Association of sleep duration and quality with atherosclerosis:

A comparative study between diabetic and non-diabetic individuals

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ABSTRACT

Tackling the global burden of diabetes and its complications continue to be a challenge. Emerging risk factors such as poor sleep have been reported to contribute significantly to this. A cross-sectional study was conducted amongst 105 individuals aged between 25 to 45 years in a South Indian population aiming to find an association between the quality and duration of sleep with atherosclerosis in diabetic and non-diabetic individuals. The sleep quality was assessed using the PSQI questionnaire, and the population was divided into 4 groups based on the sleep duration (long, normal, short, very short). The degree of atherosclerosis was measured by using the carotid intima-media thickness (CIMT). The data was analysed using SPSS Software version 20. Descriptive statistics, Chi-Square test and Independent t-test were employed. 52.4% of the subjects were diabetic individuals and 47.6% were non-diabetic individuals. A higher percentage of individuals in the diabetic group exhibited a poor quality of sleep and shorter sleep duration as compared to the non-diabetic group. The former also had a higher mean CIMT value when compared to the non-diabetic individuals. The difference between the mean CIMT values was found to be significant. A significant association was observed between the CIMT and PSQI score as well as the CIMT and average sleep duration in the diabetic population. However, amongst the non-diabetics, no such association between the CIMT and PSQI score was present, although a significant association was noted between the CIMT and average sleep duration. Shorter sleep durations may be associated with a higher risk for
atherosclerosis in diabetic as well as non-diabetics individuals. Poor sleep quality is a potential risk factor for atherosclerosis.

**Keywords:** Atherosclerosis; CIMT; diabetes; sleep duration; sleep quality; PSQI


**Introduction**

Diabetes is a chronic metabolic disease that has been given the status of a modern-day epidemic. According to a report by the WHO, it is estimated that over 400 million people worldwide currently suffer from this disease. In 2012, the global burden consisted of 1.5 million deaths being directly caused by diabetes and it was the eighth leading cause of death among individuals of both genders [1].

After decades of extensive research in the field of diabetes, it is now a well-established fact that the presence of diabetes accelerates atherosclerosis due to vascular dysfunction, caused by the underlying metabolic abnormality[2]. This may in turn precipitate cardiovascular complications in affected individuals.

With the advent of technology and fast-paced lifestyles, there has been an increasing trend of poor sleeping habits among populations of all ages. Several studies conducted previously have identified a relationship between the duration of sleep and the overall morbidity and mortality of individuals[3,4]. Both shortened as well as prolonged sleep durations have been linked to an increased incidence of atherosclerosis and cardiovascular events[5,6]. According to the National Sleep Foundation, USA the daily recommended sleep duration for an adult is 7-8 hours. Values below and above this range would be characterized as short and long sleep durations respectively[7]. Poor sleep is now an emerging risk factor for the development of non-communicable diseases (NCDs). Certain significant health conditions including diabetes mellitus, cardiovascular disease (CVD), hypertension, stroke, dyslipidaemia etc. can in fact be attributed to the duration and quality of sleep[8,9]. The normal atherosclerotic process in every person begins to occur during childhood and adolescence and continues to progress for years together[10]. However, the earliest changes can be detected due to a structural change in the blood vessels, most commonly in the carotid arteries. The carotid intima-media thickness (CIMT) has been identified as a surrogate marker for sub clinical atherosclerosis and this can be measured using a non-invasive test, namely B mode ultrasound. It has been reported that the CIMT is an independent predictor of future cardiovascular events apart from traditional risk factors[11-13].
Complications such as coronary artery disease and stroke occur due to a complex interplay between various risk factors. In diabetic individuals who are predisposed to these, identifying the risk factors and tackling them individually is of utmost importance. The fact that a simple physiological process, namely sleep plays such a crucial role in the progression of atherosclerosis, suggests the need for intervention in the form of lifestyle modification.

**Materials and Methods**

A cross-sectional study was conducted at a tertiary care teaching hospital in Southern India.

Written informed consent was taken from the participants of the study after providing detailed information regarding the purpose and potential benefits of the study. The forms were given in the local vernacular language for better patient understanding. Strict confidentiality was maintained.

**Sample Size and Selection Criteria:** A total of 105 participants were included in the study consisting of 55 diabetic persons and 50 non-diabetic persons using simple convenient sampling.

The inclusion criteria consisted of normal, healthy individuals between 25-45 years of age who were willing to participate in the study and newly diagnosed patients with type 2 diabetes mellitus or diabetic patients currently on medications between 25-45 years of age willing to participate in the study.

This study excluded participants aged <25 and >45 years of age, with type 1 diabetes mellitus, diagnosed with obstructive sleep apnoea (OSA), diagnosed with sleep disorders, on treatment for insomnia, on sedative drugs.

**Study Setting and Population**

The study subjects consisted of individuals aged between 25-45 years attending the General Medicine and Diabetology OPD of the hospital.

Demographic details such as Name, Age, Sex, Occupation etc. were collected.

(i) **Categorisation of Participants Based on The Presence/Absence of Type 2 Diabetes Mellitus**

They were divided into two major groups after being matched for age and sex, based on the presence and absence of diabetes. This was in accordance to the criteria prescribed the American Diabetes Association (ADA) for Type 2 Diabetes Mellitus.\(^{[14]}\)

Routine investigations such as fasting blood glucose, post prandial blood glucose and HbA1C were performed to confirm the presence of diabetes.

(ii) **Assessment of The Quality and Duration of Sleep**
The participants were then administered a standardized questionnaire by the principal investigator using the interview method to assess the quality of sleep of these individuals. The Pittsburgh Sleep Quality Index (PSQI) questionnaire was employed in this regard.

The quality of sleep was determined by the PSQI score which ranged from 0-21, where higher scores denoted a worse sleep quality. A global PSQI score >5 indicated a poor sleep quality. The individuals were then categorized into 4 subgroups based on the duration of sleep namely:

- Very short duration: <6 hours
- Short duration: 6 hours-7 hours
- Regular duration: 7-8 hours
- Long duration: >8 hours

(iii) Measurement of the Carotid Intima-Media Thickness [CIMT]

All the subjects of the study from both groups underwent a B Mode Ultrasound Scan performed by a qualified radiologist to quantify the degree of atherosclerosis based on the Carotid Intima-Media Thickness (CIMT). Intima-media thickness values greater than 0.9 mm (European Society of Cardiology) or over the 75th percentile (American Society of Echocardiography) was considered abnormal. A value higher than the normal range indicated an increased risk for a future cardiovascular event.

Statistical analysis

The data was analysed using SPSS Software version 20. Descriptive statistics, Chi-Square test and Independent t-test were employed.
Results

Out of the 105 participants that were included in the study, 52.4% were diabetic individuals and 47.6% were non-diabetic individuals.

Amongst the diabetic group, 72.7% of the participants demonstrated a poor sleep quality as opposed to 36% of the participants who had a poor quality of sleep in the non-diabetic group. (Fig. 1)

In the diabetic population, 45.45% of the participants had a normal sleep duration (7-8 hours), the remaining showed either very short, short or long sleep durations, the mean sleep duration being 6.64 ± 1.32 hours (Fig. 2, Table 1).

In the non-diabetic population, 52% of the participants had a normal duration of sleep whereas the remaining individuals had very short, short or long sleep durations, the mean sleep duration being 6.9 ± 1.38 hours (Fig. 2, Table 1).

30.9% of the diabetic individuals had a CIMT value >0.9 mm, however only 6% of the non-diabetic population had a CIMT value of >0.9 mm (Fig. 3).

The diabetic individuals had a higher mean CIMT value when compared to the non-diabetic individuals (Table 1). The difference between the mean CIMT values was found to be significant p < .001 (t = 4.799) using the independent t-test. A significant association was observed between the CIMT and PSQI score (p= 0.009) as well as the CIMT and average sleep duration (P=0.006) in the diabetic population using the chi-square test (Table 2).

However, amongst the non-diabetics, no such association between the CIMT and PSQI score (p= 0.266) was present, although a significant association was noted between the CIMT and average sleep duration (p=0.043) (Table 2).

Discussion

The recognition of sleep as a crucial entity in the maintenance of health and wellbeing is a widely regarded concept. The quality and duration of sleep of an individual can be affected by a multitude of factors. In recent times, comorbid illnesses such as diabetes mellitus have been associated with an increasing incidence of poor sleep quality and shortened sleep durations [17,18].
In a study conducted in a diabetic population, 33.6% of the 944 participants were found to have a poor quality of sleep as indicated by their PSQI scores\(^ {18}\). 72.7% of the diabetic individuals in our study showed a similar trend of a poor quality of sleep (Fig. 1).

The complex relationship between poor sleep and diabetes is double-sided, with each having a profound effect on the other\(^ {19}\). The incidence of poor sleep quality in diabetic patients may be accounted for by a number of reasons; either by diabetes primarily or the complications that arise due to it\(^ {20}\).

However, Trento et al in his study demonstrated an association between type 2 diabetes and sleep disruption even without the presence of complications or obesity\(^ {21}\).

Yoda et al also showed that poor glycaemic control was independently associated with impaired sleep, and consequently a decrease in the quality of sleep could possibly be significantly associated with increased carotid intima-media thickness in patients with type 2 diabetes mellitus\(^ {22}\).

Sleep has often been linked to accelerated atherosclerosis. A simple and non-invasive method employed to quantify atherosclerosis is the B-Mode Ultrasound which measures the carotid intima media thickness (CIMT), a surrogate marker for atherosclerosis. 30.9% of the diabetic participants in our study had a CIMT value >0.9 as opposed to the 6% of participants with a CIMT value >0.9 in the non-diabetic population. (Fig.3). This may imply that poor sleep in diabetic individuals can lead to atherosclerosis by complex metabolic, inflammatory and neurohumoral mechanisms in addition to the hastened atherosclerosis contributed by diabetes itself\(^ {23}\).

Several studies have demonstrated a significant relationship between the duration of sleep and increased risk of atherosclerosis. In a study conducted by Wolff et al, it was noted that there was a J-shaped association of sleep duration (5 to 11/12 h) with the carotid intima media thickness. It was also identified that both long as well as short durations of sleep were associated with an increased risk of atherosclerosis\(^ {8,24}\). Comparable results were obtained in a study conducted by Chen et al where a sleep duration of less than 5 hours per night was associated with a higher risk of carotid atherosclerosis\(^ {9}\).

The results of our study suggested a significant association between the CIMT and PSQI score indicative of the sleep quality as well as the CIMT and average sleep duration in the diabetic population. However, amongst the non-diabetics, no such association between the CIMT and PSQI score was present, although a significant association was noted between the CIMT and average sleep duration. The inference that can be drawn is that...
shorter sleep durations are associated with a higher risk of atherosclerosis in both diabetic as well as non-diabetic populations, however more so in the former.

Although there is no singular pathophysiological process that explains the progression of atherosclerosis due to impaired sleep in patients with diabetics, the process in normal individuals is complex and multifactorial\[25\].

Some theories suggest the role of increased oxidative stress which alters the morphology of the arterial vessels along with an amplified inflammatory cell recruitment\[26,27\]. Certain animal models have shown an elaboration of various inflammatory mediators and cytokines\[28\]. Other inflammation-mediated mechanisms include dysregulation of the autonomic nervous system which in turn leads to endothelial dysfunction and atherosclerotic plaque deposition\[29\]. In addition to these, various hormonal and metabolic determinants also contribute toward this extensive and gradual process.

Tackling the global burden of diabetes and its complications pertaining to atherosclerosis still continues to be a challenge. Emerging modifiable risk factors such as poor sleep have been reported to contribute significantly towards the development of atherosclerosis. However, adequate research linking these factors is still lacking. This study attempts to throw light on the importance of cultivating and maintaining good sleep hygiene with the aim of preventing the onset of metabolic diseases such as diabetes and consequently mitigating the risk of potential cardiovascular complications.

**Conclusion**

The presence of diabetes is associated with an impairment in the quality and duration of sleep. Shorter sleep durations may be associated with a higher risk for atherosclerosis in diabetic as well as non-diabetics individuals. Poor sleep quality is a potential risk factor for atherosclerosis.
References


3. Sabanayagam C, Shankar A. Sleep Duration and Cardiovascular Disease: Results from the National Health Interview Survey. Sleep. 2010 Aug 1;33(8):1037–42.


Figure 1: Sleep Quality in the Diabetic and Non-Diabetic populations

<table>
<thead>
<tr>
<th>PSQI Score</th>
<th>Diabetic</th>
<th>Non-Diabetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;5 (Poor Sleep Quality)</td>
<td>40</td>
<td>18</td>
</tr>
<tr>
<td>&lt;5 (Good Sleep Quality)</td>
<td>15</td>
<td>32</td>
</tr>
</tbody>
</table>

TOTAL NUMBER

Figure 2: Sleep Duration (in hours) in Diabetic and Non-Diabetic individuals

Figure 3: CIMT Values (in mm) in diabetic and non-diabetic individuals

Table 1: Mean Attributes: Age (In Years), PSQI Score, CIMT (In mm)

<table>
<thead>
<tr>
<th>ATTRIBUTES</th>
<th>DIABETICS N=55)</th>
<th>NON-DIABETICS (N=50)</th>
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<tbody>
<tr>
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</tbody>
</table>
### Table 2: Association of CIMT (in mm) with Other Variables Among Diabetic and Non-Diabetic Individuals

<table>
<thead>
<tr>
<th></th>
<th>DIABETIC INDIVIDUALS</th>
<th>NON-DIABETIC INDIVIDUALS</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIMT (in mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PSQI SCORE</strong>†</td>
<td>&lt;0.9</td>
<td>&gt;0.9</td>
</tr>
<tr>
<td><strong>p VALUE</strong></td>
<td>6.66%</td>
<td>93.33%</td>
</tr>
<tr>
<td></td>
<td>(N=14)</td>
<td>(N=1)</td>
</tr>
<tr>
<td><strong>&lt;5 Good Sleep Quality</strong></td>
<td>96.8%</td>
<td>3.2%</td>
</tr>
<tr>
<td></td>
<td>(N=31)</td>
<td>(N=1)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.009</td>
<td>0.266</td>
</tr>
<tr>
<td><strong>&gt;5 Poor Sleep Quality</strong></td>
<td>88.88%</td>
<td>11.11%</td>
</tr>
<tr>
<td></td>
<td>(N=16)</td>
<td>(N=2)</td>
</tr>
<tr>
<td><strong>AVERAGE SLEEP DURATION</strong></td>
<td>&lt;0.9</td>
<td>&gt;0.9</td>
</tr>
<tr>
<td></td>
<td>(N=24)</td>
<td>(N=16)</td>
</tr>
</tbody>
</table>

*CIMT: Carotid Intima Media Thickness
†PSQI: Pittsburgh Sleep Quality Index
<table>
<thead>
<tr>
<th>Duration</th>
<th>Percentage 1</th>
<th>Percentage 2</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Short</td>
<td>50% (N=6)</td>
<td>50% (N=6)</td>
<td>0.006</td>
</tr>
<tr>
<td>(&gt;6 hours)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short</td>
<td>46.66% (N=7)</td>
<td>53.33% (N=8)</td>
<td>0.043</td>
</tr>
<tr>
<td>(6-7 hours)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>88% (N=3)</td>
<td>12% (N=3)</td>
<td></td>
</tr>
<tr>
<td>(7-8 hours)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long</td>
<td>100% (N=3)</td>
<td>N=0</td>
<td></td>
</tr>
<tr>
<td>(&gt;8 hours)</td>
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</table>

**Comparison**

- Very Short Duration (>6 hours): 50% vs. 50% (p=0.006)
- Short Duration (6-7 hours): 46.66% vs. 53.33% (p=0.043)
- Normal Duration (7-8 hours): 88% vs. 12%
- Long Duration (>8 hours): 100% vs. N=0