

Common Sleep Disorders and Risk Factors in Hemodialysis Patients

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Although the function and physiology of sleep have not been fully elucidated, it is a universal need for life-forms such as human beings, and in the absence of sleep, severe physiological consequences emerge. Sleep can be defined as temporary, partial and periodic disappearance of the organism's communication with the environment and it is reversible with various severity stimuli. Sleep disorders in hemodialysis patients are frequently seen with the contribution of various risk factors. Insomnia is the most common sleep disorder in hemodialysis patients and affects the sleep quality of patients negatively. Insomnia is a lack of adequate and restful sleep despite adequate reserved time to sleep and it refers to sleeplessness. Sleeplessness can be defined as difficulty in starting sleep, and it refers insufficiency in duration, integrity and quality of sleep despite there is adequate time and chance to sleep. Anemia, anxiety, depression and many factors cause sleep disorders in hemodialysis patients. The aim of this review is to give information about the prevalence of common sleep disorders in hemodialysis patients and the risk factors that contribute to the development of these disorders.

Keywords: Hemodialysis, Sleep Disorder, Risk Factor, Prevalence, Patient.**Introduction**

Hemodialysis [HD] is the process of taking toxin loaded blood from the patient via an artificial membrane and HD machine, regulating liquid-electrolyte content of blood and giving it to the patient again [1-3]. In the early years of HD, it was used only for patients with severe uremic and terminal periods. However, with the technical development of HD treatment, ease of accessibility to HD and the fact that HD costs can be covered by health insurance, the frequency of this method has increased [4]. The dialysis process can be applied as standard HD, short daily HD, night long HD and home HD [4-6]. Standard HD treatment is the main treatment option for ESRF [End-Stage Renal Failure] patients in the world [5].

Definition, Stages and Physiology of Sleep

Although the function and physiology of sleep have not been fully elucidated, it is a universal need for life-forms such as human beings, and in the absence of sleep, severe physiological consequences emerge.

Sleep can be defined as temporary, partial and periodic disappearance of the organism's communication with the environment and it is reversible with various severity stimuli [7]. Sleep consists of two different stages in terms of cardiovascular effect. The first is NREM [non-rapid eye movement] sleep without rapid eye movements and the second is REM [rapid eye movement] sleep with rapid eye movements. 70-80% of the normal sleep period consists of NREM [6 hours] period and 20-25% [1,5-2 hours] consists of REM period. Non-REM sleep is divided into four stages and REM sleep is divided into two stages as phasic and tonic [8]. Stages of Non-REM Sleep;

- Stage 1: Constitutes 1-5% of all night sleep. It is a period of falling asleep and it has short duration. Brain activity is high at this stage, accompanied by relaxation and slow eye movements [8, 9].
- Stage 2: Constitutes 40-50% of all night sleep. It is the longest stage of sleep. There are brain activities that provide continuity of sleep [8, 9].
- Stage 3: Constitutes 3-8% of all night sleep [8].
- Stage 4: Constitutes 10-15% of all night sleep. Stage 3 and stage 4 are deep sleep stages [10].

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In the tonic phase of REM sleep, atony occurs in skeletal muscle groups and reflexes are suppressed. Blood pressure and heart rate fluctuations occur in the phasic stage characterized by rapid eye movements. In addition, irregular breathing, movement in the tongue, jaw and leg muscles are observed in this stage [9].

Normal sleep begins with stage 1 and then passes to stage 2. The frequency and height of brain waves are reduced in stage 1. In this process, the activity of the mind detaches from the conscious state, the person becomes distracted, and detaches from the outer environment. It then moves to stage 2, during which the sleeping spindles which ensure the continuity of sleep and the so-called K-complex regenerating brain activity are observed and these activities ensure that sleep is maintained. After the onset of sleep, the first REM period occurs after 70-90 minutes and this cycle is renewed every 90 minutes. REM sleep occurs in 4-6 separate episodes overnight [10, 11].

The cortical and subcortical areas of the brain are involved in initiating and sustaining sleep. Borbely[2001] describes the sleep-wake cycle in a dual process model. According to the model, the sleep-wake cycle occurs with the effect of cyclic and homeostatic factors. Cyclic factors make the tendency to sleep more or less in certain segments of the day. The hourly cycle formed by the day-night change is controlled by the suprachiasmatic nuclei which are bilateral in the hypothalamus. Homeostatic sleep impulse increases as the time spent awake increases [12].

Classification of Sleep Disorders

Sleep disorders were first classified in 1979 under the heading of Diagnostic Classification of Sleep and Arousal Disorders. This classification includes three main headings: sleep disorders insomnia, daytime sleepiness and abnormal sleep behavior. In the following years, the American Sleep Disorders Association published the International Classification of Sleep Disorders [ICSD]. In the second edition of International Classification of Sleep Disorders [ICSD-2, 2004], the clinical characteristics and definitive diagnostic criteria of 85 diseases are specified. ICSD-2 includes eight sub-titles [13, 14].

Common Sleep Disorders in Hemodialysis Patients

Insomnia is the most common sleep disorder in ESRF and HD patients with a rate of 65.9-69.1%. This is followed by excessive daytime sleepiness, obstructive sleep apnea syndrome, snoring, nightmares, narcolepsy and sleepwalking. The table shows the risk factors that cause sleep disorders in dialysis patients.

Insomnia

Insomnia is defined as a complaint of inadequate and restless sleep although enough time is left for sleep [15]. Insomnia refers to sleeplessness. Sleeplessness can be

defined as difficulty in starting sleep, and it refers insufficiency in duration, integrity and quality of sleep despite there is adequate time and chance to sleep. Complaints about insomnia in adults;

- Difficulty in starting to sleep or maintaining sleep
- Increased time of awakening in night
- Concerns about insufficient sleep duration
- Feeling that sleep is not restful

Insomnia may be acute or chronic depending on duration. Acute insomnia lasts less than four weeks and chronic insomnia lasts longer than 6 months [16]. Insomnia is the most commonly reported sleep disorder in the general population and its prevalence is between 4.4-11.7% [17]. In a study by Al-Jahdali et al. [2010], HD patients with insomnia were reported to have poor sleep quality as measured by PSQI. Studies show that insomnia is the most common sleep disorder in HD patients [18-20]. According to studies, the prevalence of insomnia is reported to be between 40-69.5% in patients receiving HD treatment [18-23]. In other words, this sleep disorder is 4-6 times more common in HD patients than the general population. In addition, HD treatment is considered as an independent risk factor in the development of insomnia [22]. Al-Jahdali et al. [2010] reported that the sleep quality of HD patients diagnosed with insomnia is poor [23]. The risk factors causing insomnia in patients receiving HD treatment are listed below. Advanced age, anemia, anxiety, depression, restless leg syndrome, obstructive sleep apnea syndrome, excessive daytime sleepiness and dialysis shift [the insomnia ratio is significantly higher in those taking HD treatment in the afternoon than morning and evening] are important risk factors in the formation of insomnia in HD patients [23-26].

Excessive Daytime Sleepiness

Excessive Daytime Sleepiness is a general symptom of ineffective, inadequate and internal sleep disorders. Daytime sleepiness is the most common complaint that causes patients to apply to sleep clinics. Sleepiness affects the general health and daily function and determines the energy and fatigue level of the individual during the day [27]. Approximately 5% of the population has excessive daytime sleepiness. It causes accidents and increases the risk of death in individual and other people [23]. Araujo et al. [2011] found that excessive daytime sleepiness prevalence was 27% in their study conducted with 400 hemodialysis patients. Risk factors for excessive sleepiness in hemodialysis patients are low hemoglobin level and presence of obstructive sleep apnea syndrome [26].

Obstructive Sleep Apnea Syndrome [OSAS]

OSAS is an important sleep disorder developing due to recurrent respiratory disorders [apnea, hypopnea] as a result of the blockages in the upper airway during sleep. Sleeplessness due to sleep splits, hypoxemia as a result of upper airway obstruction, and wake-up reactions cause sympathetic nervous system discharge and this situation causes both sleep disturbance and cardiovascular complications. Snoring, restless sleep, morning headache, gastroesophageal reflux, nocturia and decreased libido are common symptoms of OSAS [28]. Although there are scales developed to detect the risk of sleep apnea, polysomnography is the gold standard method in the diagnosis. In studies using polysomnography, the prevalence of OSAS in patients receiving HD treatment is reported to be between 34.4-65% [28-30]. According to the studies using scales, the risk of OSAS development in patients receiving HD treatment is between 31.8-71% [18, 19, 25, 31, 32]. In addition, patients with high risk of developing OSAS have been reported to be more susceptible to insomnia, RLS, snoring habits and excessive daytime sleepiness [23]. Factors that increase the risk of OSAS in ESRD; Age, Dialysis shift, Obesity, Smoking, Dialysis insufficiency [23, 32].

Restless Leg Syndrome

Restless Legs Syndrome [RLS] is defined as a common neurological disorder that may be primary or secondary, containing emotional and motor components. Pathophysiological mechanisms of central nervous system causing RLS are not fully known [33]. According to a study conducted in Turkey, RLS is seen in 30.8% of patients received dialysis treatment [34]. In a study by Al-Jahdali et al. [2010], the prevalence of RLS is reported to be 50% in ESRD patients [23]. In a study conducted by Stefanidis et al. [2013], it was reported that the prevalence of RLS was 26.6% in HD patients and that more than 80% of patients with RLS

experienced mild or moderate symptoms and 16.2% were severe or very severe [35]. According to a study conducted by Rohani et al. [2014] in Iran, sleep complaints of HD patients with RLS are reported to be more frequent. These complaints include decreased sleep time, increased dozing off duration, excessive daytime sleepiness, insomnia and frequent consumption of sedative-hypnotic agents [36]. In a study to determine RLS-related sleep disorders, RLS has been reported to be associated with excessive daytime sleepiness, poor sleep quality and insomnia [37]. In addition, RLS causes sleep deprivation, excessive daytime sleepiness, depression in patients with chronic renal failure and in this group, RLS decreases quality of life and increases mortality [38]. Risk factors of RLS in HD patients; gender [RLS is seen more common in women], age [the average age of patients with RLS is higher], presence of RLS in family history, unemployment, body mass index, history of cardiovascular disease, hypertension, antihypertensive drug use, presence of peripheral neuropathy, serum creatinine level and thyroid gland dysfunction [34-37].

Periodic Limb Movement Disorder

Periodic limb movement disorder [PLMD] was first described by Symonds in 1953 as nocturnal myoclonus, which is characterized by periodic repetitive foot, leg and / or arm movements during sleep. The etiology of the disease has not been fully elucidated. PLMD can be a primary disease and may accompany other sleep disorders. The prevalence of PLMD in the population is 3.9% and it is more common in women. PLMD is associated with restless leg syndrome and 80% of patients with RLS have PLMD [39]. Hsu et al. [2008] reported the prevalence of PLMD in HD patients as 14.7% [40]. Restless leg syndrome is the most important risk factor in PLMD.

Table 1: Common Sleep Disorders and Risk Factors in Hemodialysis Patients

Sleep Disorder	Prevalence	Risk Factors
Insomnia	<ul style="list-style-type: none"> • %40-69.5 	<ul style="list-style-type: none"> ✓ Advanced age ✓ Anemia ✓ Anxiety ✓ Depression ✓ Restless Leg Syndrome ✓ Dialysis shift is an important risk factor. The insomnia ratio is significantly higher especially in those taking HD treatment in the afternoon than morning and evening. ✓ Obstructive Sleep Apnea Syndrome ✓ Excessive Daytime Sleepiness

Excessive Daytime Sleepiness	<ul style="list-style-type: none"> • %27 	<ul style="list-style-type: none"> ✓ Low Hemoglobin Level ✓ Presence of obstructive sleep apnea syndrome
Obstructive Sleep Apnea Syndrome	<ul style="list-style-type: none"> • The risk of OSAS development in HD patients is between 31.8-71%. • Prevalence in HD patients; 37% in female, 34% in male. 	<ul style="list-style-type: none"> ✓ Age, elderly patients have higher risk of sleep apnea than young ones. ✓ Shift when dialysis applied, patients who underwent hemodialysis in the morning shift have higher risk when compared with those applied in the afternoon and evening ✓ Obesity increases the risk of sleep apnea ✓ Smoking increases the risk of sleep apnea. ✓ Dialysis insufficiency increases the risk of sleep apnea.
Restless Leg Syndrome	<ul style="list-style-type: none"> • %26.6-%50 	<ul style="list-style-type: none"> ✓ Gender [RLS is seen more common in women] ✓ Age [the average age of patients with RLS is higher] ✓ Presence of RLS in family history ✓ Unemployment ✓ Body Mass Index ✓ History of Cardiovascular Disease ✓ Hypertension ✓ Antihypertensive drug use ✓ Presence of peripheral neuropathy ✓ Serum creatinine level ✓ Thyroid Gland Dysfunction
Periodic Limb Movement Disorder [PLMD]	% 14.7	<ul style="list-style-type: none"> ✓ Restless Leg Syndrome

Conclusion

Sleep disorders in HD patients negatively affect sleep quality of patients. The most common sleep disorders in hemodialysis patients are insomnia. Obstructive Sleep Apnea Syndrome, Excessive Daytime Sleepiness, Restless Legs Syndrome, Periodic Limb Movement Disorder [PLMD] are other common sleep related disorders in hemodialysis patients. Hemodialysis treatment is one of the main risk factors for sleep disorders. Advanced age, gender, family history, anemia, anxiety, depression, restless leg syndrome, dialysis shift, obesity, body mass index, smoking, dialysis insufficiency, history of cardiovascular disease, hypertension, antihypertensive drug use and thyroid gland dysfunction are important risk factors.

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