

## ROLE OF IMPAIRED SLEEP ON DIABETES MELLITUS

Dr. Pimpalkhare Aditi Y.\*<sup>1</sup> and Dr. Gedam Lomesh P.<sup>2</sup>

<sup>1</sup>M. D. (Kriya Sharir), Assistant Professor.

<sup>2</sup>MD (Ayurved Samhita & Siddhant), Assistant Professor.

\*Corresponding Author: Dr. Pimpalkhare Aditi Y.

M. D. (Kriya Sharir), Assistant Professor.

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### ABSTRACT

**Background:** Over the past 30 years there has been an increase in the prevalence of insomnia and diabetes, both of which have serious consequences for longevity and quality of life. Because of this, various serious diseases are increasing nowadays like infertility, psychological disorders, hypertension, risk of myocardial infarction, etc. Diabetes mellitus is topmost in a line. Multiple studies have indeed shown that sleep plays an important role in the 24 hour pattern of glucose concentrations. **Objective:** To study the role of impaired sleep in Diabetes Mellitus according to modern science & ayurveda. **Methods:** following different researches in recent scientific journals, all the three main Samhitas will be referred. **Result:** Inappropriate sleep mainly disturbs carbohydrate metabolism. Higher sleep variability is associated with poorer glycaemic control. Also the quality of sleep is as important as quantity. More is the deep sleep less is the risk of developing diabetes. Also sleep deprivation may aggravate the complications of pre existing diabetes mellitus. **Conclusion:** There is an important role of sleep in maintaining normal glucose metabolism. So impaired sleep has direct action in developing diabetes mellitus.

**KEYWORDS:** glycaemic control, insomnia, diabetes mellitus.

### INTRODUCTION

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. There are very different causes for the development of diabetes right from the genetic cause to obesity, Living a sedentary lifestyle, Increasing age, alcoholism, junk food habits, etc. In the year 2000, India (31.7 million) topped the world with the highest number of people with diabetes mellitus followed by China (20.8 million) with the United States (17.7 million) in second and third place respectively.<sup>[1]</sup> Impaired sleep or Insomnia is difficulty falling asleep or staying asleep, even when a person has the chance to do so. People with insomnia can feel dissatisfied with their sleep and usually experience one or more of the following symptoms: fatigue, low energy, difficulty concentrating, mood disturbances and decreased performance in work. Though other factors such as diet and reduced physical activity have contributed to the obesity epidemic, the impact of sleep dysregulation on causing metabolic derangements is being increasingly recognized. Percentage of insomnia or impaired sleep as a cause of diabetes is increasing now a days.

Good quality of sleep is essential for good health and well-being. However, lifestyle and environmental factors are increasingly causing difficulties in sleeping.

Pressures of modern society have resulted in decreased sleep duration over the past several decades. There are several types of sleep disorders. Insomnia, sleep apnea and restless leg syndrome are some examples. Insomnia causes psychological as well as metabolic diseases. Type 2 Diabetes Mellitus is one of the metabolic end result of Insomnia. Those who are victims of insomnia have an increased risk of developing type 2 diabetes, as controlling blood sugar levels becomes difficult.

Ayurveda includes sleep as one amongst the three pillars of life. *Vagbhata* has enlisted the impaired sleep as one of the causative factors of *Prameha* i.e. diabetes.<sup>[2]</sup> In the verse of sleep as non-suppressible urge in *Sootrasthan*, temporary symptoms of insomnia are given<sup>[4]</sup> but long term effects of insomnia include diabetes is given in *Nidansthan*.<sup>[2]</sup> Obesity or leanness of the body depends on both diet as well as sleep. For the sustenance of life, sleep is as important as diet.<sup>[3]</sup>

### OBJECTIVE

1. To study the role of normal nocturnal sleep on glucose metabolism.
2. To study the role of impaired sleep in Diabetes Mellitus
3. To study the effects of impaired sleep according to *Ayurveda*.

## METHODS

1. Different researches in recent scientific journals were surveyed.
2. All the three main *Samhitas* were referred.

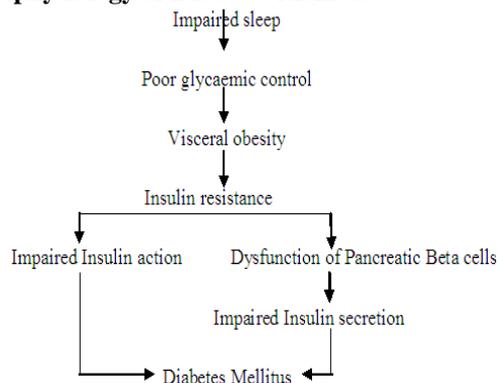
## MATERIALS

Sound Sleep is concerned with physical, mental & social wellbeing of each individual. Sleep is marked by reduced level of consciousness, diminished activity of skeletal muscles and lowered metabolic activity. Sleep is divided into two broad types: rapid eye movement (REM sleep) and non-rapid eye movement (non-REM or NREM sleep). Non-REM sleep occurs first and after a transitional period is called slow wave sleep or deep sleep. The sleep cycle of alternate NREM and REM sleep takes an average of 90 minutes, occurring 4–6 times in a good night's sleep. The first half of the night is predominantly NREM, and the second half is predominantly REM sleep. Although most mammals, whether diurnal or nocturnal, sleep in bouts, human sleep is generally consolidated in a single 7 to 9 hours period and therefore an extended period of fasting must be maintained overnight.

Metabolism is defined as the whole range of biochemical processes that occur within a living organism. It constitutes the two processes of anabolism (build up) and catabolism (break down). In simpler terms, metabolism is the amount of energy (calories) the body burns to maintain itself. Metabolism in general is associated with cell injury due to the release of free radicals. The lower metabolic rate and brain temperature occurring during non-REM sleep seem to provide an opportunity to deal with the damage done during awake and metabolically active period. During sleep the metabolism is anabolic. Anabolic hormones are preferentially secreted in sleep e.g. growth hormone. So BMR (Basal Metabolic Rate) is decreased by 10-15%. In normal subjects, during overnight sleep, blood levels of glucose remain stable or fall only minimally despite the extended fast. Thus a number of mechanisms operate here.

Impaired sleep includes sleeping late at night, altered duration of sleep (less than 6 hours or more than 9 hours), sleeping till late at morning, daytime sleep, interrupted sleep, voluntary suppression of sleep, etc. All these types disturb the circadian rhythm of body. Higher sleep variability is associated with poorer glycaemic control.<sup>[5]</sup> In sleep deprivation, bodies' ability to utilize glucose changes. Chronic sleep deprivation may cause weight gain by affecting the way our body processes and stores carbohydrates & hormones that affect our appetite.

## Pathophysiology of Diabetes Mellitus



## DISCUSSION

### Metabolic changes in sleep

BMR is decreased during normal sleep and reaches a minimum in the morning. It is more decreased in NREM than REM sleep. Glycogen stores, ATP levels & peptide synthesis increase in the brain during sleep. Brain metabolism in REM sleep is similar to wakefulness. But several hormonal changes that foster growth & repair occur during NREM sleep. For example, growth hormone is secreted in the first few hours of slow wave sleep, while cortisol levels are greatly increased during the second half of the sleep, predominantly in REM sleep. This surge in GH induces peripheral lipolysis & insulin resistance. Hence there is a relative state of insulin resistance during early phases of sleep. Conversely, most hypothalamic-pituitary-adrenocortical hormones (cortisol) are suppressed during NREM sleep.

Sleep deprivation causes following changes:

- Alterations in postprandial glucose and lipid metabolism
- Sympathetic activation - Increased catecholamines
- Hypothalamo-Pituitary-Adrenal axis alteration - Increased cortisol
- Oxidative stress
- alter immune response & increase proinflammatory markers e.g. IL-6, TNF- $\alpha$  & CRP
- Changes in adipokines - Increased Leptin

### Metabolic effects of sleep duration

When a person enters slow wave or deep sleep, nervous system activity goes down, the brain uses less glucose, and other changes occur such as an increase in growth hormone and a decrease in the activating hormone cortisol. These hormones make the body less sensitive to insulin. If specifically slow-wave NREM sleep time is restricted, there are metabolic changes that increase the risk of diabetes. In Ayurveda, it is said that one should go to sleep in the evening (first 3 hours after sunset) after taking light & suitable food.<sup>[17]</sup> One should get up in the Brahma Muhurt (the last yama i.e. 3 hours of night), after considering the condition of digestion of food.<sup>[17]</sup> So the total duration of sleep will be 6-9 hours according to season.

### Effects of sleep in the regulation of glucose metabolism

Glucose homeostasis is a balance between glucose production & glucose utilization. Insulin plays a key role in this process. Glucose homeostasis is critically dependent on the ability of pancreatic  $\beta$ -cell to release insulin both acutely (i.e., acute insulin response to glucose or  $\beta$ -cell responsiveness) and in a sustained fashion. Insulin inhibits hepatic glucose production & by stimulating glucose uptake by insulin sensitive tissues such as muscle and fat and non-insulin-dependent tissues, such as the brain. Glucose tolerance refers to the ability of the body to metabolize exogenous glucose & return to a baseline level of blood glucose. Glucose tolerance is typically optimal in the morning & reaches its maximum in the middle of the night. This diurnal variation appears to be due to reduction in insulin sensitivity. Sleep deprivation decreases glucose tolerance in humans. The pattern of glucose secretion during nocturnal sleep deprivation differs significantly from the pattern during nocturnal sound sleep and it is likely due in part to the absence of slow wave sleep and growth hormone secretion in the beginning of the night.

Daytime sleep was associated with marked elevations of glucose levels and insulin secretion, which indicates that sleep, exerts modulatory influences on glucose regulation independently of time of day. Glucose utilization appears lowest during non-REM sleep and highest during wake, with intermediate levels during REM sleep.<sup>[7]</sup> A sleep duration of 6 hours or less or 9 hours or more is associated with increased prevalence of DM and Impaired Glucose Tolerance.<sup>[8]</sup>

### Effects of sleep on Insulin Resistance

Under normal conditions, Akt, serine-threonine kinase (also known as protein kinase B), is activated in the presence of insulin. Then it signals the uptake of glucose into the cells. Insulin resistance indicates that greater amounts of insulin are required to metabolize the same amount of glucose. The beta cells in the pancreas try to keep up with this increased demand for insulin but at one point beta cells fail. Over time, insulin resistance can lead to prediabetes and type 2 diabetes. Both  $\beta$ -cell responsiveness and insulin sensitivity are influenced by sleep. One night of sleep deprivation and 6 months on a high-fat diet could both impair insulin sensitivity to a similar degree, according to research presented at the Obesity Society Annual Meeting in Los Angeles, CA.<sup>[6]</sup>

### Effects of Sleep on Appetite Hormones

The appetite center is believed to be located in the arcuate nucleus of the hypothalamus, which in turn is influenced and regulated by peripheral hormones such as leptin and ghrelin. Leptin is an appetite suppressant hormone produced by adipose tissue, and ghrelin is released from the stomach primarily in response to fasting and promotes the feeling of hunger. Sleep duration seems to play an important role in the regulation of human leptin and ghrelin levels. In case of insomnia,

hormone of hunger (ghrelin) increases and hormone of satiety (leptin) decreases. This makes a person feel hungrier than when well-rested. Differences in energy balance between sleep restriction and sleep extension do not entirely explain the differences in appetite regulation since the laboratory studies kept energy intake and activity levels constant for both bed time conditions. Sleep loss therefore may alter the ability of leptin and ghrelin to accurately signal energy requirements. Acute total sleep deprivation appears to be associated with an increase in leptin levels relative to daytime concentrations but more extended sleep deprivation seems to result in a decrease of leptin levels.<sup>[7]</sup>

### Normal Sleep

- Reduced insulin sensitivity
- Reduced insulin secretory response to elevated glucose level
- Decrease cerebral glucose use related to slow-wave sleep
- Reduction in peripheral glucose use

### Sleep deprivation

- Impaired glucose tolerance
- Increased appetite and hunger (elevation of ghrelin and reduction of leptin)
- Increased sympathetic nervous system activity  
Alterations in counter-regulatory hormones (growth hormone and cortisol)
- Increased proinflammatory markers

### Effects of impaired sleep according to Ayurveda

*Ayurveda* defines sleep, in context to psychology, as retirement of mind from the surrounding.<sup>[9]</sup> In *Ayurveda*, the overall effects of sleep are concluded in the single verse in contrast to the symptoms of sleep deprivation.<sup>[10]</sup> *Aacharyas* have mentioned that sleep is very important even for the existence of life. In *Ayurveda*, sleep is considered among the three pillars important for the sustenance of life.<sup>[11]</sup> Sleep is also included in 13 *Adharneeya vegas* along with other life threatening symptoms like *shwas* (breathlessness), *kasa* (coughing) etc. If there's insufficient sleep at night, it is advised to take sleep in daytime but before food.<sup>[12]</sup> Because sleeping just after food will cause indigestion.<sup>[13]</sup> Daytime sleep is therapeutically indicated in certain conditions also; e.g. for any type of pain, hiccough, indigestion, loose motion, more thirst, deprived sleep because of travelling, in anger, grief etc.<sup>[14]</sup> Day sleep is strictly contraindicated in obese, persons eating regular unctuous substances, persons having vitiation of Kaphadosha, having Kapha prakriti & in persons consuming cumulative poisonous substances like alcohol etc.<sup>[15]</sup> So impaired sleep can lead to Kapha dosha vitiation, then obesity & ultimately it will lead to Prameha i.e. diabetes. Patient of DM desires to stand instead of walking, to sit instead of standing, to lie on a bed instead of sitting, & to get into the sleep instead of lying simply.<sup>[16]</sup>

## CONCLUSION

- Lack of NREM sleep is more harmful than lack of REM sleep.
- Deep sleep with longer duration is much concerned with the regulation of blood glucose.
- Glucose homeostasis is a sum of glucose tolerance & insulin sensitivity. Sleep deprivation hampers insulin sensitivity & causes insulin resistance which will lead to diabetes in chronic cases.
- Impaired sleep causes imbalance between leptin & ghrelin hormones. So body becomes confused when to demand for food as the body's biological clock is disturbed. This excessive hunger is the main cause of obesity in sleep deprivation.
- In Ayurveda there's so much emphasis given on the proper sleep. A detailed treatment is explained for the diseases of sleep deprivation & also excess sleep. A clear reference is given that impaired sleep leads to Obesity & Prameha i.e. diabetes
- So one should take care of own sleep wake cycle to avoid the sequential hazards.

## Clinical Application of the Study

1. Proper history of sleep wake cycle has to be taken in each metabolic disease.
2. Sleep chart should be prescribed to the obesity patients along with diet chart.
3. In patients doing shift duty, keep control on diet, avoid overeating (Adhyashana), follow the rules of daytime sleep, etc.
4. In insomnia patients check GTT periodically to diagnose prediabetes & diabetes.
5. For daytime sleepers, e.g. housewives, explain the rules given in Ayurveda.
6. Ratricharya should be advised in metabolic disorders<sup>[17]</sup>

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