symptoms, improve sleep quality and increase the quality of life of patients. With the right selection of treatment, it is possible to achieve a significant reduction in the manifestations of restless legs syndrome and prevent its further progression [22].

Conclusions

Restless legs syndrome is a multifactorial disease that requires a comprehensive approach to diagnosis and treatment. The inclusion of biochemical markers such as TSH, HIF-1, and IL-6 can significantly improve the accuracy of diagnosis and select personalized treatment. Optimization of diagnostics using scales, laboratory tests, and individualized therapeutic methods helps improve the quality of life of patients and improve their general condition.

Conflict of interest. The authors declare no conflict of interest.

Acknowledgments: Parts of the manuscript were translated from kazakh language to English using artificial intelligence (ChatGPT, OpenAI, GPT-4). The translation was subsequently reviewed and edited for accuracy by the authors.

References

1. Bhatia S, et al. Thyroid Dysfunction and Its Association with Restless Legs Syndrome: A Review of the Literature. Endocr Rev. 2020; 41(6):1025-1037.
2. Zhao X, et al. Role of HIF-1 in the pathogenesis of Restless Legs Syndrome. Front Neurol. 2022;13:692437.
3. Andrei Vlasie, Simona Corina Trifu, Cristiana Lupuleac, Bianca Kohn, Mihai Bogdan Cristea Restless legs syndrome: An overview of pathophysiology, comorbidities and therapeutic approaches (Review). Exp Ther Med. 2021 Dec 30;23(2):185. doi: 10.3892/etm.2021.11108
4. Samson G Khachatryan, Raffaele Ferri, Stephany Fulda, Diego Garcia-Borreguero, Mauro Manconi, Maria-Lucia Muntean, Ambra Stefani Restless legs syndrome: Over 50 years of European contribution. J Sleep Res . 2022 Jul 9;31(4):e13632. doi: 10.1111/jsr.13632
5. Federico Castillo-Álvarez , María Eugenia Marzo-Sola Restless legs syndrome. Pathophysiology, diagnosis and treatment. Med.Clin (Barc). 2025 Jan 24;164(2):84-90. doi: 10.1016/j.medcli.2024.05.026. Epub 2024 Aug 28.
6. Schormair B, et al. Genetic Insights into Restless Legs Syndrome: Novel Approaches to Diagnosis and Therapy.J Clin Neurol. 2019;15(2):181-191.
7. Xiao-Min Xu , Jiang-Hai Ruan, Tao Tao , Shu-Li Xiang, Ren-Liang Meng, Xiu Chen Role of vitamins in the pathogenesis and treatment of restless leg syndrome: A systematic review and meta-analysis. PLoS One. 2025 Mar 10;20(3):e0313571. doi: 10.1371/journal.pone.0313571. eCollection 2025.
8. Winkelman JW, Berkowski JA, Del Rosso LM, et al Treatment of restless legs syndrome and periodic limb movement disorder: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. J Clin Sleep Med. 2025 Jan 1;21(1):153-199. doi: 10.5664/jcsm.11392.
9. Mohammadi MM, Ahmadi M, Vaisi Raygani AA. The Effect of Superficial Heat-Cold Application on the Sleep Quality of Patients With Restless Leg Syndrome: A Systematic Review and Meta-Analysis. Nurs Open. 2024 Nov;11(11):e70080. doi: 10.1002/nop2.70080.
10. Lanza G, Mogavero MP, Ferri R, Pani T. Motor cortex excitability in restless legs syndrome: A systematic review and insights into pathophysiology via transcranial magnetic stimulation. Sleep Med Rev. 2025 Feb:79:102027. doi:10.1016/j.smrv.2024. 102027. Epub 2024 Nov 20.
11. Karolina Poplawska-Domaszewicz , Silvia Rota, Mubasher A Qamar , K Ray Chaudhuri The complexities in the differential diagnosis of restless legs syndrome (Willis-Ekbom disease). Expert Rev Neurother. 2025 Feb; 25(2):157-173. doi: 10.1080/14737175.2025.2450639. Epub 2025 Jan 14.
12. He Y, et al. Effects of Iron Deficiency and Supplementation in Restless Legs Syndrome: A Review. Neuropharmacology. 2020;164:107912.
13. Diego Garcia-Borreguero, Jed Black, Christopher J Earley, et. al. International Restless Legs Syndrome Study Group (IRLSSG) Rethinking clinical trials in restless legs syndrome: A roadmap. Sleep Med Rev 2024 Oct:77:101978. doi: 0.1016/j.smrv.2024.101978. Epub 2024 Jul 18.
14. John W Winkelman, J Andrew Berkowski, Lourdes M DelRosso et al. Treatment of restless legs syndrome and periodic limb movement disorder: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. J Clin Sleep Med 2025 Jan 1;21(1):153-199. doi: 10.5664/jcsm.11392.
15. Kaplan Ö, Başer M, Karaçam Z Effect of Non-Pharmacological Methods Used for Restless Leg Syndrome in Pregnancy on the Severity of the **Syndrome** and Sleep: A Systematic Review and Meta-Analysis. Altern Ther Health Med. 2024 Jun; 30(6):32-38.

16. González-Parejo P, Martín-Núñez J, Cabrera-Martos I, Valenza MC. Effects of Dietary Supplementation in Patients with Restless Legs Syndrome: A Systematic Review. Nutrients. 2024 Jul 18; 16(14):2315. doi: 10.3390/nu16142315.

17. Li S, et al. Serum Cytokine Changes and Their Role in Restless Legs Syndrome. Clin Neurol Neurosurg. 2021;201:106421.

18. Burini A, Pellitteri G, Merlino G, Nilo A, Tereshko Y, Dolso P, Gigli GL, Valente M. Current and emerging pharmaceutical strategies for the treatment and management of **r**estless legs syndrome. Expert Rev Neurother. 2024 Oct; 24(10):997-1009. doi: 10.1080/14737175.2024.2385947. Epub 2024 Jul 31.

19. Song P, Wu J, Cao J, Sun W, Li X, Zhou T, Shen Y, Tan X, Ye X, Yuan C, Zhu Y, Rudan I The global and regional prevalence of restless legs syndrome among adults: A systematic review and modelling analysis. Global Health Epidemiology Research Group (GHERG).J Glob Health. 2024 Jun 7;14:04113. doi: 10.7189/jogh.14.04113.

20. Zhou X, Du J, Liang Y, Dai C, Zhao L, Liu X, Tan C, Mo L, Chen L The Efficacy and Safety of Pharmacological Treatments for Restless Legs Syndrome: Systemic Review and Network Meta-Analysis. Front Neurosci. 2021 Oct 26;15:751643. doi: 10.3389/fnins.2021.751643. eCollection 2021.

21. Raimova MM, Yodgarova UG. Pathogenetic Aspects of Restless Feet Syndrome. Br Med J 2021;1(1.2): 34-41.

22. Raimova MM, Yodgarova UG, Boboev KK, Mamatova ShA, Yadgarova LB. Modern pathogenetic mechanisms of restless legs syndrome development. Journal of Neurology and Neurosurgical Research. 2021;(1),45-52.

Raimova Malika Mukhamedjanovna, Doctor of Medical Sciences, Professor of the Department of Nervous Diseases. Folk Medicine, Tashkent State Dental Institute, Tashkent, Uzbekistan. malikamed-74@yandex.ru
https://orcid.org/0000-0002-5933-3665

Yodgarova Umida Gaybulloyevna, PhD, Associate professor of the Department of Nervous Diseases. Folk Medicine, Tashkent State Dental Institute, Tashkent, Uzbekistan.
umidayodgarova2425@mail.ru
https://orcid.org/0000-0002-7846-4417

Sadykova Karlygash Zharylkasynovna, PhD, Head of the Department of "Special Clinical Disciplines", Khoja Ahmed Yasawi International Kazakh-Turkish University
e-mail: *karlygash.sadykova@ayu.edu.kz*
https://orcid.org/0000-0002-9120-8565