OBSTRUCTIVE SLEEP APNEA
AND
ISCHEMIC HEART DISEASE STUDY

A dissertation submitted to
The Tamil Nadu Dr. M.G.R Medical University, Chennai,
in partial fulfillment of the degree of
M.D. Branch XVII (Respiratory Medicine) Examination

DEPARTMENT OF RESPIRATORY MEDICINE
CHRISTIAN MEDICAL COLLEGE
VELLORE- 632004
TAMIL NADU

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CERTIFICATE

This is to certify that the dissertation entitled **"Obstructive Sleep Apnea and Ischemic Heart Disease"** is the bonafide original work of Dr. Keshavan. V towards the MD Branch-XVII (Respiratory Medicine) Degree examination of the Tamil Nadu Dr.M.G.R Medical University, Chennai to be conducted in April 2014.

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ABBREVIATIONS

1. AHI- Apnea hypopnea index
2. CABG- Coronary artery bypass grafting
3. CAD- Coronary artery disease
4. CPAP- Continuous positive airway pressure
5. CVD- Cardiovascular disease
6. DALY- Disability adjusted life year
7. ESS- Epworth sleepiness scale
8. IHD- Ischemic heart disease
9. ODI- Oxygen desaturation index
10. OSA- Obstructive sleep apnea
11. OSAS- Obstructive sleep apnea syndrome
12. PSG-Polysomnography

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1. ABSTRACT

BACKGROUND:

IHD is the leading cause of mortality and morbidity in the world. OSA has been established as one of the important modifiable risk factors for IHD. However, it is often undiagnosed and therefore, untreated. Though studies linking IHD and OSA have been published among western populations, there is a paucity of data from India about OSA and IHD. This study aims at identifying the relation between OSA and IHD among a cohort of patients diagnosed with IHD.

METHODOLOGY:

This study was a prospective observational study conducted among 70 patients undergoing evaluation for IHD at the Department of Cardiology, CMC Vellore. Data was collected using a standardized proforma. Subsequently, screening for OSA was performed using a portable screening device, the Apnea Link device.

RESULTS:

The prevalence of OSA and OSAS among the study cohort was 75.7% and 18.6% respectively. Nearly 50% of patients with OSA had mild OSA. The prevalence of metabolic syndrome and syndrome Z was 77.1% and 58.6% respectively.
There was a statistically significant association between severity of OSA and severity of IHD based on coronary angiography and also presence of apneic episodes.
Presence of snoring and apneic episodes were found to be important risk factors for development of OSA.

CONCLUSION:

This study is the first study from South Asia that attempts to study the relation between OSA and IHD in a cohort of patients with IHD.
It establishes that OSA is more prevalent among IHD patients as compared to the general population, with a majority of patients having mild OSA. This also reveals the importance of screening for OSA among IHD patients, especially those with a history of snoring and apneic episodes.

2. INTRODUCTION

Ischemic heart disease is one of the leading causes of death worldwide. While it was earlier believed to be more prevalent in the developed nations, recent data has established IHD to be a vitally important public health issue even among developing nations. A study has also demonstrated the increased prevalence of risk factors for IHD among south Asians and a resulting increased prevalence of IHD in this group as compared to other populations. Analysis of data from India also suggests that IHD is currently the leading cause of mortality in this country.

Advances in the knowledge about the etiology, risk factors and pathogenesis of IHD will play a vital role in the management of IHD in the future.

Obstructive Sleep Apnea is characterized by recurrent episodes of either partial or complete airway obstruction that results in fragmented sleep and intermittent hypoxemia. Community based studies done in North India have estimated the prevalence of OSA to be around 9%. Other studies have established the role of OSA as an important risk factor for IHD. However, it frequently remains undiagnosed and untreated in a majority of patients with one study estimating that 93% of women and 82% of men with moderate to severe obstructive sleep apnea remain undiagnosed and subsequently untreated.

Thus, screening for OSA is of vital importance as timely detection and appropriate treatment of underlying OSA may play a role in both fastening the recovery process after an ischemic event and also in the prevention of subsequent recurrence of ischemic events.

Despite the high burden of morbidity and mortality due to IHD in India, there is a paucity of data regarding OSA and IHD. This study aims to identify the relationship between OSA and IHD in a tertiary care hospital in South India.

3.AIM AND OBJECTIVES

AIM:

To examine the relationship between OSA and IHD in a cohort of patients diagnosed with IHD.

OBJECTIVES:

1. To assess the prevalence of OSA
2. To assess the prevalence of OSAS
3. To assess the severity of OSA
4. To assess the prevalence of metabolic syndrome and syndrome Z
5. To study the patterns of sleep disordered breathing
6. To identify the risk factors for development of OSA
7. To study the relationship between OSA and:
    a. Severity of IHD based on coronary angiography
    b. LV systolic function
    c. Body Mass Index
    d. Waist Circumference
    e. Neck Circumference

4.REVIEW OF LITERATURE

4.01 The Global Burden of IHD

IHD is the leading cause of morbidity and mortality in the world. (1)(2)(3)(4)While the prevalence was initially estimated to be higher in high income countries, recent data suggests that it is a major public health concern even among middle and low income countries.(5)

It has also been established that south Asians have a higher prevalence of risk factors for IHD, as compared to other parts of the world and this results in a higher prevalence among this population. (6)

4.02 Mortality in IHD

Data from the WHO from 2008, estimated that IHD is the single largest cause of death worldwide causing 7,249,000 deaths and accounting for 12.7% of total global mortality.(7)

While IHD related mortality appears to be decreasing in high-income countries, it appears to be increasing in middle and low income countries and currently, middle and low income countries account for nearly 80% of all IHD related deaths.(7)(8)

The Global burden of Disease study estimates that the annual global mortality due to IHD will be over 11 million by 2020.(9)

4.03 The Economic impact of IHD

Data from the UK, published in 2002, estimates the total annual cost related to IHD to be over 7 billion pounds and it was the leading public health problem in terms of economic impact.(10)

Data from the European Union published in 2003, estimates the annual economic impact of IHD on health care costs to be 169 billion euros, which is an average of 3724 euros per capita per year. A total of 62% of this amount was related to direct costs and 21% to productivity loss.(11)

Data from The US published in 2004, estimates the total annual cost related to IHD to be over 40 billion dollars.(12)

4.04 The Indian Scenario

The available data from India also suggests that it is the leading cause of morbidity and mortality. Data published in 2007 estimates that 32% of all deaths were related to IHD.(13)Other studies report that the prevalence of IHD is increasing.(14) The prevalence of IHD in India among general population aged between 35- 64 years is around 10%.(15)

Mortality rates vary from region to region, ranging from 10% of all deaths in Meghalaya to 49% in Punjab. Punjab (49%), Goa(42%), Tamil Nadu (36%) and Andhra Pradesh (31%) have the highest IHD related mortality rates.(16)

The WHO has estimated that India lost 9 billion dollars in national income from premature deaths due to cardiovascular disease in 2005. (17)
These losses are expected to cumulatively lead to 237 billion US dollars over the next 10 years.(17)

The Global burden of disease study suggests that there will be a rise in the number of Disability adjusted life years (DALY) due to IHD in the coming years in India—from a figure of less than 25 million DALYs in 1990, to over 30 million in 2020.(9)
This is alarming, not just because of the increase in prevalence of IHD, but due to the fact that it will increasingly manifest in the economically active groups in society.

4.05 Obstructive Sleep Apnea and Obstructive Sleep Apnea Syndrome

Obstructive sleep apnea is the pathological occurrence of recurrent episodes of apnea and hypopnea during sleep owing to partial or complete pharyngeal obstruction, which leads to oxygen desaturation and sleep fragmentation.(18)(19)

The occurrence of sleep apnea along with functional impairment like early morning fatigue and increased daytime somnolence is termed Obstructive sleep apnea syndrome.(20)(21)

Apnea is defined as an episode of complete cessation of airflow lasting for atleast 10 seconds. Hypopnea is defined as an episode of reduction of airflow (>50%) that results in a decrease of arterial oxygen saturation of atleast 4%.(22)

Apnea-hypopnea index is the ratio of the total number of apneic and hypopneic episodes and the total hours of sleep. Oxygen desaturation index is defined as the ratio of the total number of desaturation events (≥ 4% desaturation) and the total hours of sleep.(23)

4.06 Metabolic syndrome and Syndrome Z

Metabolic syndrome is characterized by the presence of hypertension, dyslipidemia, increased blood glucose levels and abdominal obesity.

The definition of metabolic syndrome as per the National cholesterol education program/ adult treatment panel (NCEP/ATP) III is the presence of any 3 of the following features:(24)

- Abdominal obesity, defined as a waist circumference in men ≥102 cm (40 in) and in women ≥88 cm (35 in).
- Serum triglycerides ≥150 mg/dLor drug treatment for elevated triglycerides.
- Serum HDL cholesterol <40 mg/dL in men and <50 mg/dLin women or drug treatment for low HDL.
- Blood pressure ≥130/85 mmHg or drug treatment for elevated blood pressure.
- Fasting plasma glucose (FPG) ≥100 mg/doll or drug treatment for elevated blood glucose.

Patients with obstructive sleep apnea are often overweight and obese and demonstrate features of metabolic syndrome. Syndrome Z is defined as the co-occurrence of OSA and metabolic syndrome.(25)(26)

Obesity is emerging as a major public health problem worldwide, especially in developing countries like India. A study among adult Indians in urban areas has estimated 30-65% of population to be overweight, obese or have features of abdominal obesity. (27) There is also a difference in the prevalence of metabolic syndrome among urban areas and rural areas, with increased rates in urban areas.(28)

Abdominal obesity has been identified as a risk factor for cardiovascular disease.(29)Studies have also suggested that it may be more important in the pathogenesis as compared to generalized obesity.(12)(30) Commonly used measurements of abdominal obesity include waist circumference and waist-hip ratio. It has also been shown that both these measurements can be used to predict risk of cardiovascular events.(31)

Waist circumference can be measured easily and is less cumbersome as compared to waist-hip ratio. Further, changes in waist-hip ratio may not accurately reflect the extent of obesity or fluctuations in weight. Therefore, waist circumference is preferred over waist-hip ratio as measurement of abdominal obesity.(32)

It has also been proposed that neck circumference may play a role in development of OSA(33) A study published in Turkey established the relationship of neck circumference and metabolic syndrome and OSA(34)

However, data suggests that the current definitions of overweight status and obesity among western population may not be applicable for Asian Indians and that Asian Indians may be at risk for development of obesity related complications at lower levels of Body mass index (BMI) and waist circumference (WC).(35)

Subsequently, in 2009, the consensus statement for diagnosis of obesity, abdominal obesity and metabolic syndrome for Asian Indians was published.(32)

<u>According to this statement, obesity, abdominal obesity and metabolic syndrome were defines as follows:</u>

1. <u>Obesity:</u>

   Normal BMI: 18.0-22.9 kg/m2

   Overweight: 23.0-24.9 kg/m2

   Obesity: >25 kg/m2

2. <u>Abdominal Obesity: (based on waist circumference)</u>

   Men: 90 cm, women: 80 cm

3. <u>Metabolic syndrome: (presence of any 3 of the following):</u>

   - Abdominal obesity, defined as a waist circumference in men ≥ 90cm and in women ≥80 cm.

- Serum triglycerides ≥150 mg/dL or drug treatment for elevated Triglycerides.
- Serum HDL cholesterol <40 mg/dL in men and <50 mg/dL in women or drug treatment for low HDL.
- Blood pressure ≥130/85 mmHg or drug treatment for elevated blood pressure.
- Fasting plasma glucose (FPG) ≥100 mg/dL or drug treatment for elevated blood glucose.

A study that compared OSA among normal weight, overweight and obese individuals revealed that OSA was less common among normal weight individuals as compared to the other groups and that in normal weight individuals, age and gender were predictive factors for OSA.(36)

Data among south Asian population suggests that a majority of patients with OSA are not obese. Compared to the obese OSA patients, they have less prevalence of hypertension and severity of OSA is mild.(37)

While it is well known that obesity is a risk factor for OSA, a recent study has established a positive association between severity of OSA and likelihood of increased BMI over a duration of 5 years.(38)

The relationship between OSA and metabolic disorders is multi-directional and complex.(39)(40)

Obesity is considered to be one of the main causes for OSA.It is also likely that metabolic syndrome may play a role in development of OSA. Conversely, OSA may

be a risk factor for metabolic disorders like hypertensionand insulin resistance.(41)(42)(43)(44)Both Human and animal studies have revealed the relationship between OSA and dyslipidemia, independent of obesity.(45)(46)(47)

Studies in a western population had shown that the prevalence of metabolic syndrome is higher in patients with OSA(48)(49)

Subsequently, data from India has revealed that OSA is independently associated with metabolic syndrome in Asian Indians.(50)(51)

It has also been proposed that OSA may be one of the manifestations of metabolic syndrome.(52)(53)

It has also been shown that metabolic syndrome is significantly associated with cardiovascular disease and can also predict cardiac morbidity and mortality in healthy subjects with a family history of ischemic heart disease.(54)

4.07 Mechanisms of cardiovascular pathogenesis in Obstructive sleep apnea

OSA has been thought to cause cardiovascular disease through a combination of various factors:(55)(56)(57)(58)(59)(60)(61)(62)(63)(64)

- Intermittent hypoxia
- Inflammation
- Oxidative stress that can cause atherosclerosis
- Endothelial dysfunction

Intermittent hypoxia is recognized as the pivotal feature of OSA. This leads to activation of selective inflammatory pathways that cause increased expression of inflammatory cytokines, chemokines and adhesion molecules. This leads to vascular endothelial dysfunction.(65)(66) It has also been shown that OSA is associated with endothelial dysfunction, independent of obesity.(67) It has also been shown that the degree of endothelial dysfunction is dependent on the severity of intermittent hypoxia.(68) Studies among patients with OSA and IHD have estimated the lowest nocturnal saturation values to be between 86.1-86.7%. (21)(69)

It has also been shown that episodes of hypopnea with desaturation of atleast 4% are associated with increased cardiovascular risk and that there is no risk with hypoxic epsiodes of lesser severity.(70) The mechanisms postulated to explain the cardiovascular pathogenesis include myocardial ischemia and cardiac arrhythmias.(71)

Animal models have also proven the role of intermittent hypoxia in increasing susceptibility to myocardial infarction.(72)
This has been shown to occur due to increased oxidative stress.(73)
The oxidative stress has been shown to be due to activation of NADPH oxidase and other free oxygen radicals.(74)

The other molecular biomarkers of endothelial dysfunction include:(75)(76)(77)(78)

- Endothelial nitric oxide synthase (eNOS)

- Tumour necrosis factor- alpha induced protein 3 (TNF- AIP 3)
- Hypoxia inducible factor 1 alpha (HIF 1 alpha)
- Vascular endothelial growth factor (VEGF)
- C-reactive protein (CRP)
- Brain natriuretic peptide (BNP)
- Heart type fatty acid binding protein (h FABP)
- Neopterin

Serum Adiponectin is another protein bio-marker for OSAS and it is shown to significantly decreased among patients with moderate and severe OSAS.(79)

It has been proven that the frequency of non-calcified coronary plaques are higher among patients with OSA than among non-OSA patients.(80) Patients with OSA also have more number of vessels involved and greater severity of stenosis.(81)

Even among patients with no history of IHD, the presence of OSA is associated with increased risk of subclinical atherosclerosis.(82)
Autonomic dysfunction has also been documented in patients with OSA.(83)(84)(85) Abnormally elevated sympathetic activity is implicated in the development of secondary hypertension.(86)

It has been shown that in patients with heart failure and OSA, the degree of daytime somnolence is less as compared to patients with OSA alone. Also, in this group the degree of daytime somnolence does not correlate with the AHI. This is postulated to

be due to increased sympathetic activity in patients with heart failure and OSA.(87)

It has also been shown that the prevalence of OSA increases with age in both sexes and the relative risk has been calculated as 2.2 with each 10 year increase in age.(88)

4.08 Obstructive Sleep Apnea and Ischemic Heart Disease

The Earliest population based studies had documented the relationship between snoring and hypertension and between snoring and IHD.
Subsequently, numerous recent studies have suggested the role of OSA as an important modifiable risk factor for IHD.(89)(90)(91)(92)(93)(94)(95)(96)(97)(98)(99)(100)

Studies done among patients with IHD, estimate the prevalence of OSA to be between 50-65%.(101)(102)(21)(103)
Data also suggests that a majority of patients with OSA and IHD have mild OSA.(21)(103)

Studies showing association between OSA and IHD

Author Name (Reference number in bibliography)	Study group characteristics	OSA prevalence
De Olazabal (100)	N= 17 male patients with IHD proven by angiography	65%
Andreas (101)	N= 47 male patients, 3 female patients with IHD proven by angiography	50%
Mooe (21)	N= 142 male patients with IHD proven by angiography	61%
Mooe (102)	N= 102 female patients with IHD proven by angiography	54%

Studies have also estimated the relative risk for IHD in people with OSA as compared to controls to be between 4.1-4.5.(21)(103)

A meta-analysis estimated the relative risk for IHD in patients with moderate and severe OSA to be 1.40 and 2.65 respectively.(104)

A follow-up study published in 2011 done among patients with acute ST elevation myocardial infarction, showed that the risk of recurrence of ischemic events was higher among patients with OSA and the survival rate was correspondingly lower.(105)

It has also been shown that the severity of OSA is an important predictor of mortality due to cardiovascular events.(106)(107)

The severity of OSA has been found to be associated with increased risk of IHD as shown in the Sleep heart health study.(108)

Single photon emission CT studies have shown impaired ventricular function and decreased coronary reserve among OSA patients as compared to controls.(109)
OSA has also been determined to be an important factor in the development and progression of heart failure.(110)(111)

Conversely, cardiac status has also been found to affect the severity of OSA as established by a recent study conducted in patients with acute myocardial infarction and OSA, wherein an improvement in left ventricular function after the acute event was found to correlate with an alleviation in the sleep apnea.(112)
Even among patients with cardiac failure, treatment of underlying OSA has been shown to associated with better mortality outcomes.(113)

OSA is also associated with increased risk of sudden cardiac death. Nocturnal Hypoxemia, which is an important feature of OSA, has been determined to be an important risk factor for sudden cardiac death.(114)

Thus, it has been suggested, based on available data that all patients with IHD should be screened for OSA and that all patients with OSA should be screened for IHD.(115)(116)

4.09 Screening for Obstructive sleep apnea

OSA is frequently undiagnosed and one study estimated that 93% of women and 82% of men with moderate and severe OSA remain undiagnosed.(117)
A lack of awareness among treating physicians is cited as the primary reason for the deficit in diagnosis and treatment.(118)
Although full polysomnography is the diagnostic test of choice, a screening device that provides reliable information and is simple and easy-to-use would be useful.(119)

The Apnealink device is a single channel screening tool for sleep apnea that measures airflow through a nasal cannula connected to a pressure transducer, thereby providing AHI. Studies comparing the device to Polysomnography, have demonstrated the high sensitivity and specificity of the device.(120)(121)(122)(123)(124)

STOPBANG questionnaire:

The STOPBANG questionnaire is a simple and easy to use screening tool for OSA.
It was initially developed as a screening tool for use among surgical patients. Initial studies had revealed high sensitivity for OSA.(125)

1. Snoring: Do you snore loudly (loud enough to be heard through closed doors)?	
Yes	No
2. Tired: Do you often feel tired, fatigued, or sleepy during daytime?	
Yes	No
3. Observed: Has anyone observed you stop breathing during your sleep?	
Yes	No
4. Blood pressure: Do you have or are you being treated for high blood pressure?	
Yes	No
5. BMI: BMI more than 35 kg m^{-2}?	
Yes	No
6. Age: Age over 50 yr old?	
Yes	No
7. Neck circumference: Neck circumference >40 cm?	
Yes	No
8. Gender: Male?	
Yes	No

High risk of OSA: Yes to ≥3 questions.
Low risk of OSA: Yes to <3 questions.

Other studies have revealed that a STOPBANG score of 5-8 identified patients with high probability of moderate and severe OSA.(126)(127)

Subsequently, The STOPBANG questionnaire was adapted for an Asian population with the BMI cut-off changed to 30 kg/mt^2. (128)

Pictorial Epworth Sleepiness Scale:

The Epworth sleepiness scale was developed in 1991 and has become one of the most

commonly used questionnaires for increased daytime somnolence.(129)

As it is designed to be self-administered, many patients often have difficulty understanding and completing the ESS.

Subsequently, a pictorial version of the ESS was developed and published in 2011. (130)

It was found to be comparable to the standard ESS and a majority of patients found it to be very easy and preferred it over the standard ESS.

A score ≥ 11 is considered to be abnormal.

Pictorial Epworth Sleepiness Scale

Name: _____ Date: ___/___/___ Hospital No: _____ Date of Birth: ___/___/___

In contrast to just feeling tired, how likely are you to doze off or fall asleep in the following situations? Even if you have not done some of these things recently, try to work out how they would affect you.

Use the following scale to choose the most appropriate number for each situation.

Situation (Please tick box)	0 No chance of dozing	1 Slight chance	2 Moderate chance	3 Definitely would doze
Sitting and reading	☐	☐	☐	☐
Watching TV	☐	☐	☐	☐
Sitting inactive in a public place (e.g. Theatre or a meeting)	☐	☐	☐	☐
As a passenger in a car for an hour without a break	☐	☐	☐	☐
Lying down to rest in the afternoon when circumstances permit	☐	☐	☐	☐
Sitting and talking to someone	☐	☐	☐	☐
Sitting quietly after lunch without alcohol	☐	☐	☐	☐
In a car, while stopped for a few minutes in traffic	☐	☐	☐	☐

total sleepiness score / 24

4.10 Grading of severity of Obstructive sleep apnea

The severity of OSA is graded as follows:(119)

Severity of OSA	AHI
1.Mild	5-15
2.Moderate	16-30
3.Severe	>30

4.11Treatment for Obstructive sleep apnea

CPAP was first described as a possible treatment for OSA in 1981 by Sullivan.(131) Subsequently, it has been established that CPAP is the standard treatment for OSA.(132)(133)(134)(135)

Studies have also established that treatment with CPAP reduces risk of future ischemic cardiac events.(136)(137)(138)

The mechanisms postulated to explain the action of CPAP in OSAS are:(139)(140)

1. reduced upper airway resistance due to prevention of sleep induced collapse of the airway
2. stimulation of mechanoreceptors leading to increased airway tone.
3. Role in opposing inflammation, oxidative stress and endothelial dysfunction

Other studies have shown that the application of CPAP would eliminate snoring as well as obstructive sleep apnea.(141)

Subsequent studies have also shown that long term adherence to CPAP is around

70%, which is comparable to therapies for other chronic disorders.(142)(143)(144)(145)

4.12 The Global Scenario

Studies done in general adult populations in the west have estimated the prevalence of OSA to be between 3-7% and OSAS to be between 1-4%.(146)(20)(147)

4.13 The Indian Scenario

A population-based study done in New Delhi, estimated the prevalence of OSA and OSAS to be 9.3% and 2.8% respectively.(148) Another population based study, also from New Delhi, estimated the prevalence of OSA and OSAS to be 13.74% and 3.57%.(149)

A study, done in Orissa, among an urban population, estimated the prevalence of metabolic syndrome to be 33.5%.(150) Another population based study from Jaipur showed the prevalence of metabolic syndrome to be 31.6%.(151) Another population based study from Mumbai has estimated the prevalence of metabolic syndrome to be 19.52%.(152) A hospital based study done among patients with OSA has estimated the prevalence of metabolic syndrome to be 74%.(153)

A study from New Delhi among general population has estimated the prevalence of syndrome Z to be 4.5%.(154) However, hospital based studies among patients with OSA has estimated the prevalence of syndrome Z to be between 65-79%.(155)(153)

4.14 Relevance of this study

OSA has been shown to be a significant independent modifiable risk factor for IHD. There is a paucity of data from India about prevalence of OSA among the general population and among those diagnosed with IHD, as compared to western populations. Thus, any advances in the scientific knowledge about the pathogenesis of OSA and its relationship with IHD will have a vital role in management of IHD in the future.

This is particularly significant, when we consider that:

1. IHD is the most common cause of mortality and morbidity in India
2. Reports suggest that the prevalence of IHD is on the rise
3. In the future, IHD will increasingly occur among the economically active groups in society, which would result in enormous losses to the economy, both in terms of direct and indirect medical expenditure

This study attempts to study the following in a cohort of IHD patients:

1. Prevalence of OSA, OSAS, metabolic syndrome and syndrome Z
2. Severity of OSA
3. Patterns of sleep disordered breathing
4. Relationship between OSA and:
    - Severity of IHD, based on angiography
    - LV systolic function
    - BMI
    - Waist circumference
    - Neck circumference

This is the first study from South Asia that attempts to look at these aspects.

5. MATERIALS AND METHODS

5.1 STUDY DESIGN

This is a prospective observational study done among patients who are undergoing evaluation of Ischemic Heart Disease at The Department of Cardiology, CMC Vellore.

Study Setting:

CMC, Vellore is a 2200 bedded, tertiary care, multi-specialty teaching hospital located in Tamil Nadu, which caters to the demands of not only people from Tamil Nadu, but from all over India.

5.2 IRB APPROVAL

This study was reviewed and cleared by the Institutional Review Board (IRB Min. 7751 dated 06/02/2012) and The Ethics Committee, CMC, Vellore.

5.3 INCLUSION CRITERIA

1. Patients willing to give informed signed consent
2. Patients of both sexes, aged between 30-85 years
3. Diagnosis of Ischemic heart disease-

- Patients with a history of documented myocardial infarction (STEMI/NSTEMI) (> 90 days before date of informed consent)
- Patients who had undergone PTCA previously (with/ without stent)(>90 days before date of informed consent)
- Patients who had undergone CABG previously (> 1 year before date of informed consent)
- Patients in whom diagnosis of IHD was made by coronary angiography

5.4 EXCLUSION CRITERIA

1. Patients who have already been initiated on long term domiciliary oxygen therapy
2. Patients who have been diagnosed with severe and very severe COPD (Fev1/FVC< 70% and Post bronchodilator Fev1<50%)

5.5 STUDY DURATION

The duration of the study was 16 months. (01/04/2013- 31/07/2013)

5.6 DATA COLLECTION

A standardized profoma was used for collection of relevant data during assessment and this included demographic data, medical history, clinical assessment and investigations. The data was subsequently entered onto a standardized Microsoft Excel spread sheet.

5.7 STUDY METHODOLOGY

All adult patients, who were admitted for evaluation of IHD at the department of Cardiology were screened. Among these patients, those who satisfied the inclusion criteria, those willing to give informed signed consent for the study and those willing to undergo a sleep study with a portable screening device were included.

The patients and the relatives were initially explained about:

1. Clinical manifestations of Obstructive sleep apnea

2. The aim of this study wherein it was planned to study the relationship between OSA and IHD.
3. The methodology of this study wherein screening for OSA was planned using a portable screening device at the bedside

They were then given the patient information sheet, in a language that they could comprehend. Subsequently, if the patients were willing to participate in the study, signed consent was obtained on the consent form.

Subsequently, a brief history was obtained that included details of co-morbidities and details of sleep pattern and sleep disordered breathing. A brief physical examination was also performed that included general examination and assessment of vital signs. Relevant data was noted from the laboratory investigations performed as well as findings from the 2D Echocardiogram. All the data was entered into the proforma.

The proforma also had a pictorial version of the ESS and the patients were requested to enter the appropriate information.

Subsequently, the portable screening device was connected in the night once the patient was ready to go sleep and it was disconnected the next morning. The data was subsequently retrieved from the device for analysis.

5.8 ANALYSIS

Microsoft Excel was used for data entry and Statistical Package for Social Sciences (SPSS) Version 16 was used for analysis.

The data was divided into continuous and nominal varieties and was analysed appropriately. The data was expressed as mean (standard deviation) for continuous variables and rates for nominal variables. The pearsons's correlation coefficient was calculated for continuous variables. The differences between means were analysed using independent t test or one way ANOVA as appropriate.

Differences were considered significant for p values less than 0.05.

6. RESULTS

Table I. CLINICAL CHARACTERISTICS OF PATIENTS- A

	Cases (N= 70)
1. Age (years)*	56.76 (8.76)
2. Male gender**	55 (78.6%)
3. Diabetes Mellitus**	37 (52.9%)
4. Hypertension**	46 (65.7%)
5. Dyslipidemia**	18 (25.7%)
6. Hypothyroidism**	3 (4.3%)
7. BMI (Kg/Mt^2)*	28.04 (3)
8. Neck Circumference (cms)*	38.85 (2.12)

9. Waist circumference (men)(cms)*	88.47 (9.32)
Waist circumference (women)(cms)*	84.80 (10.75)
10. Weight (Kg)*	73.57 (8.63)
11. Metabolic Syndrome**	54 (77.1%)

* Mean (Standard deviation)

** Number (Percentage)

Criteria for definition of Metabolic syndrome: (presence of any 3 of the following): (32)

- Abdominal obesity, defined as a waist circumference in men ≥ 90cm and in women ≥80 cm.
- Serum triglycerides ≥150 mg/dL or drug treatment for elevated Triglycerides.
- Serum HDL cholesterol <40 mg/dL in men and <50 mg/dL in women or drug treatment for low HDL.
- Blood pressure ≥130/85 mmHg or drug treatment for elevated blood pressure.
- Fasting plasma glucose (FPG) ≥100 mg/dL or drug treatment for elevated blood glucose.

Table II. CLINICAL CHARACTERISTICS OF PATIENTS- B

	Cases (N=70)
1. **History of Myocardial Infarction***	17 (24.3%)
2.**Type of Myocardial Infarction**	
a. ST elevation MI	14 (82.4%)
b. Non ST elevation MI	3 (17.6%)
3. **Results of Coronary Angiography***	
a. Single vessel disease	22 (31.4%)
b. Double vessel disease	20 (28.6%)
c. Triple vessel disease	16 (22.9%)
d. Minor Coronary artery disease	12 (17.9%)
4. **Number of patients who underwent Coronary Angioplasty ***	34 (48.6%)
5. **Number of patients who underwent Coronary Angioplasty followed by Coronary artery Stenting ***	33 (47.1%)

6. **Number of patients who underwent Coronary Artery Bypass Grafting Surgery***	4 (5.7%)

* Number (Percentage)

Table III. 2D ECHOCARDIOGRAM RESULTS

LV systolic function (Ejection fraction)	Cases (N=70)
1. **Normal (EF> 55%)***	48 (68.6%)
2. **LV systolic dysfunction***	22 (31.4%)
a. mild (EF: 45-54%)	4 (18.2%)
b. moderate (EF: 36-44%)	16 (72.7%)
c. severe (EF: ≤ 35%)	2 (9.1%)

* Number (Percentage)

** The grading of LV systolic function in terms of LV ejection fraction:(157)

1. Normal: LV EF ≥ 55%
2. Mild LV dysfunction: LV EF: 45-54%
3. Moderate LV dysfunction: LV EF 36-44%
4. Severe LV dysfunction: LV EF ≤ 35%

Table IV. PATTERNS OF SLEEP DISORDERED BREATHING

Sleep Pattern	Cases (N=70)
1.**Presence of snoring****	54 (77.1%)
2.**Does snoring affect other people****	45 (83.3%)
3.**Loudness of snoring** (156)**	
a. loud as breathing	1 (1.9%)
b. loud as talking	3 (5.6%)
c. louder than talking	23 (42.6%)
d. very loud	27 (50%)
4.**Frequency of snoring****	
a. almost everyday	41 (75.9%)
b. 3-4 times per week	12 (22.2%)
c. 1-2 times per week	1 (1.9%)
5.**Occurence of breathing pauses**	25 (46.2%)
6.**Frequency of breathing pauses**	
a. almost everyday	25
7.**Presence of Morning fatigue****	53 (75.7%)
8.**Presence of Morning fatigue and increased Daytime somnolence****	13 (18.6%)
9. **STOPBANG criteria positive (≥3)****	65 (92.8%)
10. Pictorial Epworth Sleepiness scale	7.90 (3.16)

score among all 70 patients*	
11. Pictorial Epworth Sleepiness scale score among 53 patients with OSA*	9.01 (2.69)
12. Pictorial Epworth Sleepiness scale score among 13 patients with OSAS*	12.61 (1.50)

* Mean (Standard deviation)

**Number (Percentage)

Table V. SLEEP STUDY RESULTS

	CASES (N=70)
1.Presence of Obstructive Sleep Apnea (AHI≥5)**	53 (75.7%)
2. Presence of Obstructive Sleep Apnea Syndrome**	13 (18.6%)
3.Presence of Syndrome Z**	41 (58.6%)

4. Mean Apnea Hypopnea Index among the entire group of 70 patients	18.27 (17.54)
5. Mean Oxygen Desaturation Index among the entire group of 70 patients	21.04 (18.51)

6. Mean Apnea Hypopnea Index among the 53 patients diagnosed with OSA*	23.75 (16.79)
7. Mean Oxygen Desaturation Index among the 53 patients diagnosed with OSA*	27.06 (17.39)

8. Mean Lowest Oxygen saturation among the 53 patients diagnosed with OSA*	73.71 (13.48)

9. Mean Apnea Hypopnea Index among the 13 patients diagnosed with OSAS*	32.53 (19.64)
10. Mean Oxygen Desaturation Index among the 13 patients diagnosed with OSAS*	35.15 (20.87)
11. Mean Lowest Oxygen saturation among the 13 patients diagnosed with OSAS*	72.61 (13.42)

* Mean (Standard deviation)

**Number (Percentage)

Table VI. SEVERITY OF OBSTRUCTIVE SLEEP APNEA

	N= 53
Apnea hypopnea index*	
5-15	26(49.1%)
16-30	13(24.5%)
>30	14(26.4%)
Oxygen desaturation index*	
5-15	22(41.5%)
16-30	11(20.8%)
>30	20(37.7%)

* Number (Percentage)

Table VII. OSA AND LOUDNESS OF SNORING (52 PATIENTS)**

Loudness of snoring	Number of patients	AHI*	ODI*
Loud as breathing	1	11	24
Loud as talking	3	26.67 (32.39)	21.22 (21.22)
Louder than talking	21	22.47 (15.57)	27.09 (16.01)
Very Loud	27	25.59 (16.47)	27.59 (19.03)

* Mean (standard deviation)

** 53 patients were diagnosed to have OSA. In this group, 1 patient did not snore.

Table VIII. OSA AND APNEIC EPISODES (52 PATIENTS)**

	Patients having history of apneic episodes	Patients without history of apneic episodes	p value
Number of patients	25	27	-----
AHI*	30.40 (17.44)	18.29 (14.01)	0.008
ODI*	33.44 (19.07)	21.74 (13.81)	0.014

* Mean (standard deviation)

** 53 patients were diagnosed to have OSA. In this group, 1 patient did not snore.

Table IX. OSA AND SEVERITY OF IHD (53 patients)

	Minor CAD	Single vessel disease	Double vessel disease	Triple vessel disease
Number	9	16	17	11
AHI*	18.56(13.51)	17.44(12.31)	25.41(17.63)	34.64(19.3)
ODI*	21.78(14.34)	20.50(13.95)	27.71(19.28)	39.91(15.64)

	Single vessel disease	Double vessel disease	Triple vessel disease	p value
Number	16	17	11	-----
AHI*	17.44(12.31)	25.41(17.63)	34.64(19.3)	0.036
ODI*	20.50(13.95)	27.71(19.28)	39.91(15.64)	0.018

* Mean (Standard deviation)

Table X. OSA AND LV SYSTOLIC FUNCTION **(53 patients)

	Normal LV EF≥ 55%	Mild LV dysfunction LV EF: 45-54%	Moderate LV dysfunction LV EF: 36-44%	Severe LV dysfunction LV EF≤ 35%
Number	36	2	13	2
AHI*	21.36(16.18)	17(4.24)	30.31(18.56)	31(19.79)
ODI*	24.58(16.28)	24(21.21)	34(18.88)	29.50(28.99)

	Mild LV dysfunction	Moderate LV dysfunction	Severe LV dysfunction	p value
Number	2	13	2	-----
AHI*	17(4.24)	30.31(18.56)	31(19.79)	0.623
ODI*	24(21.21)	34(18.88)	29.50(28.99)	0.790

* Mean (Standard deviation)

PEARSON'S CORRELATION COEFFICIENT

AHI and LV EF	-0.218
ODI and LV EF	-0.215

** The grading of LV systolic function in terms of LV ejection fraction:(157)

Normal: LV EF ≥ 55%

Mild LV dysfunction: LV EF: 45-54%

Moderate LV dysfunction: LV EF 36-44%

Severe LV dysfunction: LV EF ≤ 35%

Table XI. OSA AND BMI (53 patients)

	Overweight	Obese	p value
Number	6	47	-----
AHI*	16.67(7.60)	24.66(17.47)	0.277
ODI*	19.17(9.06)	28.06(17.99)	0.242

* Mean (Standard deviation)

PEARSON'S CORRELATION COEFFICIENT

AHI and BMI	0.08
ODI and BMI	0.169

PEARSON'S CORRELATION COEFFICIENT

AHI and weight	0.013
ODI and weight	0.105

Table XII. OSA AND WAIST CIRCUMFERENCE (53 patients)

Men: (42 patients)

	< 90 cms	> 90 cms	p value
Number	23	19	-----
AHI*	27.17(15.47)	22.68(20.04)	0.417
ODI*	28.22(16.94)	25.79(19.01)	0.664

Women: (11 patients)

	< 80 cms	> 80 cms	p value
Number	6	5	-----
AHI*	14.50(6.71)	23.70(16.90)	0.274
ODI*	25.50(16.19)	28.40(19.45)	0.793

* Mean (Standard deviation)

Table XIII. OSA AND NECK CIRCUMFERENCE (53 patients)

	< 40 cms	>40 cms	p value
Number	36	17	-----
AHI*	21.42(15.24)	28.71(19.24)	0.142
ODI*	26.86(17.03)	27.47(18.62)	0.907

* Mean (Standard deviation)

PEARSON'S CORRELATION COEFFICIENT

AHI and NC	0.255
ODI and NC	0.124

Table XIV. THE SIGNIFICANCE OF NOCTURNAL DESATURATION IN PATIENTS DIAGNOSED WITH OSA

Lowest nocturnal oxygen saturation and LV systolic dysfunction (17 patients)

	Mild LV dysfunction	Moderate LV dysfunction	Severe LV dysfunction	p value
Number of patients	2	13	2	-----
Lowest nocturnal oxygen saturation	68 (25.45)	69.38 (17.09)	75 (18.38)	0.908

* Mean (Standard deviation)

PEARSON'S CORRELATION COEFFICIENT

LV ejection fraction vs. Lowest nocturnal oxygen saturation	0.133

Lowest nocturnal oxygen saturation and severity of IHD (44 patients)

	Single vessel disease	Double vessel disease	Triple vessel disease	p value
Number of patients	16	17	11	-----
Lowest nocturnal oxygen saturation	75.18 (14.44)	77.11 (12.40)	65.90 (14.13)	0.1

Table XV. The Risk factors for OSA among IHD patients (70 patients)

	Number (70)	OSA (53)	No OSA (17)	p value
Diabetes	37	27	10	0.592
Hypertension	46	34	12	0.772
Dyslipidemia	18	11	7	0.116
Hypothyroidism	3	3	---	1.000
Metabolic syndrome	54	41	13	0.589
BMI (mean)	---	28.32	27.15	0.162
Neck Circumference (mean)	---	39.35	37.29	<0.001
Presence of snoring	54	52	2	<0.001
Occurrence of apneic episodes	25	25	---	<0.001

Table XVI. Odds Ratio of snoring and OSA among IHD patients

Out of 70 patients, there were 53 patients diagnosed with OSA.

Out of 70 patients, there were 54 patients who had a history of snoring.

Out of the 54 patients with a history of snoring, 52 patients had OSA.

Out of the 16 patients who did not have a history of snoring, 1 patient had OSA.

	OSA positive	OSA negative
Snoring present	52	2
Snoring absent	1	15

Therefore in the study cohort, the odds ratio that a patient with snoring would have OSA is 390.

A total of 70 patients with a diagnosis of IHD were included in the study.

Clinical characteristics of patients (Table I, II)

Among the patients included, nearly 80% of the patients were men and the mean age was 56.7 years. While Diabetes and hypertension were present in over 50% of patients, over 25% of patients had dyslipidemia.
The mean BMI was 28 and nearly 80% of patients had features of metabolic syndrome.

17 patients had a history of myocardial infarction with over 80% of these patients having had a ST elevation MI.
Over 30% of patients had single vessel disease on angiography. 20 patients had double vessel disease with 16 patients having triple vessel disease.

Nearly 50% of patients underwent coronary angioplasty. All these patients, with the exception of 1 patient, underwent coronary artery stenting. 4 patients underwent CABG.

Figure I. Presence of comorbidities among the cohort of 70 patients

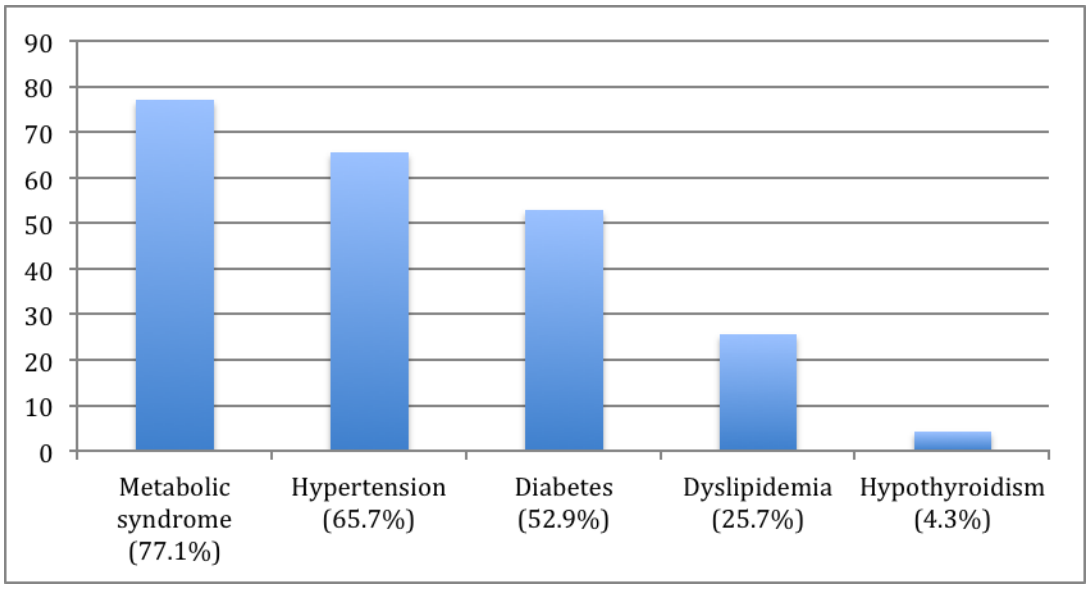
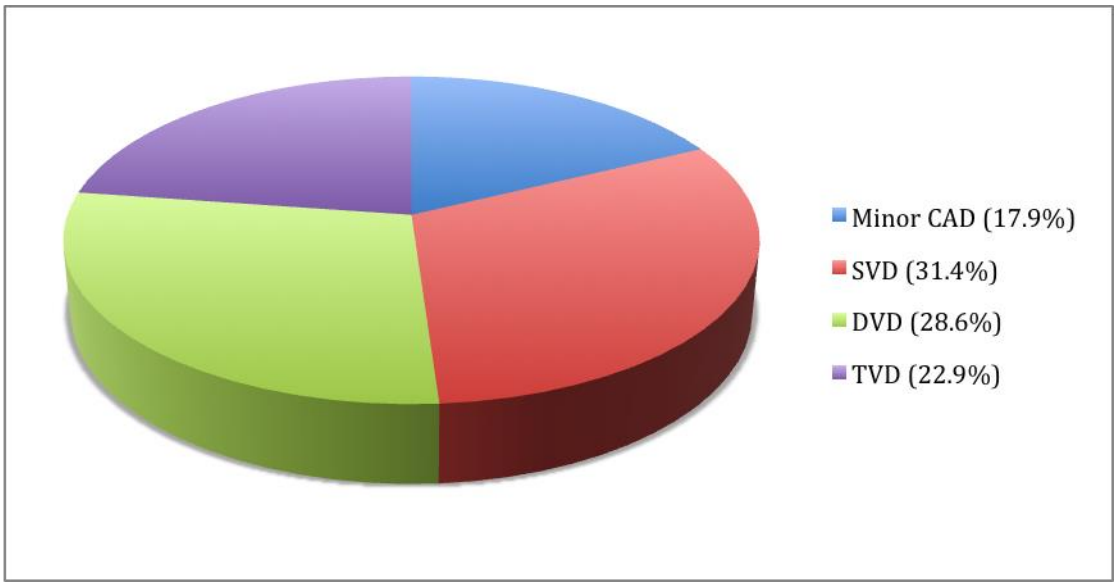


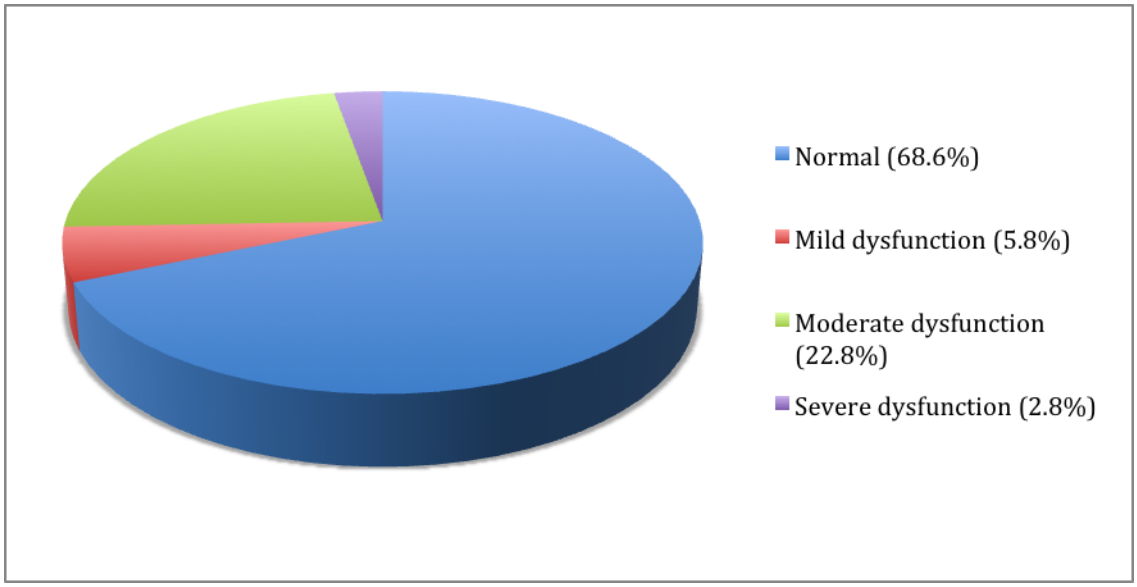
Figure II. Results of Coronary Angiography (70 patients)



2D Echocardiogram results (Table III)

Of the 70 patients, nearly 70% had normal LV systolic function. Among the 22 patients who had LV systolic dysfunction, over 70% had moderate LV dysfunction.

Figure III. LV Systolic function based on 2D Echocardiogram (70 patients)



Patterns of sleep disordered breathing (Table IV)

Of the 70 patients, 54 patients gave a history of snoring with 50% of these patients having very loud snoring. Over 75% of these patients also gave a history of daily snoring.

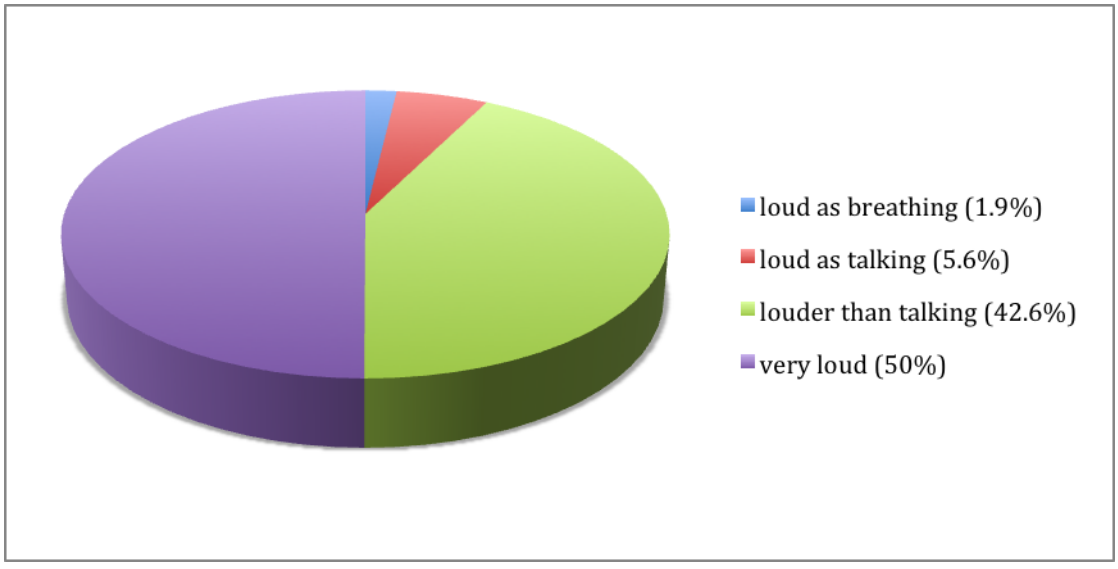
Of the 54 patients who had a history of snoring, 25 patients gave a history of apneic episodes occurring daily.

Over 75% of patients gave a history of morning fatigue while only 18.6% gave a history of increased daytime somnolence along with morning fatigue.

The STOPBANG criteria were positive in over 90% of patients.

The mean Epworth score in the entire group was 7.90. However, it was 9.01 and 12.61 among the 13 patients diagnosed with OSA and OSAS respectively.

Figure IV. Loudness of snoring (54 patients)

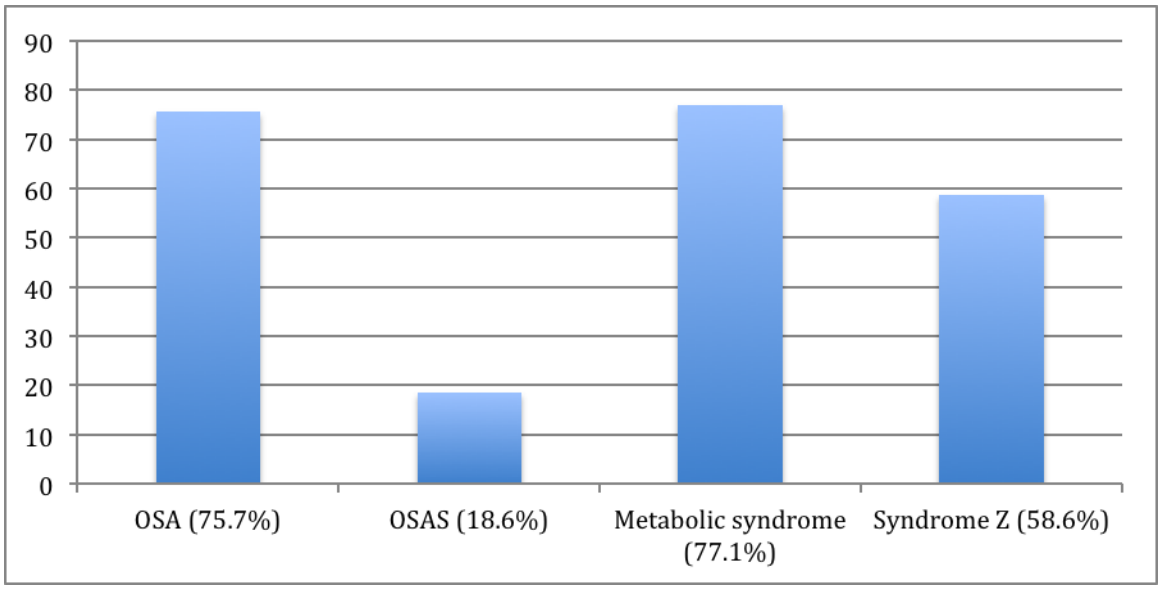


Sleep study results (Table V)

Of the 70 patients, over 75% of patients had OSA while the prevalence of OSAS was 18.6%. Nearly 60% of patients had features of syndrome Z.

The mean AHI and ODI in the entire group of 70 patients was 18.27 and 21.04 respectively. Among the 53 patients who were diagnosed to have OSA, the mean AHI was 23.75 and the mean ODI was 27.06. The mean lowest oxygen saturation among the 53 patients diagnosed with OSA was 73.71%. The mean AHI and ODI among the 13 patients diagnosed with OSAS was 32.53 and 35.15 respectively.

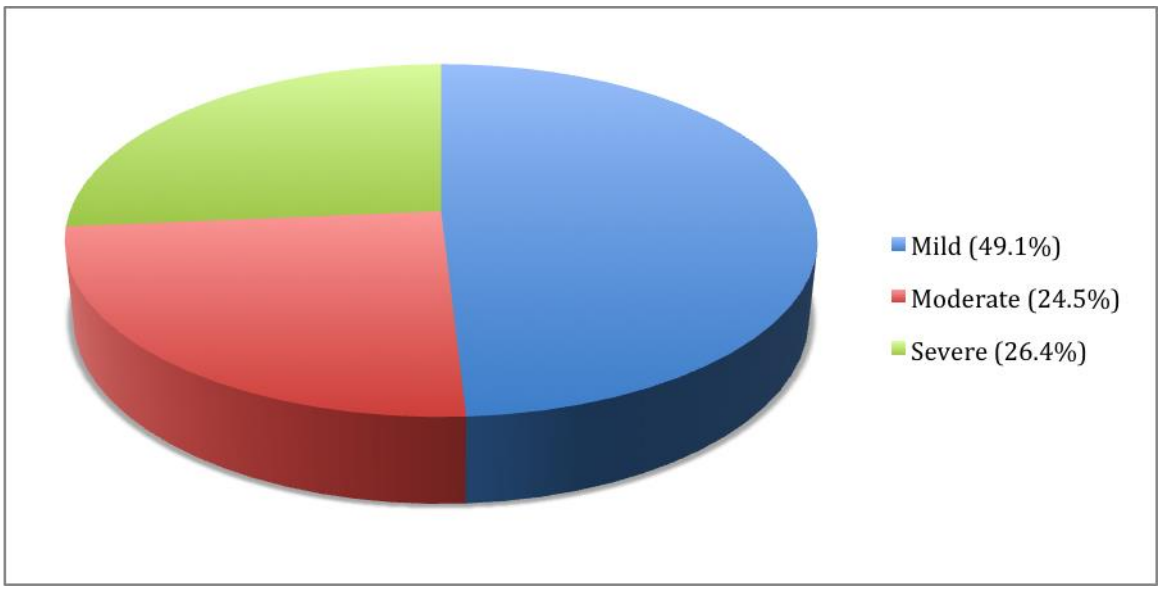
Figure V. Prevalence data (70 patients)



Severity of OSA (Table VI)

Of the 53 patients who were diagnosed with OSA, nearly 50% of patients had mild OSA.

Figure VI. Severity of OSA (53 patients)



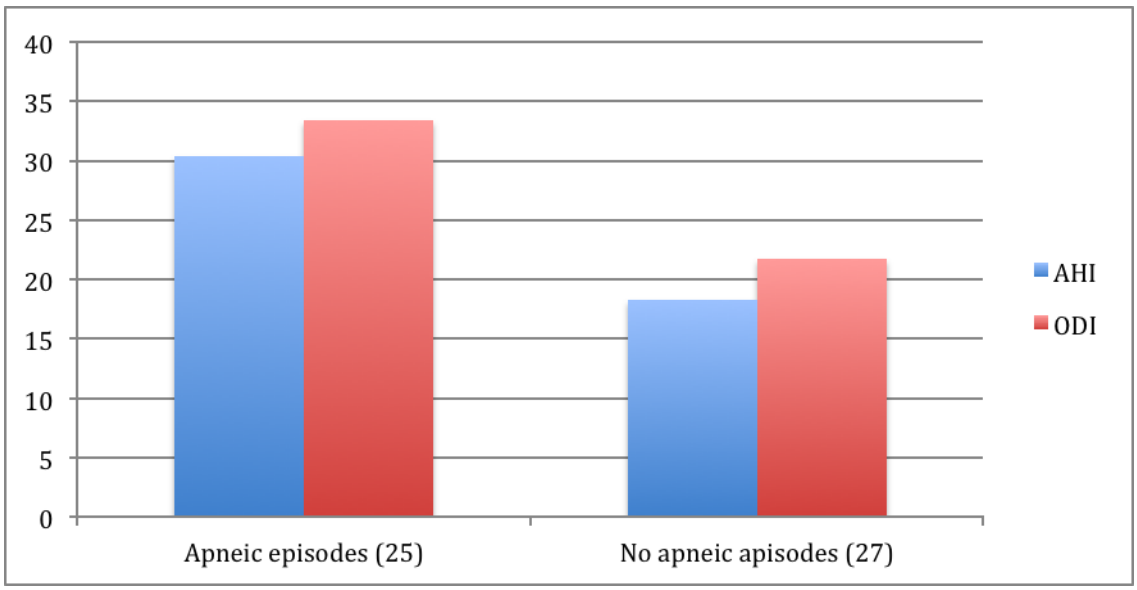
OSA and Loudness of snoring (Table VII)

The analysis of the AHI and ODI on the basis of the loudness of snoring did not reveal any association.

OSA and Apneic Episodes (Table VIII)

The analysis of the AHI and ODI among the 25 patients who had a history of apneic episodes found it to be significantly higher when compared to the AHI and ODI values among the 27 patients who did not have a history of apneic episodes.

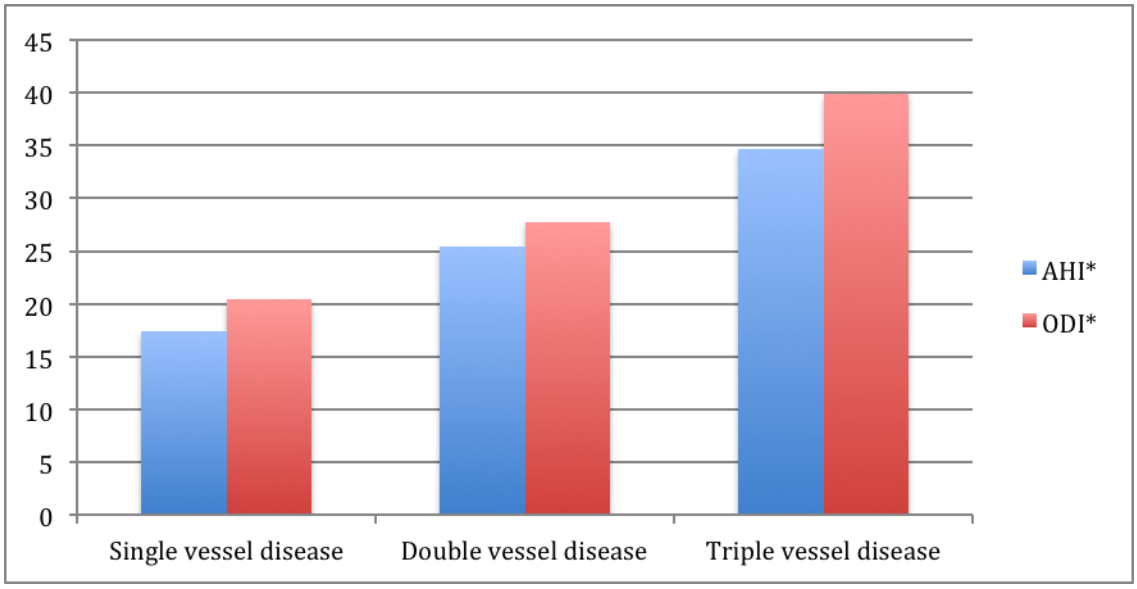
Figure VII. Severity of OSA and Apneic episodes (52 patients)



OSA and severity of IHD (Table IX)

The mean AHI and ODI among the triple vessel disease group were higher when compared to the other groups. This was found to be statistically significant.

Figure VIII. OSA and severity of IHD



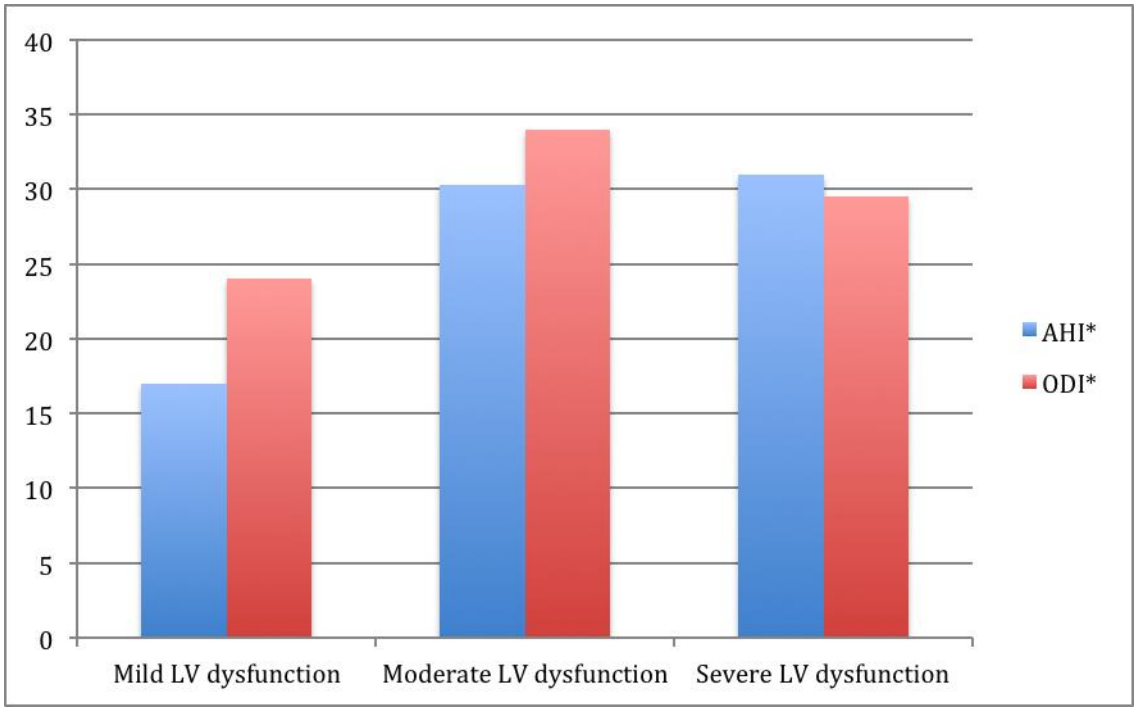
OSA and LV systolic function (Table X)

Of the 53 patients with OSA, nearly 70% had normal LV systolic function. Among the 17 patients with LV systolic dysfunction, over 75% had moderate LV dysfunction.

A comparison of the AHI and the severity of LV dysfunction showed that more severe OSA was present in patients with severe LV dysfunction. However, there was no statistically significant difference.

The pearsons's correlation coefficient revealed a weak negative relation between AHI, ODI and LVEF.

Figure IX. OSA and LV systolic dysfunction



OSA and BMI (Table XI)

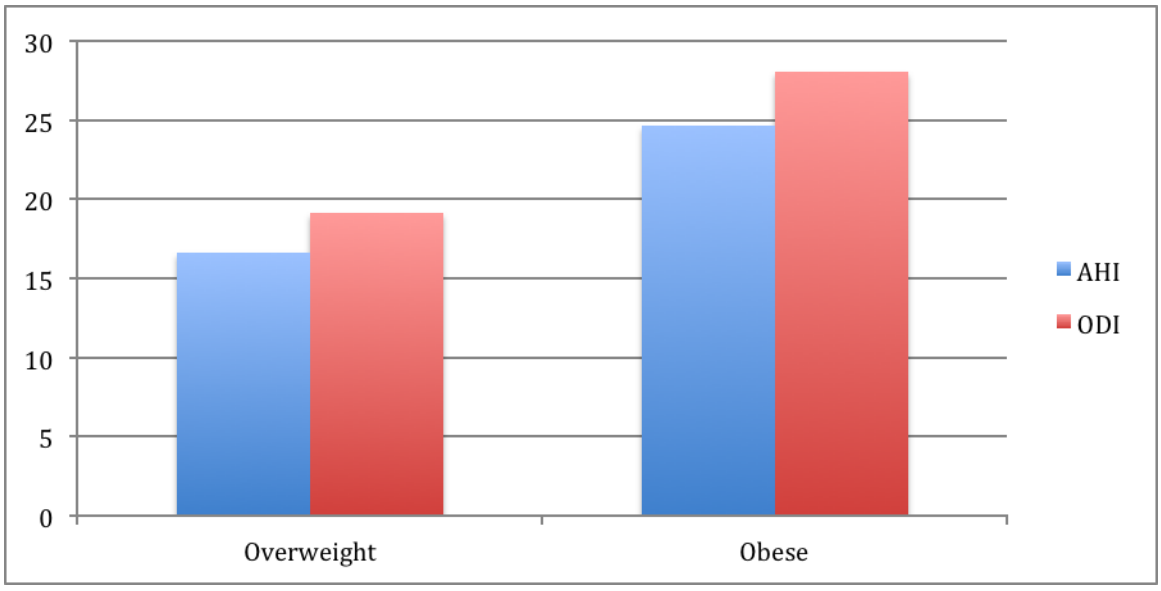
The mean AHI and ODI were higher in the obese group as compared to the overweight group.

However, the difference was not statistically significant.

The pearsons's correlation coefficient revealed a weak positive relation between AHI, ODI and BMI.

Also, the pearsons's correlation coefficient revealed a weak positive relation between AHI, ODI and weight.

Figure X. OSA and BMI



OSA and waist circumference (Table XII)

The data among the women revealed that the mean AHI and ODI was greater among those women with abdominal obesity.

However, among the men, the AHI and ODI was less among those with abdominal obesity. However, there was no statistically significant difference among both groups.

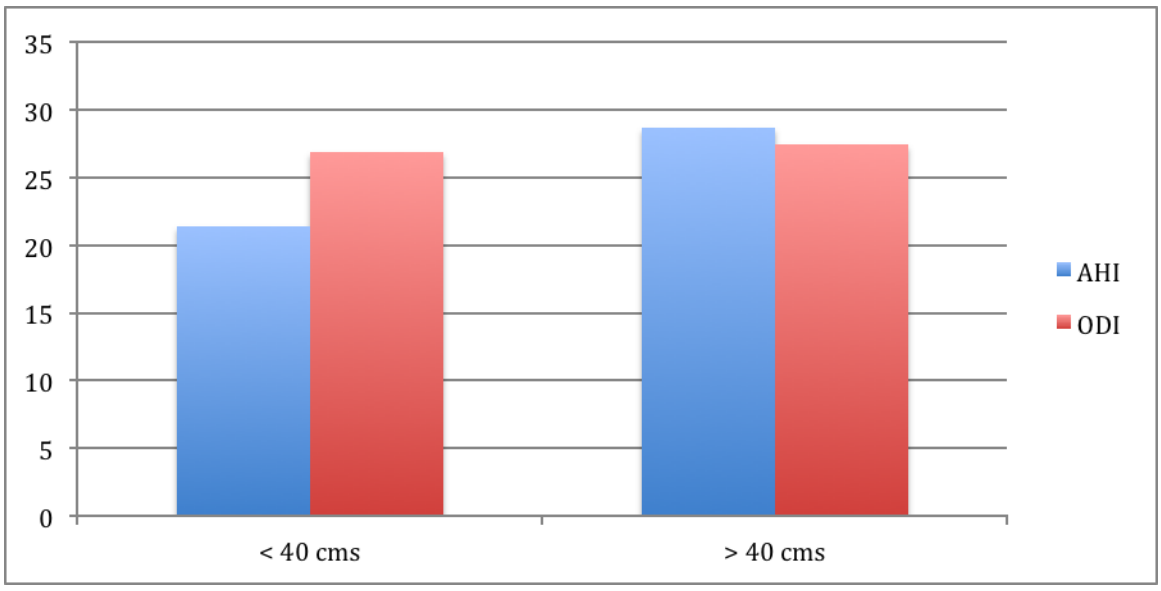
OSA and neck circumference (Table XIII)

Analysis reveals that both the AHI and ODI were increased in the group with neck circumference more than 40 cms.

However, there was no statistically significant difference between the groups.

The pearsons's correlation coefficient revealed a weak positive relation between AHI, ODI and neck circumference.

Figure XI. OSA and neck circumference



The significance of nocturnal desaturation in patients diagnosed with OSA (Table XIV)

An analysis of the lowest nocturnal desaturation values among patients with LV systolic dysfunction did not reveal any association.

The pearsons's correlation coefficient revealed a weak positive relationship.

Also, analysis of the lowest nocturnal desaturation values with severity of IHD based on angiography, did not reveal any association.

The risk factors for OSA among IHD patients (Table XV)

Among the various factors analysed regarding risk of OSA among IHD patients; neck circumference, presence of snoring and presence of apneic episodes were identified to be the significant risk factors.

Odds ratio of Snoring and OSA among IHD patients (Table XVI)

Out of 70 patients, there were 53 patients diagnosed with OSA.

Out of 70 patients, there were 54 patients who had a history of snoring.

Out of the 54 patients with a history of snoring, 52 patients had OSA.

Out of the 16 patients who did not have a history of snoring, 1 patient had OSA.

In this cohort of IHD patients, the odds ratio that a person with snoring would have OSA was 390.

7. DISCUSSION

The results indicate that sleep disordered breathing is highly prevalent among patients with IHD.

We have used the ApneaLink device in this study. This is a portable screening device for OSA and has been validated previously. Its ease of use has also been demonstrated.

The prevalence of OSA and OSAS in this cohort of patients with angiography proven IHD is estimated to be 75.7% and 18.6% respectively. This data is similar to previous studies from western populations that have estimated the prevalence of OSA among IHD patients to be between 50-65%.

Studies showing association between OSA and IHD

Author Name (Reference number in bibliography)	Study group characteristics	OSA prevalence
De Olazabal (100)	N= 17 male patients with IHD proven by angiography	65%
Andreas (101)	N= 47 male patients, 3 female patients with IHD	50%

	proven by angiography	
Mooe (21)	N= 142 male patients with IHD proven by angiography	61%
Mooe (102)	N= 102 female patients with IHD proven by angiography	54%
Present Study	N= 55 male patients, 15 female patients with IHD proven by angiography	75.7%

However, there is a paucity of data regarding prevalence of OSAS among IHD patients. While more than 75% of patients in our cohort had OSA, less than 20% had evidence of functional impairment like morning fatigue and increased daytime somnolence. This suggests that in a majority of patients with OSA and IHD, snoring occurs without any functional impairment. Analysis of the pictorial Epworth sleepiness scale scores further corroborates this data.

Out of the 54 patients who had a history of snoring, over 96% were diagnosed to have OSA. This data suggests the importance of history of snoring as a screening tool for OSA. While there was no association between severity of OSA and loudness of snoring, the severity of OSA was found to be significantly associated with presence of

apneic episodes with more severe OSA being present among those patients with history of apneic episodes.

Neck circumference, presence of snoring and presence of apneic episodes were identified as risk factors for development of OSA among IHD patients. The Odds ratio that a person in this cohort who had snoring, would have OSA was 390.

Among the 53 patients diagnosed with OSA, nearly 50% of patients had mild OSA. This is again similar to previous studies done that have estimated that more than half of the patients with OSA and IHD have mild OSA.

Nocturnal desaturation is one of the most important consequences of OSA, especially in patients with IHD. Intermittent hypoxia is associated with myocardial ischemia and arrhythmias in patients with IHD. The mean lowest oxygen saturation among the 53 patients with OSA in our study was 73.7 %. However, data from other studies have estimated the lowest saturation to be around 86%. The significance of this difference is yet to be confirmed. However, it was not found to be associated with either LV systolic function or severity of IHD.

Analysis revealed that the severity of OSA was significantly associated with severity of IHD with patients with triple vessel disease having more severe involvement as compared to single and double vessel disease..
However, while the severity of OSA was related to severity of LV systolic dysfunction, BMI, waist circumference and neck circumference, it was not statistically significant.

This has to be considered in the background of the relatively small sample size. This could have led to a type II error that limited the power of statistical analysis.

This is the first study from South Asia that attempts to study the relation between OSA and IHD in a cohort of patients with IHD. Also, the data regarding OSA, LV dysfunction, severity of IHD, patterns of sleep disordered breathing and metabolic parameters is novel and there have been no other previous studies regarding these factors from South Asia.

8. CONCLUSIONS

1. The prevalence of OSA in the cohort of patients with angiography proven IHD is greatly increased as compared to the prevalence among the general population.
2. This confirms the role of OSA as a significant independent modifiable risk factor for IHD.
3. The severity of OSA is found to be significantly associated with the severity of IHD based on angiography and also, presence of apneic episodes.
4. Neck circumference, presence of snoring and presence of apneic episodes were identified as risk factors for OSA in this cohort.
5. This indicates the importance of screening for OSA among all patients with IHD, and especially among those with a history of snoring associated with apneic episodes.

9. LIMITATIONS

We were unable to obtain a control group for the study in order to perform a case-control analysis. This was due to the fact that we were unable to perform corresponding sleep studies on the required number of normal individuals.

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11. ANNEXURE

11.1 PATIENT INFORMATION SHEET

Christian Medical College, Vellore
Department of Pulmonary Medicine

OBSTRUCTIVE SLEEP APNEA AND ISCHEMIC HEART DISEASE STUDY

Information sheet

You are being requested to participate in a study to determine the prevalence of obstructive sleep apnea in people with ischemic heart disease.

If you take part what will you have to do?

If you agree to participate in this study, your base line data will be collected including results of investigations like blood tests and ECG and 2D Echocardiogram. You will also need to undergo a physical examination conducted by the investigator. Subsequently, you will be instructed about the portable apnea-link device that will be used for over-night monitoring during the study and you will be given the portable device. You can use the device at your residence and there is no need for hospital admission. Once the study is completed, you will need to return the device to the investigator.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?

We do not expect any injury to happen to you because of taking part in this study.

Will you have to pay anything extra to take part in the study?

You will not incur any extra charges for taking part in this study.

What happens after the study is over?

You may or may not benefit from the study that you are a part of. However the conclusions drawn from this study will be useful to manage similar patients in future.

Will your personal details be kept confidential?

The results of this study may be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical records may be reviewed by people associated with the study, should you decide to participate in this study.

11.2 PATIENT CONSENT FORM

Christian Medical College, Vellore

Department of Pulmonary Medicine

OBSTRUCTIVE SLEEP APNEA AND ISCHEMIC HEART DISEASE STUDY

Consent Form

Study Serial Number:
Participant's name:
Age (in years):

I_____
son/daughter of _____

(Please tick boxes)

(i) I confirm that I have read and understood the information sheet dated for the above study
and have had the opportunity to ask questions. [ ]
(ii) I understand that my participation in the study is voluntary and that I am
free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]
(iii) I understand that the Investigators involved with the study, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]
(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s) [ ]
(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:_____
Date: _____/_____/_____
Signatory's Name: _____

Signature of the Investigator: _____
Date: _____/_____/_____
Study Investigator's Name: _____

11.3 CASE PROFORMA

Christian Medical College, Vellore

Department of Pulmonary Medicine

OBSTRUCTIVE SLEEP APNEA AND ISCHEMIC HEART DISEASE STUDY

CASE PROFORMA

---

1. Date
2. Name
3. Age
4. Sex
5. Hospital number
6. Presence of Diabetes Mellitus- Y/N
7. Presence of Hypertension- Y/N
8. Presence of Dyslipidemia- Y/N
9. Presence of Thyroid Disorders- Y/N
10. If yes, type of thyroid disorder (hyperthyroidism/ hyperthyroidism)
11. Presence of snoring- Y/N
12. Loudness of snoring-
    loud as breathing/ loud as talking/ louder than talking/ very loud
13. Frequency of snoring-
    Almost every day/ 3-4 times per week/ 1-2 times per week/ 1-2 times per month
14. Does the snoring affect other people- Y/N
15. Occurrence of breathing pauses- Y/N
16. Frequency of breathing pauses-
    Almost every day/ 3-4 times per week/ 1-2 times per week/ 1-2 times per month
17. Presence of morning fatigue- Y/N
18. Increased daytime somnolence- Y/N
19. History of myocardial infarction- Y/N
20. If yes- type: STEMI/ NSTEMI
21. Coronary Angiogram-
    Normal/ SVD/ DVD/ TVD/ Minor artery disease
22. Angioplasty- Y/N
23. Stenting- Y/N
24. CABG- Y/N
25. Weight
26. Height
27. BMI
28. Neck circumference
29. Waist circumference
30. Sleep study reports: AHI, ODI

31. 2D ECHO- Normal/ Abnormal
32. LV ejection fraction
33. STOPBANG score
34. Presence of OSA- Y/N
35. Severity of OSA
36. Presence of Metabolic syndrome
37. Presence of Syndrome Z
38. Pictorial Epworth sleepiness scale score

Pictorial Epworth Sleepiness Scale

Name: _____ Date: ___/___/___ Hospital No: _____ Date of Birth: ___/___/___

In contrast to just feeling tired, how likely are you to doze off or fall asleep in the following situations? Even if you have not done some of these things recently, try to work out how they would affect you.

Use the following scale to choose the most appropriate number for each situation.

Situation (Please tick box)	0 No chance of dozing	1 Slight chance	2 Moderate chance	3 Definitely would doze
Sitting and reading	☐	☐	☐	☐
Watching TV	☐	☐	☐	☐
Sitting inactive in a public place (e.g. Theatre or a meeting)	☐	☐	☐	☐
As a passenger in a car for an hour without a break	☐	☐	☐	☐
Lying down to rest in the afternoon when circumstances permit	☐	☐	☐	☐
Sitting and talking to someone	☐	☐	☐	☐
Sitting quietly after lunch without alcohol	☐	☐	☐	☐
In a car, while stopped for a few minutes in traffic	☐	☐	☐	☐

total sleepiness score / 24

11.4 MICROSOFT EXCEL DATA SHEET

12. LIST OF TABLES

13. LIST OF FIGURES

TABLE OF CONTENTS

id	dt	age	sex	bp	dm	dysli
1	03/05/2013	59	1	1	1	2
2	07/06/2013	59	1	1	2	2
3	20/12/2012	54	1	1	1	2
4	17/01/2013	50	1	1	2	2
5	03/06/2012	53	2	1	1	2
6	11/05/2013	55	1	2	2	1
7	07/01/2013	53	1	2	2	1
8	14/09/2012	65	1	2	2	2
9	07/02/2013	62	2	1	1	1
10	04/05/2013	66	1	1	2	1
11	12/06/2013	83	1	2	2	2
12	07/05/2013	47	1	2	2	2
13	08/06/2013	74	2	1	1	1
14	10/12/2012	69	1	2	2	2
15	02/06/2013	55	1	1	2	2
16	14/01/2013	57	1	1	1	1
17	27/05/2013	58	1	1	1	2
18	03/06/2013	68	2	1	1	1
19	06/01/2013	65	1	1	1	2
20	12/05/2013	62	1	1	1	1
21	10/06/2012	40	2	1	1	2
22	18/01/2013	46	1	2	2	1
23	06/05/2013	56	1	2	2	2
24	13/05/2013	50	1	1	1	2
25	30/01/2013	56	1	1	1	2
26	10/05/2013	55	2	1	1	1
27	04/06/2013	60	1	1	2	2
28	27/01/2013	50	1	1	2	2
29	14/05/2013	54	1	1	2	1
30	08/05/2013	47	1	2	2	1
31	08/01/2013	50	1	1	1	1
32	15/05/2013	50	1	2	1	2
33	28/05/2013	74	1	1	1	2
34	03/01/2013	32	1	2	2	2
35	21/05/2012	65	2	2	1	2
36	05/05/2013	47	1	1	2	2
37	20/05/2013	59	1	1	2	2
38	14/06/2013	54	1	1	1	1
39	10/06/2013	59	2	1	2	2
40	14/02/2013	58	2	1	1	2

41	14/06/2012	56	2	1	1	1
42	10/07/2013	53	1	1	1	2
43	22/01/2013	65	1	2	2	2
44	14/01/2013	55	1	1	2	1
45	06/06/2013	47	1	1	2	2
46	13/12/2012	70	1	2	2	2
47	30/05/2013	44	1	1	2	2
48	21/02/2013	62	1	1	1	1
49	20/12/2012	57	1	2	2	2
50	28/06/2012	60	2	1	1	2
51	30/12/2012	41	1	1	1	2
52	30/01/2013	51	1	2	1	2
53	05/02/2013	43	1	1	2	2
54	21/06/2012	59	2	2	1	2
55	19/05/2013	70	1	2	2	2
56	29/05/2012	58	2	1	1	2
57	09/05/2013	50	1	1	1	2
58	24/05/2013	55	1	2	1	2
59	17/05/2013	64	1	2	2	2
60	26/05/2013	47	1	2	2	2
61	23/05/2013	63	1	2	1	2
62	13/06/2013	68	1	2	1	2
63	18/06/2013	48	1	1	1	2
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65	02/05/2013	57	2	1	2	1
66	03/04/2012	62	1	1	1	2
67	13/05/2012	56	1	1	2	2
68	24/06/2013	65	1	2	1	2
69	26/06/2013	59	1	1	2	2
70	24/03/2013	52	2	1	1	2

thy	thyyes	presnor	loudnes	fresnor	affeoth	occubre	
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	1	2		5	2	2
	2	1	1	5	2	2

bypass	bmi	wc	apnea	echo2d	lvef	slvd	
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	2	24.6	79	11	1	56	
	2	30.4	89	20	2	42	2
	2	26.8	80	64	1	58	
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	2	27.3	85	25	2	39	2
	2	26	90	45	2	30	3
	2	23	70	9	1	57	
	2	26.5	81	1	1	56	
	2	22	72	1	1	57	
	1	24	82	1	1	56	
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	2	29	80	2	1	55	
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2	24.6	84	10	1	57	
2	28.3	97	6	1	58	
2	31.1	101	10	1	58	
2	26.5	80	5	1	58	

desind	ids	picscr	osa	osasev	metsyn	synz	
	28	2	9	1	2	1	1
	7	2	8	1	1	2	2
	16	1	12	1	2	2	2
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15	2	8	1	1	1	1
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11	2	6	1	1	1	1

stopbang	nc	wt
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5	38	68
8	42	80
6	42	68
5	36	66
6	41	70
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4	39	68
3	35	78
3	38	72
4	40	76
3	37	69
3	35	70
3	35	69
3	36	70
1	38	70
1	36	74
3	38	84
3	38	70
3	38	76
6	38	80
6	40	78
7	40	74
7	41	74
5	40	74
8	43	88
5	41	70
5	38	68
4	36	67
6	40	70
5	42	76
5	39	70
7	42	78
4	39	67
5	38	70

6	38	105
6	42	78
5	38	76
7	42	74
4	38	66
7	42	84
5	40	70
8	40	76
6	40	80
4	36	60
5	38	84
4	35	74
5	42	80
6	38	68
6	41	78
4	38	60
7	42	76
6	40	76
4	39	70
3	38	74
4	38	70
6	41	103
4	39	64
6	41	96
4	38	66
5	39	78
5	36	68
3	38	78
6	42	88
2	38	68