Sleep Disorders in Individuals With High Risk for Diabetes in Indian Population

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Abstract
Background: Sleep restores physiology and neurochemical components of our body and is essential for physical and mental health. Sleep disorders (SDs) are associated with insulin resistance and metabolic disorders. The association between SDs and diabetes needs to be understood in the Indian population.
Purpose: The purpose was to investigate the association between SD and diabetes in the Indian population.
Methods: As a part of nationwide Niyantra Madhumeha Bharata Abhiyan-2017 (NMB-2017), a cross-sectional study was conducted and data was collected from seven zones of India, after screening through the Indian Diabetes Risk Score (IDRS). The sleep quality was assessed on a scale of 1 to 4 (very good = 1, very bad = 4). The time taken to fall asleep (sleep latency) was assessed on a scale of 0 to 5 (“0” = nil and “5” = >1.5 h). Stress was assessed by the perceived stress scale.
Results: Bad sleep quality was positively (odds ratio 1.055, CI [1.001, 1.113], and P < .01) associated with self-reported known diabetes. Increased sleep time (sleep latency) was associated significantly with IDRS high risk (odds ratio 1.085, CI [1.008, 1.168], and P = .01), with an average sleep latency (maximum range 5 [>1.5 h], mode 2 [10 to 30 min]) minutes. Moderate stress was significantly associated with bad sleep quality (odds ratio 1.659).
Conclusion: A positive association of bad sleep quality and stress with diabetes, and an increased sleep latency in the IDRS high-risk population point to the role of modifiable risk factors. Behavioral modification and stress reduction by using yoga may be beneficial in the better management of diabetes.

Keywords
Sleep quality, diabetes, Indian diabetes risk score, stress

Introduction
Sleep is a biological process involving both physiological and neurochemical aspects of life.1,2 Circadian rhythm and sleep homeostasis influence each other and regulate the sleep–wake cycle.3 Sleep can be considered as a health indicator.4 The quality of sleep decides the physical and mental wellbeing of an individual,3 especially slow-wave sleep or deep sleep has been demonstrated to be practically identified with optimal recovery and neuroplasticity.5–6 Seven to eight hours of night sleep is medically considered to be good enough to refresh the body.
Sleep promotes and performs important restorative functions for body homeostasis.2 Sleep deprivation or inadequate sleep is directly associated with sleep disorders (SDs) and other health issues, such as mood disturbance,7 impaired memory,8 metabolic disorders like diabetes, obesity,9 and hypertension.10 It is estimated that approximately

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20% to 30% of the general population has one or the other type of SD.\textsuperscript{11}

It has been seen that common health conditions such as diabetes, cardiovascular, neurological, urinary, or respiratory disorders are some of the major SD-associated comorbidities.\textsuperscript{12} Low quality of sleep has been reported in 38.4% of diabetes patients. Homeostasis model assessment of insulin resistance showed a strong association of obstructive sleep apnea (OSA) with high insulin resistance, excessive body weight or obesity, and hypertension.\textsuperscript{13} Another study showed a lack of sleep or fragmented sleep leads to insulin resistance, gain in body weight, type 2 diabetes,\textsuperscript{14,15} and hypertension.\textsuperscript{16,17} The duration of sleep also plays a major role as a diabetes risk factor. Tan et al.\textsuperscript{18} in their review on the effect of sleep duration on diabetes individuals showed that both short-duration sleep (≤5 and 6 h/night) and long-duration sleep (>8 h/night) are detrimental to diabetes individuals.\textsuperscript{19,20}

India, the second-most populous country, reports around seven million new diabetes patients every year, and SDs are common amongst these patients.\textsuperscript{21} Previous studies show that type 2 diabetes mellitus (DM) patients have a higher prevalence of insomnia, increased daytime sleep, and increased rapid eye movement sleep timing. OSA and DM are common amongst the aged and obese individuals. Both OSA and DM are associated with a higher risk of developing cardiovascular complications, resulting in increased morbidity and mortality.\textsuperscript{22} Earlier studies on short sleep or disturbed sleep suggest impaired glucose tolerance in healthy individuals.\textsuperscript{22} However, an association between SDs and diabetes is poorly understood in the Indian population. Hence, our study explored the prevalence of SDs in individuals with a high risk for diabetes, based on Indian Diabetes Risk Score (IDRS) which is a validated simple screening tool used to detect undiagnosed individuals with DM or those at a higher risk of developing DM.\textsuperscript{23}

**Figure 1. Trial Profile**

| Phase 1 3 months | Level 1 | Screening forms with IDRS and Known DM | 1,62,330 |
|------------------|---------|---------------------------------------|----------|
| IDRS high risk   | IDRS moderate risk | IDRS low risk |
| Rural-77,870 (48%) | Urban- 84,360 (52%) |
| Rural 24,096 (48%) | Level 2 assessment (blood test) | 50,199 |
| Urban 26,103 (52%) |
| Self-reported DM | Invited for intervention | High Risk 42,738 |
| 7,461 |
| Reasons for no response |
| a. Time constraints: out of town for business |
| b. Weather: Snowfall J&K, Hot(>45°C) - Odisha |
| c. Heavy rains: Karnataka, Maharashtra |
| d. Political: State election-UP |
| e. Agitation: Road blockages Manipur |
| f. Not interested in yoga |
| Rural-6,571 (40.1%) | Detailed data in high risk group 16,383 |
| Urban- 9,812 (59.8%) |
| Analyzed for sleep factor 16,383 |
Methods

Study Design
As a part of nationwide trial, the data was collected from seven zones of India (east, west, central, north, northeast, northwest, and south) in 2017 (the details have been published in methodology of our part 1 paper). In short, the sampling process was divided into seven levels. With the help of 1,200 volunteers for diabetes movements, 35 senior research fellows, 2 research associates, and 7 zonal coordinators, this cross-sectional survey was completed. IDRS was used to identify high-risk individuals.

Participants
A total of 1,62,330 subjects [rural, 77,870 (48%); urban, 84,360 (52%)] were screened. Of these, 50,199 subjects [rural, 24,096 (48%); urban, 26,103 (52%); IDRS high risk, 42,738; self-reported DM, 7,461] with IDRS high risk and self-reported DM were selected for detailed investigations. Data for a sleep factor analysis was acquired from 16,383 subjects [rural, 6,571 (40.1%); urban, 9,812 (59.8%)].

Outcome Measures
An initial survey was done to screen the participants by the IDRS to identify high-risk individuals. IDRS consists of four parameters: age, family history, physical activity, and waist circumference. A score of 0 to 30 is considered as low risk, 30 to 50 moderate risk, and ≥60 as high risk.

Sleep Assessments: To measure sleep habits, there was a sleep questionnaire comprising six questions. Of these, the two most important questions were taken for the present sleep analysis.

(a) Sleep quality: During the past month, how would you rate your sleep quality overall? (Score 1, very good; 2, fairly good; 3, fairly bad; and 4, very bad.)

(b) How long has it taken you to fall asleep each night? (None 0; at least 10 min, 1; 10 to 30 min, 2; 30 min to 1 h, 3; 1 to 1.5 h, 4; and >1.5 h, 5.)

Stress: Stress was measured by using an analog scale questionnaire which contained six questions related to work, family, health, financial, social, and other stress. It measured levels of stress from 0 (none) to 10 (severe).

Perceived Stress Scale: Perceived stress was measured by using the perceived stress scale which contains 10 questions related to feelings and thoughts in the last month. It was associated with internal consistency (Cronbach’s α) of 0.82 and convergent validity of 0.64–0.71.25

Statistical Analysis
Data was uploaded via Mobile Apps by trained field personnel under the supervision of senior research fellows. The data set was analyzed using the SPSS software for biostatistical analyses.

To calculate the odds ratio, ordinal regression was implemented; reference was set to sequential contrast for all ordinal variables. For known diabetes and known hypertension, unknown diabetes and unknown hypertension were the references, respectively. For IDRS high risk, IDRS low risk was the reference category. For obesity, normal was the reference. Regression was done to analyze the association of overall stress with overall sleep quality and that of overall depression with sleep quality.

Ethical clearance was obtained from the ethical committee of Indian Yoga Association.

Results
Table 1 represents the demographic details of 16,383 participants; the mean age of the participants was 48 years. The distribution of participants with respect to their location was as follows: urban cluster constituted 60%, and rural 40%, females constituted 53% of the study population, while males constituted 47%. The average body mass index (BMI) of the participants was 25.90, which suggest that the participants fall under the overweight category based on BMI estimates. Overall fasting blood glucose (FBG) was 117.1 mg/dL and glycated hemoglobin (HbA1c) was 6.33%.

Table 2 represents the sleep quality and sleep latency in different groups; 1.055 (1.001–1.113) is significantly associated with the status of known diabetes. Increased sleep time/sleep latency is associated significantly with IDRS high risk, with an odds ratio of 1.085 (CI [1.008, 1.168]). Bad sleep quality and increased sleep time are associated nonsignificantly with obesity and the status of known hypertension.

In Table 3, we can see that the moderate stress was significantly associated with bad sleep quality, but was not significantly associated with sleep latency/sleep time. Although moderate depression and medium perceived stress were associated positively with sleep quality, they were not significant.

Table 1. Demographic Characteristics of Participants

| Total       | N   | 16,383 |
|-------------|-----|--------|
| Age Mean (SD) |       | 47.7 (12.5) |
| Area Rural | 6,571 (40.1%) |
| Urban       | 9,812 (59.9%) |
| Gender Male | 7,700 (47.0%) |
| Female      | 8,683 (53.0%) |
| Total       | 16,383 |
| BMI Overall | 25.90 (13.80) |
| FBG         | 117.1 (54.50) |
| HbA1c       | 6.33 (1.74) |
Table 2. Sleep Quality and Sleep Latency in Different Groups

| Variables            | Sleep Quality    | Significance | Sleep Time/Sleep Latency | Significance |
|----------------------|------------------|--------------|--------------------------|--------------|
| Known diabetes       | 1.055 (1.001–1.113)* | 0.04         | .962 (0.919–1.006)       | 0.09         |
| Known hypertension   | 1.019 (0.968–1.072) | 0.46         | 1.015 (0.972–1.060)      | 0.49         |
| IDRS high risk       | 1.072 (0.982–1.170) | 0.12         | 1.085 (1.008–1.168)*     | 0.03         |
| Obesity              | 1.005 (0.939–1.076) | 0.88         | 1.009 (0.953–1.068)      | 0.76         |

*How long has it taken you to fall asleep each night? 
*During the past month, how would you rate your sleep quality overall? 

Note: 1 = very good; 2 = fairly good; 3 = fairly bad; 4 = very bad. 
Comment: There was significant predictive association between diabetes, high diabetes.

Table 3. Association Between Sleep Quality, Stress, and Depression

| Sleep Factor          | Parameter                  | Significance | Exp(B)  | 95% Wald Confidence Interval for Exp(B) |
|-----------------------|----------------------------|--------------|---------|----------------------------------------|
|                       |                            |              |         | Lower | Upper |
| Sleep time            | Minimum stress             | .368         | 1.342   | .708 | 2.544 |
|                       | Moderate stress            | .120         | 1.659   | .877 | 3.142 |
|                       | Minimal depression         | .909         | .953    | .417 | 2.180 |
|                       | Mild depression             | .913         | .955    | .422 | 2.161 |
|                       | Moderate depression        | .710         | 1.171   | .509 | 2.693 |
|                       | Moderately severe depression| .875         | .934    | .400 | 2.185 |
|                       | Perceived stress low       | .895         | .920    | .265 | 3.193 |
|                       | Perceived stress medium    | .858         | .893    | .260 | 3.072 |
| Sleep quality         | Minimum stress             | .296         | 1.417   | .737 | 2.727 |
|                       | Moderate stress            | .043         | 1.965   | 1.023 | 3.776 |
|                       | Minimal depression         | .935         | 1.036   | .449 | 2.386 |
|                       | Mild depression             | .716         | 1.165   | .511 | 2.659 |
|                       | Moderate depression        | .644         | 1.219   | .526 | 2.826 |
|                       | Moderately severe depression| .944         | 1.031   | .437 | 2.431 |
|                       | Perceived stress low       | .834         | 1.134   | .349 | 3.688 |
|                       | Perceived stress medium    | .681         | 1.278   | .397 | 4.110 |

Discussion

This pan-India data that used two general questions to assess the previous month’s sleep quality and sleep latency of the participants revealed a significant positive association of sleep quality and sleep latency with known diabetes and IDRS high diabetes risk, respectively. It was a noninterventional study. So, there is no control group. We have taken nondiabetics to compare diabetic subjects. We have done the regression analysis, and the results showed that moderate stress was significantly associated with poor sleep quality, but not associated with sleep latency.

Earlier studies showed that stress is significantly associated with the bad quality of sleep.26,27 Our study showed a significant association between moderate stress and poor sleep quality.

A previous study showed complications and durations of diabetes can influence the quality of sleep and depression in a diabetes population.28 In our study, we checked the association of sleep quality with depression and perceived stress. Even though it shows a positive association, it was not significant.

A cross-sectional study on 332 Gujarati subjects (between 13 and 20 years of age) showed that inadequate sleep does not affect the blood glucose levels in adolescents.29 That study was on adolescents, but our study was on adults; this seems to point out that although insufficient sleep does not affect the blood glucose level of adolescents, it may affect the blood glucose level of adults. Another cross-sectional study on 1,258 subjects (Indian = 855, Malay = 403) between 40 and 80 years of age showed that the abnormal sleep duration is associated with the diabetic kidney disease.30 Another review showed that poor sleep quality and short sleep duration were associated with cardiometabolic risk and adverse effects on diabetes, hypertension, obesity, and in turn some epigenetic changes.32–34 Our study showed similar results with a significant association between poor sleep quality and known diabetes. Our study did
not show any significant association between sleep quality and obesity or sleep quality and hypertension.

This is the first study from the Indian population consisting of a large sample size where an association between sleep factors and diabetes risk has been demonstrated.

In our earlier studies, we have examined various markers for different neurodegenerative disorders such as age-related macular degeneration,\textsuperscript{35-40} amyotrophic lateral sclerosis,\textsuperscript{41,42} and Parkinson’s disease,\textsuperscript{43} and described various treatment strategies for the brain and nervous system,\textsuperscript{44} and retinal degeneration.\textsuperscript{45} However, in the recent study, we did not include any biomarker to examine the sleep factor. As sleep is associated with our brain function, therefore further studies can be undertaken to examine the correlation between the neurodegenerative diseases and sleep factor in this diabetic population. Alzheimer’s disease and Brahmi (Bacopa monniera) as one of the treatment modalities for it have also been discussed in our previous review paper.\textsuperscript{46,47} An association between memory loss, sleep deficits, and the corresponding interventions such as yoga and Brahmi can add a new dimension to the research in the diabetic population. Our earlier literature has also provided evidence for the correlation between oxidative stress and neurodegenerative disorders\textsuperscript{48} and stem cell transplantation for neural disorders.\textsuperscript{49} Stress biomarkers and a sleep factor analysis for a larger diabetic population are thus warranted in future. We have developed different animal models for various diseases such as Alzheimer’s disease,\textsuperscript{50} and amnesia,\textsuperscript{51,52} and also discussed various animal models of neural metabolism for developing the treatment modalities.\textsuperscript{53} For mechanistic studies, the animal model resources can be used.

\section*{Limitation of the Study}

The limitation of the study is that a standardized validated questionnaire was not used to assess the sleep factor. So, we were unable to do the domain analysis of different variables of sleep.

\section*{Conclusion}

Poor sleep quality is associated with known diabetes, and increased sleep latency is associated with a high diabetes risk. Bad sleep quality or SD can be an indicator of diabetes, and increased sleep latency can be an indicator of IDRS high risk. However, further study is required by using a comprehensive sleep questionnaire to confirm the results in the Indian diabetes population.

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\section*{Author Contribution}

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KM & RN & AA & SSP & AS & RSK & SP \\
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Concept of manuscript & ✓ & ✓ & ✓ & ✓ & ✓ & ✓ \\
Design & ✓ & ✓ & ✓ & ✓ & ✓ & ✓ \\
Definition of intellectual content & ✓ & ✓ & ✓ & ✓ & ✓ & ✓ \\
Literature search & ✓ & ✓ & ✓ & ✓ & ✓ & ✓ \\
Data acquisition & ✓ & ✓ & ✓ & ✓ & ✓ & ✓ \\
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**Declaration of Conflicting Interests**
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Ethical Statement**
The study was conducted after obtaining the ethical clearance from the Institutional Ethics Committee (IEC) of Indian Yoga Association (IYA). Written informed consent in their native language was taken from every individual before physical/biochemical assessment. IEC registration no: CTRI/2018/03/01280.

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