



A Prospective Study on Prevalence and Assessment of Excessive Daytime Sleepiness in Diabetes and Obese Patients

Josmy Jose , C. Dhandapani

¹DEPARTMENT OF PHARMACY PRACTICE, KMCH COLLEGE OF PHARMACY

Research Article

Please cite this paper as: Josmy Jose , C. Dhandapani. A Prospective Study on Prevalence and Assessment of Excessive Daytime Sleepiness in Diabetes and Obese Patients. IJTP, 2012,3(3),338-344.

Corresponding Author:

JOSMY JOSE

DEPARTMENT OF PHARMACY PRACTICE
KMCH COLLEGE OF PHARMACY
COIMBATORE, TAMIL NADU, INDIA
E-MAIL: josmy23@gmail.com

Abstract

Excessive Daytime Sleepiness [EDS] is defined in International Classification of Sleep Disorders based on the behaviour of falling asleep, including difficulty maintaining alertness or wakefulness and unintentionally falling asleep. Diabetes Mellitus and Obesity are the two main factors contributing to EDS. The aim of the study was to determine the prevalence of EDS in diabetic and obese population. The quality and quantity of Sleep was assessed by Epworth [ESS] and Pittsburgh Scale Sleep Quality Index [PSQI]. This prospective study was done in 160 patients who were between the age group of 20-65 years. Among 160 patients, 49.4% patients had EDS. Out of which, 54.17% were females and 45.45% of them were males. Sleep loss varied by gender in diabetic patients. There was considerable difference in the ESS scores between both the genders. It was more observed in diabetic females than males. Obesity was also more common in diabetic women than in men as physical activity was less in women compared to men. A sedentary lifestyle has shown to enhance excessive day time sleepiness in diabetic patients. Sleep disturbance were seen more common in older age group of 55-65 years. Most of the patients observed with EDS had hypertension as a co-morbid disease condition. Thus it was concluded that the quality of sleep was seen to be reduced in patients with Diabetes Mellitus.

Keywords: EDS, sleep disorder, diabetes mellitus, behaviour

Introduction

Excessive Daytime Sleepiness [EDS] is defined in International Classification of Sleep Disorders based on the behaviour of falling asleep, including difficulty maintaining alertness or wakefulness and unintentionally falling asleep.¹ Excessive daytime sleepiness is one of the most common sleep-related patient symptoms affecting about 20 percent of the world population. Persons with excessive daytime sleepiness are at risk of road traffic accidents and have poorer health than comparable adults. The most common causes of excessive daytime sleepiness are sleep deprivation, diabetic mellitus, obesity, obstructive sleep apnea, sedating medications. Other potential causes of excessive daytime sleepiness consist of certain medical and psychiatric conditions and sleep disorders, such as narcolepsy.²

Diabetes is a condition of endemic proportions with increasing prevalence. By 2030, it is expected to have an effect on almost 439 million people ie about 7.7% of total world population. Among Diabetes mellitus Type 2 diabetes mellitus (T2DM) accounts for most cases of diabetes, about 85–95%. Among the factors considered responsible for this sharp increase in prevalence are- increased aged population, unhealthy diet, overweight, obesity, and a sedentary lifestyle³. There is evidence that sleep impairment should also be considered a T2DM risk factor because, in addition to some risk factors listed above, it seems to be independently associated with diabetes. Both the development and control of T2DM seem to be affected by sleep quality and duration⁵. Many researchers suggest that optimizing sleep duration and quality might improve the metabolic control of individuals with T2DM and type 1 diabetes mellitus (T1DM). On the other hand, it should also be taken into account that, poor glycemic control in T2DM and T1DM individuals may favour the development of sleep disorders.⁴⁻⁷ In addition to diabetes; overweight and obesity have been growing in prevalence at an alarming rate.⁸ Sleep loss is also increasing sharply. Chaput et al.⁹ reported that in 1960 the modal adult sleep duration was between 8.0 and 8.9 h, whereas in 2004 the number of sleeping hours of more than 30%



of adults aged 30–60 years had dropped to less than 6 hour. This clearly shows that the interacting epidemics of diabetes, obesity and sleep impairment form a vicious circle.^{10,11} The increased prevalence of metabolic disorders in our society is aggravated by endemic voluntary postponement of bed time and by the current sedentary lifestyle, leading to epidemic proportions of obese people. Sleep disorders is commonly found in patients with type 2 diabetes.¹² Diabetes and chronic loss of sleep share the fact that, both affect millions and one depends on the other. Associated with the endemic condition of diabetes in our society, chronic sleep loss is increasingly common in industrialized societies and affects about 45% of all adults.¹³ Sleep is a complex behavioural state that occupies one third of the human life span. Therefore proper sleep pattern is very much necessary to improve quality of life in diabetic and obese patients. However, there is increasing evidence that sleep also modulates the metabolic, endocrine and cardiovascular systems.¹⁴ Sleep disturbances are common and can be detrimental to the health, mood, and quality of life of people with diabetes.

A study revealed a marked reduction in glucose tolerance and insulin sensitivity after 8 nights of 5-hour bedtimes compared with 8-hour bedtimes.¹⁵ Various mechanisms have been explored and suggested that there is a potential link between poor sleep patterns and negative health outcomes like impaired glucose regulation and subsequent increased risk of type 2 DM.⁴ Evidence from cross-sectional studies suggests that a diabetic condition may involve a reduction in sleep duration or an impairment of sleep quality.¹⁶

Excessive day time sleepiness [EDS] is characterized by persistent sleepiness and often a general lack of energy, even after apparently adequate night time sleep. Sudden involuntary sleep onset and micro sleeps are common complication. Diabetes and obesity are the two main factors contributing to EDS.¹⁷

Sleep and type II diabetes

In the past, T2DM was considered a disease of older age groups. Today, it is well established that even with a higher incidence in older people, T2DM may occur at any age. This change is attributed to the spread of a “Western modern society lifestyle”, which includes higher food consumption, sedentary behaviour, and shorter sleep duration.¹⁸

Sleep deprivation has been shown to be a risk factor for impaired glucose tolerance (IGT),¹⁶ weight gain, insulin resistance, and T2DM itself¹⁹⁻²¹. At the same time, evidence from some epidemiological studies indicates that not only short (6 h or less), but also long sleep duration (9 h or more) is associated with increased prevalence of IGT and T2DM^{9,22} and with high fasting plasma glucose and high HbA1c levels.²³ A study conducted with 1139 men found that subjects reporting short sleep duration (5–6 h of sleep per night) were twice as likely to develop diabetes than those

who slept between 6 and 8 h, and those reporting long sleep duration (8 h) were more than three times as likely to develop diabetes over a period of 15 years.²⁴ The reason why more sleep negatively impacts metabolism has recently become the subject of much speculation.

Evidence for a modulatory impact of sleep on many physiological functions, including metabolic regulation and endocrine release, has been reported more than four decades ago. Night time hormonal release and glucose control are dependent on the occurrence of specific sleep stages²⁵⁻²⁷. Human sleep is composed of rapid-eye-movement (REM) sleep and stages 1, 2 and 3 of non-REM (NREM) sleep. During the deeper stage of non-REM sleep, i.e. slow wave sleep (SWS) or stage NREM 3, brain glucose utilization and sympathetic nervous activity are decreased and parasympathetic nervous activity is increased, relative to both wake and REM sleep. SWS are also associated with robust elevations of growth hormone (GH) levels, while pituitary–adrenal activity is inhibited.²⁸ Hence SWS is likely to play a major role in total body glucose regulation. More recently, orexin neurons in the lateral hypothalamus have been identified as playing a central role in the maintenance of arousal as well as feeding behaviour,^{29,30} suggesting an impact of sleep duration on appetite regulation.

Another cause of the daytime sleepiness in patients with diabetes is the increased levels of inflammatory cytokines³¹. Presently, these cytokines are accepted as mediators of sleepiness, and they are closely involved in the pathogenesis of type 2 diabetes.³²

Sleep and Obesity

Sleepiness is the inability to maintain alertness and manifests as characteristic hypersomnic behaviours and decreased functional outcomes. Not only is daytime sleepiness a common outcome of sleep disturbances, but obesity is biochemically associated with sleepiness also. That is, adipose tissue produces somnolence inducing inflammatory cytokines such as tumour necrosis factor-alpha, interleukin-1 beta, and interleukin-6.³¹

The cause of symptomatic daytime sleepiness in an obese population clearly needs further evaluation. There are many features of obesity that drive various aspects of obesity generated disease and disability. Daytime sleepiness may be related to the extent of adiposity, the distribution of adiposity, or metabolic, inflammatory, physical, mental, or psychological disturbances experienced by obese subjects.³²

The symptoms of daytime sleepiness is measured using a validated instrument, the Epworth Sleepiness



Scale (ESS).and the sleep quality of the past month is measured by Pittsburgh Sleep Quality index[PSQI]. It is hypothesized that the extent of symptomatic daytime sleepiness, measured with the ESS would correlate with one or several of these broad areas and that disturbance in these areas would explain substantial variance of the ESS scores.³³

The ESS represents a validated questionnaire containing eight items that measure a subject's expectation of dozing in eight hypothetical situations. A score greater than 10 is considered indicative of excessive daytime sleepiness and a PSQI score of six or more were considered poor sleepers.^{34,35}

To study the prevalence of Excessive Day time Sleepiness [EDS] in diabetes and obese population by assessing the quality and quantity of Sleep by Epworth[ESS] and Pittsburgh Scale Sleep Quality Index [PSQI] and also to provide patient education to improve quality and quantity of sleep.

Material and Method

Study Design:

It is a prospective observational study.

Study Site:

The study was conducted in the department of Diabetology, Kovai Medical Center and Hospital, a multispecialty hospital in Coimbatore, Tamilnadu.

Study Period:

The study was conducted over a period of five months from September 2011 to January 2012.

Study Population:

Both male and female patients diagnosed with Type II Diabetes Mellitus & Obesity within the age group of 20-65 were included in the study.

Sources of Data:

The data was collected through direct patient interview and also from various sources such as patient's case sheet, treatment chart and laboratory reports.

Study Procedure:

In this prospective observational study, both male and female patients who are diagnosed with Type II Diabetes mellitus, overweight and obese patients within the age group of 20-65 are included, the patients who do not wish to complete the questionnaire and those diagnosed with obstructive sleep apnea are excluded. Hospital Ethical Committee approval was obtained. All the patients are taken directly from the doctor's consultation room. The laboratory values and medications are noted from the patient's chart.

Data are collected and assessed by providing two questionnaires namely Epworth Sleepiness Scale [ESS] and Pittsburgh Sleep Quality Index [PSQI]. The former assess the

daytime somnolence in patients and the latter assess the sleep quality during the past month.

The Epworth sleepiness scale is a brief, valid, reliable measure used to assess the likelihood that an individual will fall asleep in a series of situations such as watching TV, sitting and reading, sitting in a car...etc. The scoring of the answers is 0-3, with 0 being "would never doze", 1 for "slight chance of dozing", 2 for "moderate chance of dozing" and 3 for high chance of dozing". A score lower than 6 distinguishes as getting enough sleep, 7-8 as tends to be sleepy and greater than 9 as very sleepy and they should seek medical advice. Pittsburgh sleep quality index (PSQI) was used to check the sleep habits of diabetic patient during the past month. For each of the questions of the questionnaire, response was classified as "not during the last month", "less than once a week", "Once or twice a week" and "three or more times a week". Individuals with a score of six or more were considered poor sleepers. Patient counselling to improve the quality and quantity of sleep were also given.

Results

The prospective study was aimed to find out the probable overall prevalence of excessive day time sleepiness in diabetic and obese patients. A total of 160 patients with Type II Diabetes Mellitus were selected as the subjects for the study who were attending diabetic clinic at KMCH, Coimbatore.

The study population consisted of 88 males and 72 females with an average age of $52.06.24 \pm 8.822$ and $50.55.14 \pm 8.838$ respectively.

The majority of patient among study population was within the age group of 56 to 65 nearly 38.7% followed by 46 to 55 with the percentage of 33.7% followed by 36 to 45 with the percentage of 22.5%. & 25-35 with a percentage of 5%.

The prevalence of Excessive Day time Sleepiness in the study population was found by Epworth Sleepiness Scale and Pittsburgh Sleep Quality index. Among the study population, 40 males and 39 females were found to have EDS were as 48 males and 33 females were found without EDS .In the study population 45.45% of males and 54.17% of females were found to have EDS. ESS score revealed that diabetic females were significantly sleepier than diabetic males during the day time. The majority of patients with EDS were within the age group of 56-65 (36), followed by 46-55 (25), followed by 36-45(14), and followed by 25-35 (4). The association of prevalence of EDS and age group was found out by using chi-square test ($p=0.300$)



indicating that age group is not significantly associated to EDS but older age group are more prone to disease.

Body mass index (BMI) was calculated. Based on the BMI study subjects were classified into three groups 18.5 to 24.9, 25 to 29.9 and \geq 30. According to ESS Scale, patients were classified as with EDS and without EDS. In the group of BMI (18-24.9) 31.2% of patients were with EDS and 68.8 % of patients were without EDS. In the group of BMI(25-29.9), 62.3% of patients were with EDS and 37.7% of patients were without EDS. In the group of BMI \geq 30 84.2% of patients were with EDS and 15.8% of patients were without EDS. It clearly indicates that BMI is highly associated with EDS ($p=0.000$) Among the subjects with EDS 37.5% of males and 25.6% of females were having BMI in the range 18-24.9(normal), 40% of males and 56.4% of females were having BMI in the range of 25-29.9 (overweight) and 22.5% of males and 17.9% of females were having a BMI (obese). It clearly indicates that obesity was significantly higher in diabetic females who had high chances of EDS than males.

Based on the physical activity study subjects were classified into two groups, one having moderate and other having sedentary physical activity. In the group having moderate physical activity 26 % were with EDS and 74% were without EDS. In the group leading a sedentary lifestyle 59.5% were with EDS and 40.5% were without EDS. It clearly indicates a strong association of EDS with physical activity ($p=0.000$). Among the subjects with EDS, 77.5% of males and 89% of females were leading a sedentary life style and 22.5% of males and 10.25% of females were having moderate physical activity. It clearly indicates that physical activity was significantly lower in diabetic females with poor sleep compared to males.

Risk factors like hypertension (36.7%), Foot Ulcer (27.8), Hypercholesteremia (11.3%) and heart disease (3.8%) were more frequent in diabetic patients with EDS.

The sleeping quality, excessive daytime sleepiness and its patterns in the diabetic population was studied using the Pittsburgh sleep quality index (PSQI). 72(91%) of patients with disturbed sleep and 79(97.5%) of patients with good sleep have never taken any medicine to help them sleep. 2(2.5%) of patients with disturbed sleep and 1 (1.2%) of patients with good sleep have taken medicine once a week to help them sleep. 5(6.3%) of patients with disturbed sleep and 1(1.2%) of patients with good sleep have taken medicine more than once in a week to help them sleep. 2(2.5%) of patients with disturbed sleep and 10 (12.3%) of patients with good sleep have never waken up in the middle of the night or early morning. 38(48.1%) of patients with disturbed sleep and 29(35.8%) of patients with good sleep have waken up once a week in the middle of the night or early morning. 39(49.41%) patients with disturbed sleep and 42(51.9%) of patients with good sleep have waken up more than once in a week. 20(25.3%) of

patients with disturbed sleep and 49(60.5%) of patients with good sleep have never taken more than 30 minutes to get sleep. 30(37.9%) of patients with disturbed sleep and 20(24.7%) of patients with good sleep have taken more than 30 minutes to get sleep once a week. 29(36.7%) of patients with disturbed sleep and 12(14.8%) of patients with good sleep have taken more than 30 minutes to get sleep more than once in a week. 1(1.3%) of patients with disturbed sleep and 2(2.9%) of patients with good sleep have never got up to use the bathroom. 4(5.1%) of patients with disturbed sleep and 12(14.8%) of patients with disturbed sleep have got up once a week to use the bathroom. 74(93.7%) of patients with disturbed sleep and 67(82.7%) of patients with good sleep have got up more than once in a week. 28(35.4%) with disturbed sleep and 52(64.2%) with good sleep never had bad dreams. 32(40.5%) of patients with disturbed sleep and 28(34.6%) of patients with good sleep had bad dreams once a week. 19(24.1%) of patients with disturbed sleep and 1(1.2%) of patients with good sleep had bad dreams more than once in a week. 24(30.4%) of patients with disturbed sleep and 56(69%) of patients with good sleep never had pain. 7(8.9%) of patients with disturbed sleep and 13(16%) of patients with good sleep had pain once a week. 48(60.8%) of patients with disturbed sleep and 12(14.9%) of patients with good sleep had pain more than once in a week.

Comparison in sleeping quality was studied in subjects using Epworth sleepiness scale (ESS). Female diabetic patients had significantly high chances of falling asleep during the day time than males; sitting and reading (30.8% vs 25%), watching TV (35.9% vs 30%) sitting inactive in a public place (12.8% vs 10%), as a passenger in a car (76.9% vs 75%), lying down to rest in the afternoon (97.4% vs 92.5%), sitting and talking to someone (7.7% vs 7.5%), sitting quietly after lunch without alcohol (2.6% vs 2.5%) and in a car while stopped for few minutes in traffic (7.7% vs 2.5%). ESS score results showed that diabetic women were significantly sleepier (54.17%) than men (45.45%) during the day-time.

Discussion

A study conducted by Abdulbari Bener et al has demonstrated a high proportion of sleep loss (60.1%) in Arab diabetic population residing in the State of Qatar. Among the studied diabetic patients, female diabetic patients (57%) were likely to have more sleep loss than male (43%) in the Arab population in Qatar.³⁵ It was also reported in a study by Suarez that Sleep quality and symptoms of poor sleep have been linked to increased risk of type 2 DM with recent evidence suggesting stronger associations in women.³⁶



In the present study, diabetic patients (49.4%) reported high chances of daytime sleepiness. Among the studied diabetic patients, female diabetic patients (54.17%) were likely to have excessive daytime sleepiness than males (45.45%). Another study done in Japan among male population, Kawa-kami et al reported a high incidence of diabetes in male subjects reporting sleeping disturbances after controlling other factors relevant to type 2 DM. These studies identify sleep as a potential factor influencing glucose control in a specific population of patients with type 2 DM.³⁷

In this study, quality of sleep varied by gender in diabetic patients. There was a significant difference observed in ESS scores between both sexes. This is in contrast with another study by Walker RD et al that no significant difference was observed in ESS scores between both genders³⁸.

Female diabetic patients had high chances of falling sleep during the daytime than men especially while sitting and reading. (30.8% vs 25%), watching TV (35.9% vs 30%) sitting inactive in a public place (12.8% vs 10%), as a passenger in a car (76.9% vs 75%), lying down to rest in the afternoon (97.4% vs 92.5%), sitting and talking to someone (7.7% vs 7.5%), sitting quietly after lunch without alcohol (2.6% vs 2.5%) and in a car while stopped for few minutes in traffic (7.7% vs 2.5%). Another study by Meisinger et al in their study demonstrated that the men and women who reported a high frequency of sleep loss had a significantly higher risk for type 2 DM.³⁹

Thus, poor diabetes control could contribute both to a higher perceived sleep debt and lower sleep quality. Sleep disturbances with DM could be caused by either physical or psychological discomfort due to the disorder. This shows that quality of life is vital for health and well being in persons with type 2 DM.

E.O Bixler et al in their study observed a strong association between EDS and BMI. Until the overweight threshold was reached, the BMI specific prevalence of EDS remained constant. Beyond this BMI threshold, the prevalence of EDS increased in an exponential manner.⁴⁰ This is in accordance with the present study. In the group of BMI (18-24.9) 31.2% of patients were with EDS and 68.8 % of patients were without EDS. In the group of BMI(25-29.9), 62.3% of patients were with EDS and 37.7% of patients were without EDS. In the group of BMI \geq 30 84.2% of patients were with EDS and 15.8% of patients were without EDS. Abdulbari Bener et al in their study found that obesity was significantly higher in diabetic females with higher chances of falling sleep during day time (51.7%) than in males (39.3%).³⁵ In the present study, among the subjects with EDS 40% of males and 56.4% of females were having BMI in the range of 25-29.9 (overweight) and 22.5% of males and 17.9% of females were having a BMI (obese). Physical activity was significantly less in diabetic females (38.6%) compared to men (50.2%).³⁶ This result is also in accordance with the

present study. In the group leading a sedentary lifestyle 59.5% were with EDS and 40.5% were without EDS. It clearly indicates a strong association of EDS with physical activity. Among the subjects with EDS, 77.5% of males and 89% of females were leading a sedentary life style.

Sleep efficiency declines with increasing age. With increasing age the homeostatic sleep mechanism weakens affecting both night time sleep efficiency and day time sleep propensity.⁴⁰ The majority of patients with EDS were within the age group of 56-65 (36), followed by 46-55 (25), followed by 36-45 (14), and followed by 25-35 (4).

Foley D et al in their study reported that that males and females with sleep disturbance were more likely to be obese to have a history of hypertension.¹² 36.7% of patients with EDS had hypertension. Hence the alarming rise in sleep loss among female population is due to rising problem of obesity and chronic diseases.

Conclusion

The study findings observed that excessive day time sleepiness is more prevalent in diabetic obese population. Sleep loss varied significantly by gender in diabetic patients. It was more observed in diabetic females than males. Obesity was also more common in diabetic women than in men while physical activity was less in women compared to men. A sedentary lifestyle has shown to enhance excessive day time sleepiness in diabetic patients. Difference was observed in the ESS scores between both genders. Sleep disturbance were seen more common in older age group of 55-65. Most of the patients observed with EDS had hypertension as a co-morbid disease.

Sleep exerts marked modulatory effects on glucose metabolism by influencing the balance and levels of hormones, including leptin, ghrelin, insulin and cortisol, in addition to the activity of the sympathetic nervous system (SNS). These physiological defence mechanisms alter glucose tolerance and sensitivity to insulin and leptin, impairing appetite regulation. Therefore, when chronically activated, these stress responses favour the development of obesity and T2DM. In addition, shorter sleepers have more opportunity for food consumption and tend to be more fatigued and less active during the day, which favour obesity. On the other hand, obesity itself, especially when central, leads to OSA, to inflammatory processes, and to the development of T2DM. Thus, we may conclude that it is difficult to isolate a cause and an effect from this neuro-endocrine-metabolic misbalance, since sleep characteristics (disorders or duration) may impact neurological and endocrine systems to promote obesity and T2DM, while obesity



and T2DM may impact sleep as well. Therefore, while obesity and T2DM are favoured and aggravated by short sleep duration or sleep disorders, sleep may be impaired by these two widespread metabolic conditions.

Thus sleep quality is seen poor in diabetic patients. To improve sleep quality, a clinical pharmacist can help patients to follow good sleep habits. The pharmacist should well explain to patients about the proper use of sleep medications if needed, tips to get good night sleep and the importance of limiting social habits like consumption of tea/coffee, alcohol and smoking habits which increase the quality of sleep of the patients and reduce the chances of excessive daytime sleepiness.

Acknowledgement

The author is indebted to the colleagues of the Department of Pharmacy Practice, KMCH, Coimbatore, Tamil Nadu, India.

References

- 1) Group a. The American Academy of Sleep Medicine: The international Classification of Sleep disorders In Group, ed. Revised. Diagnostic and coding Manual. Rochester NY: Davies Printing. Co; 1997
- 2) Pagel J.F. Excessive Day Time Sleepiness. American Family Physician. 2009 Mar; 79(5):391-396
- 3) Sicree R J, Shaw J, Zimmet P. The global burden, diabetes and impaired glucose tolerance. In: IDF diabetes atlas. 4th ed., Brussels: International Diabetes Federation. 2009. 1-105
- 4) Knutson KL, Ryden AM, Mander BA, Van Cauter E. Role of Sleep duration and quality in the risk and severity of type 2 diabetic mellitus. Arch Intern Med 2006; 166:1768-1774
- 5) Trento M, Broglio F, Riganti F, Basile M, Borgo E, Kucich C, et al. Sleep abnormalities in type 2 diabetes may be associated with glycemic control. Acta Diabetol 2008; 45:225-229
- 6) West SD, Nicoll DJ, Stradling JR. Prevalence of obstructive sleep apnea in men with type 2 diabetes. Thorax 2006; 61:945-950.
- 7) Villa MP, Multari G, Montesano M, Pagani J, Cervoni M, Midulla F, et al. Sleep apnea in children with diabetes mellitus: effect of glycemic control. Diabetologia 2000; 43:696-702.
- 8) James PT. Obesity: the worldwide epidemic. Clin Dermatol 2004; 22:276-280.
- 9) Chaput JP, Despre's JP, Bouchard C, Astrup A, Tremblay A. Sleep duration as a risk factor for the development of type 2 diabetes or impaired glucose tolerance: analyses of the Quebec Family Study. Sleep Med 2009; 10:919-924.
- 10) Van Cauter E, Spiegel K, Tasali E, Leproult R. Metabolic consequences of sleep and sleep loss. Sleep Med 2008; 9: S23-28
- 11) Pillar G, Shehadeh N. Abdominal fat and sleep apnea: the chicken or the egg? Diabetes Care 2008; 31(Suppl. 2): S303-309
- 12) Foley D, Ancoli-Israel S, Britz P, Walsh J. Sleep disturbances and chronic disease in older adults: results of the 2003 National Sleep Foundation Sleep in America Survey. J Psychosom Res 2004; 56: 497-502
- 13) Bonnet MH, Arand DL. We are chronically sleep deprived. Sleep; 1995; 18: 908-911
- 14) Resnick HE, Redline S, Shahar E et al, Diabetes and Sleep disturbances: Findings from the Sleep Heart Study. Diabetes Care; 2003; 26: 702-709
- 15) Leproult R, Holmback U, Van Cauter E, Marked decrease in insulin sensitivity following one week of partial sleep deprivation with or without circadian misalignment. Diabetes 2006; 55: A323-A324
- 16) Spiegel K, Leproult R, Van Cauter E, Impact of Sleep debt on metabolic and endocrine function. Lancet 1999; 354: 1435-1439
- 17) Excessive day time sleepiness [online]. Available from-Wikipedia, the free encyclopedia. http://en.wikipedia.org/wiki/Excessive_daytime_sleepiness.
- 18) Barone M.T.U, Menna-Barreto. L, Diabetes and Sleep: A complex cause- and- effect relationship. Diabetes Research and Clinical Practice 2011; 91:129-137
- 19) Spiegel K, Knutson K, Leproult R, Tasali E, Van Cauter E. Sleep loss: a novel risk factor for insulin resistance and type 2 diabetes. J Applied Physiology 2005; 99:2008-2019.
- 20) Mallon L, Broman JE, Hetta J. High incidence of diabetes in men with sleep complaints or short sleep duration: a 12-year follow-up study of a middle-aged population. Diabetes Care 2005; 28:2762-2767.
- 21) Gonzalez-Ortiz M, Martinez-Abundis E, Balcazar-Munoz BR, Pascoe-Gonzalez S. Effect of sleep deprivation on insulin sensitivity and cortisol concentration in healthy subjects. Diabetes Nutr Metab 2000; 13:80-83.
- 22) Gangwisch JE, Heymsfield SB, Boden-Albala B, Bujis RM, Kreier F, Pickering TG, et al. Sleep duration as a risk factor for diabetes incidence in a large US sample. Sleep 2007; 30:1667-1673.
- 23) Nakajima H, Kaneita Y, Yokoyama E, Harano S, Tamaki T, Ibuka E, et al. Association between sleep duration and hemoglobin A1c level. Sleep Med 2008; 9:745-752.
- 24) Yaggi HK, Araujo AB, McKinlay JB. Sleep duration as a risk factor for the development of type 2 diabetes. Diabetes Care 2006; 29:657-661.
- 25) Gronfier C & Brandenberger G. Ultradian rhythms in pituitary and adrenal hormones: their relations to sleep. Sleep Med Rev 1998; 2: 17-29
- 26) Steiger A. Sleep and endocrinology. J Intern Med 2003; 254: 13-22.
- 27) Van Cauter E. Endocrine physiology. In Kryger M, Roth T & Dement WC (eds.). Principles and practice of sleep medicine. 4th ed. Philadelphia: Elsevier-Saunders, 2005, pp. 266-282.
- 28) Sakurai T. The neural circuit of orexin (hypocretin): maintaining sleep and wakefulness. Nat Rev Neurosci 2007; 8: 171-181.



- 29) de Lecea L & Sutcliffe JG. The hypocretins and sleep. *FEBS J* 2005; 272: 5675– 5688.
- 30) Vgontzas AN, Papanicolaou DA, Bixler EO, Kales A, Tyson K, Chrousos GP. Elevation of plasma cytokines in disorders of excessive daytime sleepiness: Role of sleep disturbance and obesity. *Journal of Clinical Endocrinology and Metabolism* 1997;82(5):1313-1316
- 31) Pickup JC. Inflammation and activated innate immunity in the pathogenesis of type 2 diabetes. *Diabetes Care* 2004; 27:813-823
- 32) Dixon JB, Dixon ME, Anderson ML, Schachter L, O'Brien PE. Daytime sleepiness in the obese: Not as simple as obstructive sleep apnea. *Obesity*. 2007;15(10):2504-2511.
- 33) Johns MW. Daytime sleepiness, snoring, obstructive sleep apnea -the Epworth Scale. *Chest* 1993;103:30-36
- 34) Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991;14:540-545
- 35) Bener A, Al-Hamaq A.O.A.A. Sleep quality and excessive daytime sleepiness in a Arab diabetic population. *Biomedical Research* 2010;22(1): 333-340.
- 36) Suarez EC. Self reported symptoms of sleep disturbance and inflammation, coagulation, insulin resistance and psychosocial distress : Evidence for gender disparity, *Brain Behav Immun*, 2008;22:960-968
- 37) Kawakami N, Takatsuka N, Shimizu H : Sleep disturbance and onset of type 2 diabetes, *Diabetes Care*, 2004;27:282-283
- 38) Walker RD, Durazo-Arvizu R, Wachter B, Gopalsami C, Prospective difference between male and female patients with sleep apnea, *Laryngoscope*, 2001;111:1501-1505
- 39) Meisinger C, Heier M, Loewel H: MONICA/KORA Augsburg Cohort study Sleep disturbances as a predictor of type 2 DM in men and women from the general population, *Diabetologia*, 2005;48:235-241
- 40) Bixler E.O, Vgontzas A.N, Lin H.-M, Calhoun S.L, Vela-Bueno A and Kales A, Excessive daytime sleepiness in a general population sample: The role of Sleep apnea, age, obesity, diabetes and depression. *The journal of Clinical Endocrinology & Metabolism* 2005;90(8): 4510-4515

AUTHORS' CONTRIBUTIONS

Authors contributed equally to all aspects of the study.

PEER REVIEW

Not commissioned; externally peer reviewed

CONFLICTS OF INTEREST

The authors declare that they have no competing interests