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SLEEP DISORDER AND THYROID DYSFUNCTION: AN UPDATE

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Abstract

Sleep disorders are one of the major health issues facing by generations, and alterations in hormonal secretion also can be seen in these conditions. While there remains limited understanding of the clinical associations between sleep disorders and thyroid abnormalities, these conditions are common concerns impacting individuals across diverse ages, backgrounds, and genders within the broader populace. The clinical overlap between sleep disorders, change in sleep pattern and thyroid dysfunctions was observed during our evaluation of the literatures regarding sleep and thyroid. These results emphasize how critical it is to diagnose and treat thyroid dysfunction in patients suffering from these prevalent sleep problem.

INTRODUCTION

Sleep health involves a diverse set of sleep-wake routines that are customized to suit individual, social, and environmental factors, promoting overall physical and mental well-being. Achieving the best possible state of sleep is marked by personal contentment, suitable timing, sufficient duration, efficient sleep cycles, and sustained alertness throughout waking periods [1]. The duration of sleep needed varies by age and individual. Newborns typically require fourteen to seventeen hours, babies twelve to fifteen hours, young children eleven to fourteen hours, and preschoolers ten to thirteen hours. School-aged children typically need nine to eleven hours, while teenagers are advised to aim for eight to ten hours. Young adults and adults have to aim for seven to nine hours, and older adults typically find seven to eight hours sufficient for optimal health [2]. Enough time, excellent quality, right timing, consistency, and the lack of sleep disruptions or problems are key indicators of typical, healthy sleep patterns [3]. In instances of sleep deprivation, there is a rise in thyroid hormone levels. This heightened excitability within the nervous

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system, attributed to increased thyroid hormone activity, can lead to untimely wakefulness overriding the need for sleep [4]. Enhancing sleep quality and reducing stress levels may aid in the prevention of various cancer types, including thyroid cancer [5]. In the "National Family Health Survey V" (NFHS V), the prevalence of self-reported goiter was 2.9%, while it was 2.2% in NFHS IV. As per the statistics published by "Ministry of Health and Family Welfare" in 2022, the self-reported prevalence of goitre was more in female than male, that also increased with age. There was a graded increase of having thyroid disorders from poorest to richest [6]. The extent of the issue in India surpasses previous estimates from the 1960s, when around 9 million individuals were thought to be affected by goitre. Recent sample surveys indicate that iodine deficiency disorders affect over 10 percent of the population. Current estimates suggest that over 71 million individuals in the country are afflicted by goitre and other iodine deficiency disorders [7].

Sleep

Sleep is characterized as a temporary state of unconsciousness, where in consciousness withdraws from the physical world, and the subject can be awakened with appropriate sensory stimuli. Despite consuming about one-third of our lives, the time dedicated to sleep is not squandered; rather, it is crucial for the normal growth and development of both mind and body [8]**.** The mutual dependence between hormones and sleep in normal physiological functioning is widely recognized and supported by research [9].

Two different types of sleep are found by polysomnographic profiles: rapid eye movement (REM) sleep and non-REM (non-rapid eye movement) sleep. Three stages of NREM sleep are distinguished by a rise in arousal limit and a decrease in cortical electroencephalogram speed. Sleep typically continues through NREM stages N1–N3 about 45–60 minutes after it begins. In young adults, slow-wave sleep, also known as NREM stage N3, makes up 15–25% of their total nocturnal sleep duration and is mostly concentrated in the first third of the night. The initial REM sleep event often takes place during second hour of sleep. Throughout the night, NREM and REM make up for an average of 90–110 minutes. 20–25% of total sleep is REM sleep, while NREM stages N1 and N2 account for 50–60%. Age significantly affects how the sleep state is organized. During childhood, slow-wave sleep is most prevalent and intense, and it gradually decreases throughout the second and third decades of life, coinciding with puberty [10]. Sleep contributes to neural maturation, enhances learning and memory, aids in the selective removal of synapses to discard irrelevant information, supports cognitive functions, facilitates the elimination of metabolic waste products produced during wakefulness, and conserves metabolic energy [11].

Factors Affecting Sleep

The circadian rhythm, governing our sleep cycle, is orchestrated by the hypothalamic suprachiasmatic nucleus (SCN). Within the brain, three nuclei rich in Gamma-aminobutyric acid (GABAergic) neurons play pivotal roles in promoting sleep: these include regions within the brainstem, the lateral hypothalamus, and the preoptic area. [12].

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Sleep patterns are influenced by the circadian rhythm, the function of the pineal gland, activity within the thalamocortical loop, and changes in neurochemical levels [8]. In cases of hypothyroidism, pulmonary function typically remains normal. However, dyspnea may arise due to factors such as pleural effusion, compromised function of respiratory muscle, reduced ventilatory drive, or the presence of sleep apnea [10].

Sleep Disorders [8]

A range of sleep disorders presents themselves during various phases of sleep.

Insomnia - It describes the ongoing difficulty to fall asleep even when given plenty of opportunities. It falls into one of two categories: primary, resulting from irregularities in the usual sleep cycle, or secondary, resulting from sleep disturbances brought on by underlying medical or psychological issues.

Narcolepsy – This illness is characterized by an insatiable desire to sleep and an episodic, abrupt loss of muscular tone.

Bruxism - This is a type of grinding of teeth at night that is typically connected to REM sleep nightmares. It sometimes happens when you're sleeping throughout the day.

Nocturnal Enuresis - In childhood, bedwetting throughout the night accompanied by daytime incontinence is a common problem. It may continue till adulthood. It typically happens in stages 3 or 4 of slow wave sleep, three to four hours after falling asleep.

Sleep paralysis, nocturnal paroxysmal dystonia, somnambulism, REM sleep behaviour disorder, somnolescent starts, sensory paroxysms, and sleep paralysis are examples of **parasomnic disorders** that can also be observed during sleep. Experiencing **hypersomnia**, characterized by excessive sleepiness, can result from various factors including injury to neurons in the subthalamus or hypothalamus, as well as damage to the brainstem's reticular activating system (RAS).

Obstructive Sleep Apnea (OSA)

Obstructive sleep apnea (OSA) is frequently observed in individuals during their middle years, making it a prevalent sleep disorder. It entails a decline in muscle tone and respiratory function as one drift into sleep, resulting in the blockage of the upper airway, notably in the pharynx due to reduced tonicity in the pharyngeal muscles [8].

After evaluating common accompanying conditions among individuals with both hypothyroidism and OSA, encompassing variables such as body mass index, intake of alcohol, patterns of smoking, body mass index, and demographic factors, Thavaraputta et al. utilized a multivariate logistic regression analysis to highlight a strong correlation between OSA and hypothyroidism [13]. Individuals with a diagnosis of hypothyroidism demonstrated a higher incidence of obstructive sleep apnea (OSA) in contrast to the overall population [14]. After the receival of the OSA treatment patient who have abnormal baseline levels of TSH shows improvement in this hormone [15]. Hypothyroidism and OSA may be related via mechanisms such as reduced sensitivity to hypoxia and hypercapnia,

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mucoprotein buildup in the airways causing airway resistance, elevated body mass index, and changes in respiratory muscle activity [16]. Given its high frequency seen in type 2 diabetes mellitus, acromegaly, overt hypothyroidism and Cushing syndrome, OSA should be actively tested [17].

Thyroid Disorders

Insufficient thyroid hormone levels in the blood can be seen as a result of autoimmune disease, removal of surgical thyroid gland, or, less frequently, insufficient pituitary production of thyroid stimulating hormone (TSH) is referred to as **central hypothyroidism** [18]. On the other hand, **hyperthyroidism** results from an overabundance of thyroid hormone in the blood. This condition is typically brought on by overstimulation mediated by immunoglobulins or destruction of thyroid gland, independently functioning thyroid nodules, excessive thyroid hormone intake, or, in rare cases, excessive TSH secretion by a pituitary tumour [19, 20]. Localized clumps found in the thyroid tissue are called thyroid nodules, which can indicate abnormal growth of thyrocytes. About 5% of thyroid nodules may indicate **thyroid cancer**, even though the majority are benign [21]. Mild thyroid failure in which peripheral thyroid hormone levels lies in the normal range according to laboratory reference values but mildly elevated thyroid stimulating hormone (TSH) known as **subclinical hypothyroidism** [22].

From a mechanistic perspective, thyroid hormones boost both the number and performance of mitochondria by engaging with thyroid hormone receptors situated on mitochondrial membranes in both central and peripheral neurons [23, 24]. Using the electron transport chain, mitochondria are essential for producing adenosine triphosphate (ATP). Neurons depend on ATP for the release of neurotransmitters, synaptic functions, and the maintenance of wakefulness [25]. During conditions such as sleep deprivation, or non-physiological wakefulness there's a surge in need for neuronal ATP, which is met by a transient rise in levels of circulating thyroid hormone [4]. Furthermore, ATP itself may function as an excitatory neurotransmitter, potentially facilitating the interaction between thyroid hormone activity and sleep regulation [26, 27].

Factors affecting Secretion of Thyroid Hormones

The release of thyroid hormones is induced by low basal metabolic rate, leptin, and α-melanocyte-stimulating hormone. By preventing the production of Thyrotropin Releasing Hormone (TRH), produced by hypothalamic neurons, excess iodide consumption, stress, somatostatin, glucocorticoids, and dopamine reduce the secretion of thyroid hormones [28]. Children's somatic growth and motor development are hampered by hypothyroidism, which is brought on by severe iodine deficiency. Thyrotoxicosis is the outcome of the thyroid's multifocal autonomous expansion, which is brought on by mild to moderate iodine deficits. Conversely, excess iodine is linked to the onset of hypothyroidism and thyroid autoimmunity. An abrupt rise in iodine consumption is linked to temporary hyperthyroidism in iodine-deficient environments [29].

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Thyroid Hormones and Sleep Disorders

It's been suggested that elevated T4 brought on by sleep deprivation is a physiological adaptation that promotes awake [4]. Thyroid function may be impacted by insufficient sleep. Specifically, in the population with poor sleep conditions, the T4 and Thyroid Stimulating Hormone (TSH) levels affected considerably. Additionally, associations between sleep, stress, and fT4 (free T4) scores were found, indicating that insufficient sleep may have an impact on thyroid hormones [30]. Conditions such as hypothyroidism and hyperthyroidism can also affect sleep architecture and quality while, sleep restriction can change the secretion of hormones in Hypothalamic Pituitary Thyroid (HPT) axis. When treating individuals having thyroid diseases, it is important to consider both the HPT axis and sleep [31].

DISCUSSION

Subclinical thyroid dysfunction is associated with sleep duration. Sleeping for shorter and longer time period than optimum time could raise the chance of thyroid malfunction [32]. A study conducted in a large Chinese population with sample size 15327, L. Song et al. discovered a significant correlation between poor sleep quality and subclinical hypothyroidism. Moreover, women with subclinical hypothyroidism, young people, and slim people are more prone to have trouble in sleeping [33]. Among the workers having work in different time schedules, higher TSH levels were more closely linked to night workers than day workers. Subclinical hypothyroidism was more likely to occur in night shift workers [34]. Because their molecular clocks are altered, rotating night shift workers are more likely to acquire thyroid nodules than persons who work during the day [35]. Many symptoms that affect almost all bodily systems, including the sleep system, can be linked to thyroid disease. Thyroid dysfunction which is not treated, can undoubtedly impact one’s capacity to have restful, healthy sleep, despite the fact that current research conducted by Green ME et al., indicates that thyroid hormone levels can’t be considered as indicators of sleep disturbance. Thyroid and sleep issues frequently coexist, despite the fact that sleep disturbance is not one of the symptoms that physicians most frequently link with thyroid disorders [36].

CONCLUSION

This article concludes that several studies have found, sleep disorders may act as a cause of thyroid dysfunction, and sleep deprivation causes variation of thyroid hormone levels in serum. Change in normal sleep pattern also can cause alterations in thyroid hormone levels, vice versa. As per the current information, very few studies have been conducted on the correlation of sleep disorder and thyroid dysfunction. A few studies don’t support the correlation of thyroid disorders with sleep disorders. Due to the availability of limited data, more studies need to be done for a better conclusion.

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