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The Severity of Obstructive Sleep Apnea and Hypertension Among Middle aged Asians

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Abstract

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Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

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Abstract

This study examined the prevalence rate of obstructive sleep apnea (OSA) as an independent variable in association with hypertension as an outcome. Studies conducted outside of the United States suggest that differences in craniofacial features among middle-aged Asians increase the prevalence of OSA in comparison to Caucasians with similar age and lower BMI. No similar study had been conducted in the United States. The sufficient component cause theory guided this study and was able to describe the association between OSA and hypertension among middle-aged Asians. The objective of this cross sectional retrospective study was to determine the prevalence rate of OSA and the association between OSA and hypertension among a sample of 462 middle-aged Asian patients. Also, the study evaluated the association of 8 clinical parameters: age, gender, smoking, body mass index, Mallampati score, Epworth Sleepiness Scale and Apnea-Hypopnea-Index, and hypertension. The logistic regression analysis showed that OSA is associated with hypertension. The model containing the 8 variables was statistically significant, x^2 (8, N = 462) = 139.59, p < .000). Age was the strongest predictor among the 8 variables. This study showed that OSA is common among middle-age Asians. This research may necessitate the need to evaluate to change current medical awareness, diagnosis, and treatment of OSA and hypertension among Asians, which could reduce the cardiovascular disease (CVD) morbidity and mortality.

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Dedication

I would like to dedicate this to my son Giancarlo and my husband Nick.

Acknowledgments

I would like to thank my family, friends and faculty members who have inspired and supported me throughout my academic journey.

Table of Contents

List of Tables

List of Figures

Chapter 1: Introduction to the Study

Introduction

Hypertension, the most important modifiable and major risk factor for adverse cardiovascular disease (CVD) affects approximately 70 million people in the United States (Roger et al., 2012). However, it has been suggested that some racial and ethnic groups have much higher rates of hypertension than the general population (Mirrakhimov et al., 2013; Yoon et al., 2010). These variations in prevalence in cardiovascular risk factors also occur among subgroups (Egan et al., 2010). Hypertension prevalence rates differ among subgroups of the Asian population (Watson et al., 2009). In the MultiEthnic Study of Atherosclerosis (MESA study), the rate of hypertension among Chinese (n = 803) was 35.2 (Moran et al., 2007). The Pan Asian Cohort Study (2013) revealed that the age-and sex-adjusted prevalence rate of hypertension among various Asian subgroups compared to Non-Hispanic Whites using electronic medical records of 216,768 patients over 18 years of age was 34.9% (99% CI, 34.5-35.3%) versus 38.9% (99% CI, 38.6-39.2%; Powell et al., 2013). The adjusted hypertension rates were 51.2 % (50.7-53.2%) for Filipinos, 29.8% (29.1-30.4%) for Chinese, 30.7% (28.0-33.5%) for Koreans, 30.8% (28.7-32.8%) for Vietnamese, 36.9% (35.9-37.8%) for Asian Indians, and 38.2% (36.5-39.9%) for Japanese (Powell et al., 2013, p. 10). These variations in cardiovascular risk factors associated with hypertension are obviously modulated by race/ethnicity and prevalent comorbidities (Aronow et al., 2011).

Evidence suggested that hypertension is highly prevalent among obstructive sleep apnea (OSA) patients (Baguet et al., 2006). Numerous studies have confirmed that the intermittent airway occlusion exhibited during nocturnal sleep typical in obstructive sleep apnea evoked acute transient increases in nighttime blood pressure which consequently produced sustained daytime hypertension (Borgel et al., 2004). Studies have shown that about 30%-40% of hypertensives have some form of OSA (Worsnop et al., 1998). Systemic hypertension is also prevalent among an estimated 50%-60% of OSA patients (Silverberg et al., 2001). Additionally, 40% of patients with systemic hypertension have undiagnosed OSA (Silverberg et al., 1997).

In the last few decades, studies throughout the world have led to the recognition that the many mechanisms linking hypertension significantly affect the pathophysiological mechanisms of OSA (Kapa et al., 2008; Lopez-Jimenez et al., 2008; McNicholas et al., 2007; Quan & Gersh, 2004). Both OSA and hypertension are complex disorders modulated by a number of risk factors (Villanueva et al., 2005). Race is an important risk factor in development of OSA and hypertension (Yaggi & Strohl, 2010). Asians are contemporarily classified as Asians/ Pacific Islanders in the United States (Villanueva et al., 2005, p. 420). Such national descriptors do not accurately convey genetic variation in the prevalence of hypertension among middle aged Asians with OSA. Moreover, craniofacial structure is an important and often ignored risk factor among Asians (Villanueva et al., 2005, p. 21). Interethnic comparison in craniofacial morphology might be used to explain any variation in risk for OSA-hypertension.

The next few sections of Chapter 1 cover the study's background, problem statement, purpose, research questions and hypotheses, theoretical framework, nature, definitions, assumptions, scope and delimitations.

Background

In the years following early notions concerning whether OSA is an independent risk factor for hypertension, numerous large epidemiologic studies provided substantial proof that OSA does increase the risk for hypertension (Punjabi, 2008). The Sleep Heart Study, a cross-sectional study of 6,132 patients aged 40 and above, by employing in-home polysomnography, showed that in a significant number of patients, OSA was independently associated with hypertension (Nieto et al., 2000). The association, although quite modest, revealed that adjusted odds ratio for AHI > 30 (versus AHI < 1.5) was 1.37 (95% CI 1.03-1.83; Nieto et al., 2000, p. 1832). The Wisconsin Heart Study, a prospective study using in-laboratory polysomnography, also demonstrated that OSA was associated with hypertension. The Wisconsin study also revealed that the adjusted odds ratio of OSA (AHI > 30) to hypertension was 3.1 (95% CI 1.7-5.7; Nieto et al., 2000, p. 1832). Furthermore, the odds ratio for the development of new onset hypertension associated was 2.89 (95% CI 1.46 > 5.64 for AHI >15 versus 0; Peppard et al., 2000).

However, the interpretations of these epidemiologic studies in relation to Asian populations have several limitations. First, the OSA studies conducted in the past have largely described the prevalence of OSA and OSA's association to hypertension predominantly among White populations. Second, the interpretation of data linking OSA

to hypertension should be construed cautiously as minority populations often have additional risk factors. Third, limited studies in the literature have been conducted that have specifically investigated racial variations in OSA as an independent risk factor for hypertension.

Given the significant impact of OSA on cardiovascular morbidity and mortality, identification of OSA as an independent risk factor for hypertension among the diverse susceptible Asian subgroups may lead to physician improvements in the diagnosis, treatment, and control of these diseases. Additionally, the results generated from this research would lead to the creation of larger epidemiological studies cross sectional studies involving this vulnerable population.

Statement of the Problem

Obstructive sleep apnea is a major public health issue, with 2-6% of the population experiencing severe obstructive sleep apnea (Cantolla et al., 2009; Punjabi, 2008; Vozoris, 2012). The current literature indicates that the repeated arousals and intermittent hypoxemia associated with obstructive sleep apnea are principal in the pathogenesis of hypertension (Guillot et al., 2013; Mohsenin et al., 2009; Ryan et al., 2013). The risk of hypertension intensifies with increasing severity of obstructive sleep apnea even after adjusting for risk factors like obesity and age (Duran-Cantolla et al., 2009; Peppard et al., 2000; Sforza & Roche, 2012). There are no published scientific reports on the general prevalence of OSA among Asians. Hui et al., (2006) and Kim et al., (2004) estimated that the OSA prevalence rate among Asians was 4%. In a recent

systematic review of the literature, Mirrakhimov et al. (2013) found that among 47,957 Asian subjects, OSA prevalence were estimated to be about 3.7% to 97.3%. This analysis also showed that the risk factors associated with OSA were male gender, older age, higher BMI, higher waist-to-hip ratio, greater neck circumference, arterial hypertension, smoking, snoring, and daytime sleepiness (Mirrakhimov et al., 2013, pp.9-10).

However, the data are conflicting for these ethnic groups (i.e., Asians; (Genta et al., 2008; Ip et al., 2001; Kawaguchi et al., 2011). The accumulated findings from large scale studies of sleep-diagnosed OSA patients, random cohorts of the general population, case-controlled, and intervention studies found no consistent evidence of obesity and gender differences in the prevalence of obstructive sleep apnea with hypertension among Asians (Genta et al., 2008; Ip et al., 2001; Mirrahkimov et al., 2013; Villanueva et al., 2005).

OSA is an independent risk factor for hypertension (Bixler et al., 2000; Kasiakogias et al., 2013; Marin et al., 2012; Nieto et al.,2000; Tsioufis et al., 2011; Young et al., 2000). There are ethnic differences in the prevalence and severity of OSA (Villanueva et al., 2005). Craniofacial features seem to play a role in the differences in prevalence and severity among Asians (Duran et al., 2001).

Santa Clara County has 1.8 million residents, among whom 33.7% are Asians, (U.S. Census Data, 2012). Health disparities exist among Asians in this county, with certain subgroups experiencing higher prevalence of risk factors. There is a significant

association of these two diseases in terms of cardiovascular morbidity and mortality. In order to understand the burden of these diseases, there is a need to understand what the prevalence of OSA and hypertension among Asians is. Hence, the purpose of the study was to address this gap and to determine the role of other risk factors, such as age, gender, smoking, body mass index (BMI), Mallampati score (MS), Epworth Sleepiness Scale (ESS), and Apnea-Hypopnea Index (AHI) that influence the prevalence rate of OSA and its association with hypertension among middle aged Asians residing in San Jose, CA.

Purpose of the Study

The main purpose of this quantitative cross-sectional study was to determine: (a) the prevalence rate of OSA among middle-aged Asian patients (Chinese, Filipino, Vietnamese, Asian Indians, Korean, Taiwanese, Japanese, and Singaporean) in San Jose, CA.; (b) the association between OSA and hypertension; and (c) the association of other risk factors: age, gender, smoking, body mass index (BMI); Mallampati score (MS), the Epworth Sleepiness Scale (ESS) and Apnea-Hypopnea Index (AHI) with hypertension as the outcome.

Research Questions and Hypotheses

The overarching research question concerned the association of OSA and other risk factors as related to hypertension among middle-aged (40-60+ years old) Asians living in San Jose, CA. To answer the above research question, the following subquestions were examined.

Research Question 1. What was the association between OSA and hypertension among a sample of middle-aged Asians living in San Jose, CA?

Null Hypothesis 1. There was no association between OSA and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Alternative Hypothesis 1. There was an association between OSA and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Research Question 2. What was the association between age and hypertension among a sample of middle aged-Asians living in San Jose, CA?

Null Hypothesis 2. There was no association between age and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Alternative Hypothesis 2. There was an association between age and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Research Question 3. What was the association between gender and hypertension among a sample of middle-aged Asians living in San Jose, CA?

Null Hypothesis 3. There was no association between gender and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Alternative Hypothesis 3. There was an association between gender and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Research Question 4. What was the association between smoking status and hypertension among a sample of middle-aged Asians living in San Jose, CA?

Null Hypothesis 4. There was no association between smoking status and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Alternative Hypothesis 4. There was an association between smoking status and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Research Question 5. What was the association between body mass index (BMI) and hypertension among a sample of middle-aged Asians living in San Jose, CA?

Null Hypothesis 5. There was no association between body mass index (BMI) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Alternative Hypothesis 5. There was an association between body mass index (BMI) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Research Question 6. What was the association between Mallampati score (MS) and hypertension among a sample of middle-aged Asians living in San Jose, CA?

Null Hypothesis 6. There was no association between Mallampati score (MS) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Alternative Hypothesis 6. There was an association between Mallampati score (MS) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Research Question 7. What was the association between the Epworth Sleepiness Scale (ESS) and hypertension among a sample of middle-aged Asians living in San Jose, CA?

Null Hypothesis 7. There was no association between the Epworth Sleepiness Scale (ESS) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Alternative Hypothesis 7. There was an association between the Epworth Sleepiness Scale (ESS) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Research Question 8. What was the association between the Apnea-Hypopnea Index (AHI) and hypertension among a sample of middle-aged Asians living in San Jose, CA?

Null Hypothesis 8. There was no association between the Apnea-Hypopnea Index (AHI) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Alternative Hypothesis 8. There was an association between the Apnea-Hypopnea Index (AHI) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

The analysis determined the association between OSA, age, gender, smoking status, body mass index, Mallampati score, the Epworth Sleepiness Scale, and Apnea-Hypopnea Index to hypertension. Means, standard deviation, and frequency of distribution were calculated for continuous independent variables such as age, gender, ethnicity, sex, and BMI.

Theoretical Foundation

The theoretical guide for this study was the sufficient component causes model. This model, which, emerged in the epidemiological literature in 1976, described the many contributing determinants, and risk factors that make up the multifactorial etiologies involved in the association between OSA, and hypertension among middle-aged Asian patients.

The sufficient component causes model, pioneered by Rothman (1976), is an epidemiological model that defines a sufficient cause as "a complete causal mechanism" that eventually leads to the development of a disease (Flanders et al., 2006; VanderWeele et al., 2006). This model considers the development of a disease either through a complete causal mechanism, or through a minimum set of conditions or factors, that, if present in a given individual, will be sufficient for the outcome to ensue (Rothman et al., 2008).

According to the major proponents of this model, health conditions are outcomes of complex component interrelationships of various predisposing factors that must be present or have occurred for the disease to manifest (Rothman et al., 2008, pp. 6-8). The sufficient cause component model seeks to identify the possible set of conditions critical to the development of illness by recognizing the constellation of component causes of conditions, factors causing the condition(s), and factors that act in unification to cause the condition (Rothman et al., 2008, pp. 7-8). The sufficient component cause model is characterized by a number of features; for instance, a cause not single but consists of a

minimal set of conditions or events, each component in a sufficient cause is called a *component cause*, and there is no need to identify all of the component causes to prevent the disease outcome (Aschengrau & Seage, 2008). This *component cause* together constitute a sufficient cause for the outcome in question. In order to fully understand all the risk factors, exposure, and contributory causes of the disease, the model requires complete understanding or investigation of the diseases (Timmreck, 2006, p. 209).

The sufficient component cause theory guided this study and made it possible to describe the association between OSA and hypertension among middle-aged Asians in the United States. Studies have shown that the independent association of OSA to hypertension is affected by the increased sympathetic activity in response to hypoxemia and hypercapnia that lead to chemo reflex activation, which increase the peripheral vascular tone (Phillips & Somers, 2003). This sympathetic response continues even into daytime normoxia (Phillips & Somers, 2003, p. 381). Chemoreceptors, both peripheral and central, are inhibited, leading to decreased ability to breathe (Sadikot, 2008). The subsequent hypoxemia can stimulate the augmented production of many circulating vasoconstrictors that raise blood pressure (Phillips & Somers, 2003, p. 382). The consistent cycles of increased sympathetic stimulation, renin-angiotensin system, endothelial dysfunction, cerebral blood flow alterations, oxidative stress, and systemic inflammation also contribute to an increase in heart rate and blood pressure. The presence of risk factors (e.g., obesity; craniofacial morphology) in sleep apnea likely indicates an increased susceptibility to hypertension (Phillips & Somers, 2003, p. 383).

The key constructs of this model supported the belief that *component causes* or risk factors (e.g., body mass index (BMI), Mallampati score (MS), Epworth Sleepiness Scale (ESS), and apnea-hypopnea index (AHI) together constitute a sufficient cause model for the OSA-hypertension association. The table below shows how these risk factors are associated with certain causes of OSA as an independent predictor of hypertension as guided by the sufficient component cause theory.

Table 1

OSA Risk Factors as Guided by the Sufficient Component Cause Theory

Causes	Risk factors	Measurement
Sympathetic stimulation	Apnea/and/ or hypopnea	AHI index/Epworth Sleepiness Scale
Renin-angiotensin system	Age, smoking	Systolic and diastolic measurement
Endothelial dysfunction/systemic inflammation Oxidative stress	Obesity	BMI
Cerebral blood flow alterations	Craniofacial features, gender	Mallampati score

Note Adapted from "Epidemiology and The Web of Causation: Has Anyone Seen The Spider? by N. Krieger, 1994. *Social Science Medicine*, *39*(7), pp 887-903.

Detailed discussion of the model will be discussed in the next chapter.

Nature of the Study

I employed a quantitative cross-sectional study to determine the relationship between OSA as an independent variable and hypertension as the outcome among middle-aged Asian patients. The advantage of using this type of study was that it allowed me to examine the associations between variables within a short period of time based on biological plausibility and past research (Newman et al., 2007). The main variables that the study assessed were obstructive sleep apnea, as the independent variable and

hypertension as the dependent variable. Other risk factors including age, gender, smoking, OSA severity (measured by apnea-hypopnea index [AHI]), body mass index (BMI), daytime sleepiness (measured by Epworth Sleepiness Scale [ESS]), and craniofacial characteristics (measured by Mallampati score [MS] were assessed for their role in the development of hypertension as the outcome in association with OSA using ANOVA.

Three sleep study clinics were used to assess the participants who partook in an overnight polysomnography in a real life sleep clinic in San Jose, CA. The study variables and other demographical information including age, sex, history of smoking, etc were collected and analyzed using paper and electronic medical records.

Definition of Terms

Apnea is the absence of airflow for 10 seconds in the presence of continued respiratory effort (Hahn & Somers, 2007, p. 943).

Apnea-hypopnea index (AHI) is the total number of apneas and hypopneas divided by the total number of hours of sleep (Banno et al., 2007, p.402).

Asians refer to the group of people living in Asia. The Behavioral Risk Factor and Surveillance system categorizes this group into seven groups; namely, Asian Indian, Filipino, Chinese, Vietnamese, Korean, Japanese and other Asians (Palanaippan et al., 2010).

Body mass index is a reliable measure to determine body fat for individuals. It is calculated based on a person’s weight and height.

Hypertension also called *high blood pressure,* is based on the measured force of blood against the walls of the arteries as the heart pumps blood to the body (Victor, 2011).

Hypopnea is a reduction in airflow ≥ 50% for 10 seconds with 4% drop in arousal and saturation (Hahn & Somers, 2007, p. 943). Hypopnea is clinically significant when associated with an oxyhemoglobin desaturation event or with a central nervous system arousal characterized by EEG changes or alpha activity (Hirskowitz & Kryger, 2005).

Epworth Sleepiness Scale is a scale to measure daytime sleepiness by using a questionnaire. A score of 10 or more is considered sleepy.

Mallampati score is a grading scale to assess the tonsil and visibility of the tonsillar fossa. Class 1 shows that the entire tonsil is visible, Class 2 shows that only half of the tonsil fossa is visible, Class 3 shows clear visibility of the soft and hard palate and Class 4 shows only the hard palate (Mallampati et al., 1985).

Obstructive sleep apnea syndrome (OSAS) is clinically defined as AHI ≥ 5 per hour with symptoms or more than 15 without symptoms (Hahn & Somers, 2007, p. 943). This condition is characterized by breathing cessation caused by obstruction of the upper airway (Hirskowitz & Kryger, 2005).

Oxygen desaturation index (ODI) is the number of oxyhemoglobin desaturation events per hour of sleep (Hirskowitz & Kryger, 2005).

Polysomnography (PSG) is the method used to consistently measure nasal pressure, oxygen saturation, electroencephalogram, electro-oculogram, chin and lower

extremity electrocardiogram, chest, and abdomen plethysmography (Hahn & Somers, 2007, p. 943).

Assumptions

The basic assumption of this study was that it was conducted among study subjects who had consented to participate voluntarily. Due to the voluntary nature of this study, it is hoped that the results were not influenced by a high degree of bias. The study used secondary data obtained from sleep clinics in San Jose, CA. Walden University Institutional Review Board with approval number 03-25-14-0153639 approved the use of secondary data from three sleep study clinics in San Jose, CA. The adoption of secondary data presents an opportunity to develop primary data in future research. It is also assumed that the sleep metrics used, including AHI, polysomnograms, and other metrics, were suitable to measure the study variables.

The secondary data i.e., electronic medical records system used in this study represented real world data that reflected fairly accurately actual physician practice compared to observational data (Dean et al., 2009). It was assumed that the respondents were accurately diagnosed according to symptoms and clinical presentations. It was also assumed that participants' gender did not significantly affect physicians and other allied health professionals diagnosis of the conditions.

I also assumed that craniofacial features influenced the relationship between OSA and hypertension. The craniofacial abnormality subjects the pharynx to be a risk of airway closure independent of soft tissue influences. The Mallampati Scoring System as

marker for craniofacial abnormality was scored typically by physicians who were assumed to be able to identify the four anatomical landmarks in the oropharyngeal region.

Scope and Delimitations

This study was about the prevalence rate of OSA as an independent variable in association with hypertension as an outcome among middle aged Asians. Due to the large number of potential participants in the study population, the study only focused on a sample of 462 Asians in three sleep study clinics located in San Jose, CA during the period from January 1, 2008 to December 31, 2011. The generalizability of this epidemiological study may be limited to certain Asian Americans living in San Jose, CA and may not be representative of the United States, as a whole. It is known that diseases, regardless of etiology, are affected by multifactorial causes. As the study focused only on OSA and hypertension as the outcome, the study is most relevant in this particular area. The data and results of the study were derived from electronic and paper medical records, in which study participation among the subjects and the medical practitioner were assumed to be voluntary. Thus, the study was subjected to inherent limitations of such methods, including biases related to patient population, selection and reporting. The potential biases related to patient population, selection, and reporting were reduced by randomly sampling patient population within three sleep clinics used in this study. The potential bias was also eliminated by obtaining the appropriate number of patients to power the study, judiciously designing the study, guaranteeing that sample methods were

reliable, and employing procedures using standardized methods to accurately measure the data collected (Peat & Mellis, 2002).

Limitations

A limitation of this study was that the sample was drawn from Santa Clara County only. This affects the generalizability of the study to the other counties. In order to address this issue, the study used the correct *t*-value for alpha which is 0.05. The study employed data obtained from electronic medical records (EMR) and paper medical records which were basically designed for clinical care and not research. EMR provide the researchers with easy access to patient data, large cohorts, patient-level diagnoses, treatment data, and billing, and laboratory information. However, limitations in the use of EMR include information entered being decided by the provider, information entered in free text, scanned images, flexibility in terminology, a minimal number of required fields, and important data irrelevant to clinical care is missing (Terry et al., 2010). Another limitation of the use of secondary data is the lack of clinical detail (Gallin & Ognibene, 2012). This is especially true because certain EMR data sets will contain clinical data relevant to physician payments (Gallin & Ognibene, 2012, p. 375). Another limitation of the study was the inability of the researcher to provide the temporal sequence of the exposure and the outcome (Ho et al., 2008). In order to assure that the tools for the analysis and data generated were valid and reliable, I checked for bias, and cross checked the data looking at both paper and electronic records if both were available (Babbie, 2010). Validity issues in this study might stem from bias in data collection,

subject selection, and inadequate procedures (Creswell, 2009). In order to address these issues, I validated the codes used by the practitioners by confirming with the current International Classification of Diseases Manual, randomly sampling patients in the study sleep study clinics chosen for the study, and setting inclusion and exclusion criteria for patient selection. To validate the research findings, I looked at existing literature to confirm which specific variables would throw light on the relationship between the variables and covariables (to determine the accuracy of findings), and construct validity (if the theoretical model applied well in this study) (Creswell, 2009, pp. 149- 190).

The limitations associated with this data analysis also included variation in software platforms used by the clinics for their EMR systems, medical terminology, clinical data, (i.e., laboratory results), and units of measurement (Dean et al., 2009). In order to address these issues, the researcher ensured that standardized coding practices were adopted at each clinic, similar medical terminologies were used; and laboratory results were reported in the same units of measurement (Dean et al., 2009, p. 613).

Significance

There are very limited published scientific data on the general prevalence of OSA among Asians. This study uniquely addressed an important public health issue among a segment of the population that has significantly grown in number in the San Jose, CA area for the last few years. This study was able to provide much needed data on the prevalence of OSA and the associated risk factors between OSA and hypertension. The valuable insights that may be acquired from this study could pave the way for additional

scientific pursuits that could lead to better understanding of OSA and hypertension among middle aged Asians.

This study also adds to the epidemiologic understanding of OSA as the independent variable and hypertension as an outcome among middle-aged Asians in San Jose, CA. OSA-hypertension research studies conducted among high risk Asian groups can generate valuable public health insight into the disease and its risk factors. This is critically important especially when studies involving OSA do not adequately synthesize or provide clarity regarding the health differences among Asian Americans. Because there are still a great number of underdiagnosed and undertreated Asian patients in San Jose, CA, the results generated from this research can lead to successful identification, screening, treatment, and management of OSA and hypertension especially among high-risks middle-aged Asians, thus creating positive social change for those individuals and their families and community. This study can also foster social change by empowering members this ethnic group to advocate for themselves and collectively challenge service providers, government agencies, and other institutions to ensure equal access to healthcare, and available services. Additionally, this study may create positive social change by fostering improvements in health outcomes and the lives of Asians who have been suffering from OSA and hypertension for a long time.

Summary

The prevalence of OSA and hypertension in the United States continues to rise. The various structural and functional cardiac dysfunctions associated with OSA have

important pathologic consequences to the development of hypertension. Numerous observational and epidemiologic studies have been designed to better understand the association of OSA and hypertension and the consequences they have for CVD among Caucasian patients. OSA data among Asians are very limited.

Hypertension outcomes associated with OSA have been measured by polysomnography specifically using the Apnea-Hypopnea Index (AHI) as a common metric. Body mass indexes (BMI), Mallampati scores (MS), and the Epworth Sleepiness Scale (ESS) are also common metrics used in OSA studies.

Research efforts in the field of sleep apnea have provided intense and consistent results linking OSA to hypertension. The epidemiologic data from various human populations that are consistent with the mechanistic theory that supported the study are summarized in the next chapter.

Chapter 2: Literature Review

The literature review provided the basis for the need to examine the prevalence rate of OSA and its association to hypertension among middle aged Asian patients. In the last three decades, investigations have shown significant linkages between OSA and hypertension, as well as their important implications on long term effects on cardiovascular morbidity and mortality. Mechanistic, animal, human interventional and epidemiological studies have revealed that systematic changes in blood pressure in OSA together with the presence of significant confounders are major contributors to the development of hypertension. Although this association between OSA and hypertension had been reported in the literature, systematic investigations to address the question of whether similar associations are seen among Asians have rarely occurred. The unique craniofacial anatomic features among Asians may be the delineating difference (e.g., retrognathia) that can predispose Asians to develop OSA leading to hypertension. The theoretical foundation that guided this dissertation was the sufficient component cause model. This sufficient component cause model may be used to describe the association of OSA and hypertension as these diseases are highly associated with a number of significant risk factors (Dopp et al., 2007; Stehbens, 1985). The associated risk factors are significantly associated with the development of the disease, and if these risk factors are modified by intervention, it reduces the occurrence of the disease. The complete airway obstruction experienced during sleep leads to apnea or cessation of breathing, whereas the experienced caused by partial airway obstruction leads to hypopnea and

elevated $PCO_{2,}$ (Banno & Kryger, 2007, p. 401). A recent review of the literature showed that this theoretical construct provided a clear view of how these various risk factors work together to impact the OSA and the development of hypertension among middle-aged patients (Bixler et al., 2001; Bixler et al., 1998; Duran et al., 2001, Ip et al., 2001, Peppard et al., 2000; Young et al., 2002).

The empirical basis of this research is supported by peer-reviewed journals. The search for relevant articles to support the aforementioned evidence was made using medical search terms, subject headings, reference lists, key words and "related articles" links using MEDLINE, PUBMED, Medscape, CDC, NIH, Science, and Walden University library databases. The search terms to obtain these scientific articles included *obstructive sleep apnea, hypertension, sufficient component cause model, sympathetic activation, apnea cardiovascular adverse effects, age, craniofacial characteristics, AHI index, obesity, ethnicity sleep apnea, multicausation, hypertension risk factors, hypertension trends, OSA risk factors, Asians,* and *Asian Americans*. Sources to support this dissertation were obtained either in digital format or as traditional printed versions of scientific articles. The search of these articles was limited to those published between 1995 and 2012 and written in English. The articles chosen were from epidemiologic research. This dissertation was also supported with multiple books to provide years of scientific research on obstructive sleep apnea and hypertension.

This chapter provided a review of OSA, hypertension, relevant theoretical constructs, and the pathophysiologic evidence to support OSA's linkage to hypertension.

The chapter also provides systemic epidemiologic review of the literature to support the contributory role of OSA to hypertension. This chapter also contains a discussion of the current challenges of the outcomes of these research areas.

Obstructive Sleep Apnea: Introduction

The majority of cases of hypertension have unknown causes, whether hypertension could be considered primary or essential (Kaplan, 2011). Additionally, the severity of hypertension is largely determined by specific demographic features (age, sex, race, etc.), the magnitude of vascular damage from high blood pressure, and the presence of other risk factors (Kaplan, 2011, p. 15). The complicated etiology and pathophysiology of hypertension emanate from the heterogeneous nature of the disease (Izzo & Black, 2003). Multiplicative factors modulate blood pressure control (Heilperm, 2008). Epidemiologic studies have revealed that OSA in combination with other CV risk factors is associated with hypertension, which predispose patients to the risk of both cerebrovascular and ischemic heart disease (U.S Department of Health and Human Services, 2004, p. 1). The effective management of hypertension has been associated with considerable improvements in aged-adjusted death rates from stroke and heart disease irrespective of gender, age, race or socioeconomic status (U.S. Department of Health and Human, 2004, p. 1). However, follow-up studies conducted with multiple populations have indicated that morbidity and mortality rates are higher among patients receiving antihypertensive drug treatments compared to untreated patients with similar levels of blood pressure (Ben-Dov et al., 2007). These studies indicate that modest CVD

improvements could be due to: partial reduction in blood pressure, irreversible organ damage from hypertension, and other risk factors not properly addressed (Kaplan, 2011, p. 8). The strategic management of hypertension comes with knowledge of evaluation of other important risk factors. Clustering of this hypertension associated risk factors occurs approximately 50% of the time (Caceres et al., 2012). Identification of these associated risk factors can lessen the degree of coronary events, stroke, peripheral disease, or heart failure (Kaplan, 2011, p. 10). The numerous pathological mechanisms involve with OSA increase the risk of hypertension (Calhoun & Harding, 2010). Peppard et al., (2001) showed that even after adjustment of known risk factors for hypertension, there was a twofold risk increase for patients with AHI of 5-15/ hour and threefold increase for patients with AHI > 15 (Peppard et al., 2000, p. 1378).

Definitions: Obstructive Sleep Apnea and Hypertension

Diagnosis of *hypertension*, defined as blood pressure of 140mmHg/80 mmHg, is often challenge by the fact that considerable variability in measurements occurs (Kaplan, 2011). Sources of variation include inappropriate equipment, inaccurate reading, incorrect positioning of the arm, and observer bias (Kaplan, 2011, p. 25). Chang et al., (2002) reported 64-82% residual variability with systolic and diastolic measurements from inaccuracy of the device. In order to establish accuracy for in home, in office or in clinical studies, patients are advised to prevent marked changes induced by activity and position, keep a diary of activities, use computer-assisted diaries, use electronic monitors and obtain average values within the 24 hours (Kaplan, 2011, p. 39).

It is important to establish the clinical definition of OSA in order to fully comprehend the key differences between the sensitivity, specificity and predictive value of the various diagnostic techniques used in various studies (Frederick & George, 1999, p. 356). Guilleminault & Dement (1976) defined OSA as cessation of airflow for 10 seconds with 30 apneic events observed in both REM and NREM sleep observed during seven hours of sleep study (Frederick & George, 1999, p. 357). The diagnosis of OSA is confirmed by Apnea-Hypopnea Index (AHI) or Respiratory Disturbance Index (RDI) ≥ 5 events /hour during a polysomnography with monitored respiratory parameters (Kushida, et al., 1997). OSA is a chronic condition involving a characteristic closure of the airway at the supraglottic area (Mansfield & Naughton, 2005). This effect converges at the apnea termination, which causes the recurrent brief arousals throughout the night (Mansfield & Naughton, 2005, p. S2). OSAs are associated with variable drop in arterial oxygen saturation (SAO2) of various intensities (Mansfield & Naughton, 2005, p. S2). The International Classification of Sleep Disorders, 2nd edition, categorically diagnoses OSA as follows:

A. At least one of the following:

- complaints of unintentional sleep episodes during wakefulness, daytime sleepiness, unrefreshing sleep, fatigue or insomnia;
- awakenings with breath holding, gasping, or choking;
- bed partner reports loud snoring, and or breathing interruptions during the patient's sleep.

B. Polysomnography with the following results:

- scoreable respiratory events (apneas + hypopneas + Respiratory Effort – Related Arousals (RERA)/hr. of sleep ≥ 5/hr.);
- evidence of respiratory effort during all or a portion of each respiratory event (In the case of RERAs, respiratory effort is best detected by esophageal manometry); or

C. Polysomnography with the following:

- score able respiratory events (apneas+hypopneas+RERAs)/hr. of sleep ≥ 15/hr;
- evidence of respiratory effort during all or a portion of each respiratory event;

D. The disorder is not better explained by another current sleep disorder, medical or neurologic disorder, medication use, or substance use disorder (American Academy of Sleep Medicine, 2001).

The American Academy of Sleep Medicine defined OSA based on RERAs but not RDI (number of respiratory events per hour of monitoring time). The majority of sleep studies use RDI instead of RERA. However, most of the literature do use the OSA diagnostic criteria of AHI ≥ 5/hr. with symptoms or AHI ≥ 15/hr. with or without symptoms (Bradley & Floras, 2009). The ICD definitions do not include partial obstruction or complete obstruction to diagnose OSA.

The Practice Parameters of the American Academy of Sleep Medicine established a consensus statement in 1997 the evidence based recommendations for the diagnosis and management of OSA. Based on this evidence based guideline, the diagnosis of OSA must be established with sleep history, physical examination, and standard sleep testing (in laboratory polysomnography (PSG), or home testing with portable monitors (PM; Epstein et al., p. 266, 2009). PSG is routine test for clinical diagnosis and indicated for patients with high pretest likelihood of moderate to severe OSA (i.e., obese, heart failure, coronary artery disease, history of transient ischemic stroke, or significant arrhythmias (Epstein et al., 2009, p. 266). Diagnosis should be obtained in one of three settings: 1.as routine health maintenance evaluation; 2. as part of evaluation for patients with symptoms of OSA; and 3. as part of comprehensive evaluation of patients' high risk for OSA (Epstein et al., 2009, p. 264). The important features that are clinically relevant in the diagnosis for OSA includes increased neck circumference (>17 inches for men and 16 inches for women), body mass index (BMI > 30 kg/m^2), modified Mallampati score of three or four, presence of retrognathia, lateral peritonsillar narrowing, macroglossia, tonsillar hypertrophy, elongated/enlarged uvula, high arched/narrow hard palate, nasal abnormalities, and/or over-jet (Epstein et. al., 2009, p. 266).

OSA and Hypertension: Theoretical Constructs

Rothman (1976) recognizing that the occurrences of certain diseases were caused by multiple causes, in which no single factor can produce the disease itself, proposed a model that he termed a "*sufficient component cause model*". According to Rothman

(1976) a "*cause*" is a state of nature, act, or event that leads, or allows either by itself, or combination with other causes, a succession of events that will lead to an "*effect*" (Rao & Enterline, 1983). The "sufficient component cause model" represented the cause that would be estimative to produce the outcome as "*sufficient*" (Rao & Entreline, 1983, p. 268). Thus, Rothman (1976) believed that a sufficient cause is an amalgamation of condition that consequently would lead to the outcome in consideration (Rao & Enterline, 1983, p. 267). According to this model, a number of component causes make up the sufficient cause, which will operate sufficiently enough under various sets of component causes to act as "*sufficient cause*" (Martin, 2008). In other words, the sufficient component cause model embodies biologic relations in the form of involvement of factors in a sufficient cause (Vanderweele, 2009).

The term "*causation*" refers to the relationship between at the least two entities: the agent and the disease (Vineis & Kriebel, 2006). The sufficient component cause theory does not imply that there is a specific cause for a given disease in a given individual but rather the disease is smartly intertwined with multiple intersections which determines the association between given exposure and frequency of disease in a given population (Vineis & Kriebel, 2006). The associations can indicate that the exposure might cause the disease or the exposures are associated with difference in "*risk factors*" (Krieger, 1994).

According to this model, sufficient cause refers to "a set of minimal conditions and events" not necessarily gratuitous, that leads to the production of the disease (Allard

& Boivin, 1993). The components of each the conditions which are part of the sufficient cause, which will be called a "*component*" of the cause (Allard & Boivin, 1993, p. 37). The assemblage of the components of the disease would then lead to the development of the disease (Allard & Boivin, 1993, p. 37). Sufficient causes are basically disease producing process, in which the accumulation of the components would be sufficient enough for the expression of the disease (Allard & Boivin, 1993, p. 37).

Rothman (1976) further refined the sufficient component cause theory to take into account confounding and effect modification to pay attention to the relationships between "*necessary* and *component causes*". Rothman developed the sufficient component cause model which incorporated the "*sufficient causal complexes*, with *five component causes*" later termed as "*causal pie model"*. By bringing attention to these factors, Rothman was able to show that the strength of the association between the component cause and outcome depended on the prevalence of other components that influenced the specified change (Krieger, 1994, p. 891). Additionally, this concept explained that diseases were caused by mixtures of conditions or multiple conditions that together contributed to the development of the disease, and that various combinations of component causes can produce the disease; and that the multiple causes need not include any component cause in common (Labarthe, 2011, p. 541).

Aschengrau and Seage (2003) outlined that the basic features of the sufficient component cause model are as follows:

1. There is no single cause for the disease but a minimal set of conditions or events that would lead to the development of the outcome.

2. Each of the component causes is important in the sufficient component cause model; however, it is not necessary to identify all of the component causes in order to avert the disease.

3. There could be a number of sufficient cause for a given disease or outcome.

4. A component cause that must be existent in every sufficient cause of a given outcome is termed “necessary cause”.

5. The biologic occurrence of the outcome must parallel with the completion of a sufficient cause.

6. The components of the sufficient cause can act at different times and not necessarily concurrently.

The sufficient component cause model can help explain the theoretical structure of sufficient causes for OSA and hypertension. A *sufficient cause* can be interpreted in this case as if the risk factor for hypertension is present, then the presence of that risk factor, in this case OSA, leads to the increase risk of the disease. Additionally, the relationship between OSA and hypertension is an example of a chronic disease caused by an array of sources and risk factors. The association between hypertension and OSA is multifactorial, with a number of unique overlapping causal mechanisms (Punjabi, 2008). The source of interaction between component causes in the sufficient component cause

model as proposed by Rothman (1976) is the combined involvement of the component causes in a sufficient cause (Rao & Enterline, 1983). This theoretical construct supports the idea that OSA involves grouping of one or more of the sufficient causes and the factor that is part of more than one sufficient cause (Martin, 2008). The *components of a sufficient* cause can be simultaneous, or can be represented by a chain of events, in which one of the components can lead to another (Martin, 2008, p. 274). The physiologic changes allied with OSA bring a plethora of various changes that contributes to the etiopathogenic mechanism of hypertension, of which a single component cause may be insufficient to root the given disease (Cantolla-Duran et al., 2009). Studies have shown that the multitude of events and sources involved with OSA that lead to the changes in hypertension physiology are; the negative intrathoracic pressure, sympathetic activation, effects of hypoxia, oxidative stress, vascular endothelial dysfunction, metabolic, and dysregulation and inflammation.

Negative Intrathoracic Pressure

In OSA, the negative intrathoracic pressures generated are from the inspiration against a closed upper airway (Adegunsoye & Ramachandran, 2012). This results to negative intrathoracic pressure as low as -80cm H20, which affects both left and right ventricular function (Adegunsoye & Ramachandran, 2012, p. 4). Numerous studies showed that negative intrathoracic pressure lead to adverse consequence to left ventricular function thru elevating left ventricular transmural pressures and increasing afterload (Buda et al., 1979; Virolainen et al., 1995).

Sympathetic Activation and Hypoxia

In OSA, the arterial PCO2 is increased with the rise in arterial PO2 and SaO2 decrease which permitted the rise of the chemical drives (Cheng et al., 2010). As the total ventilator drive is greater than the arousal threshold, the arousal is generated to allow opening of the upper airway to resume airflow (Cheng et al., 2010, p. 6). The arousal threshold is linearly related to SWA. The higher the threshold, the higher the SWA, and closer to one during NREM sleep, while when the threshold is lower, the lower SWA or closer to zero during REM sleep (Berry & Gleeson, 1997). During regular sleep cycles, cardiorespiratory homeostasis is achieved through the coordination of both the respiratory and cardiovascular system (Khoo et al., 2011). The cardiorespiratory control mechanisms are direct consequences of variations in brain states that typically transpired during alternating cycles of NREM and REM sleep (Verrier et al., 2005). The CNS activations dynamically fluctuate to affect heart rate, blood flow, and ventilation (Verrier et al., 2005, p. 193). REM-induced surges facilitate the activation of sympathetic and parasympathetic nerve activity causing the surges and pauses in heart rhythm (Verrier et al., 2005, p. 193). In NREM stage, the coupling of the respiratory activity and cardiorespiratory centers resulted to the normalization of respiratory sinus arrhythmia, (Verrier et al., 2005, p. 193). NREM stage allowed stable sympathetic activity (Verrier, et al., 2005, p. 193). The cardiorespiratory homeostasis achieved during sleep is often altered among OSA patients. The mitigating effects of repeated arousals and intermittent hypoxia characteristic of OSA lead to restructuring of the control

mechanisms (Verrier et al., 2005, p. 194). These types of changes lead to interference in compensatory mechanisms to assist blood pressure management and remove forebrain influences on hypotension or hypertension (Verrier et al., 2005, p. 194).

Hypoxia is also an important intermediate mechanism that increased the development of hypertension among OSA patients (Leung et al., 2012). These pathological effects acutely lead to hemodynamic and autonomic changes that alternate between the apneic and ventilator phases (Leung et al., 2012, p. 221). Heart rate and blood pressure increase happens five to seven seconds after the apneic termination (Leung et al., 2012, p. 221). The OSA related sleep arousal accordingly leads to peak in respiration with the pits of SaO^2 (Leung et al., 2012, p. 221). The hypoxia experienced during OSA contributes to reduction in myocardial oxygen demand, depression of the myocardial contractility, and elevation of left ventricular afterload (Leung et al., 2012, p. 221). The sympathetic activation caused the hypoxia driven events which increased heart rate (Leung et al., 2012, p. 221). The relationship between these intermediates is shown in the figure below.

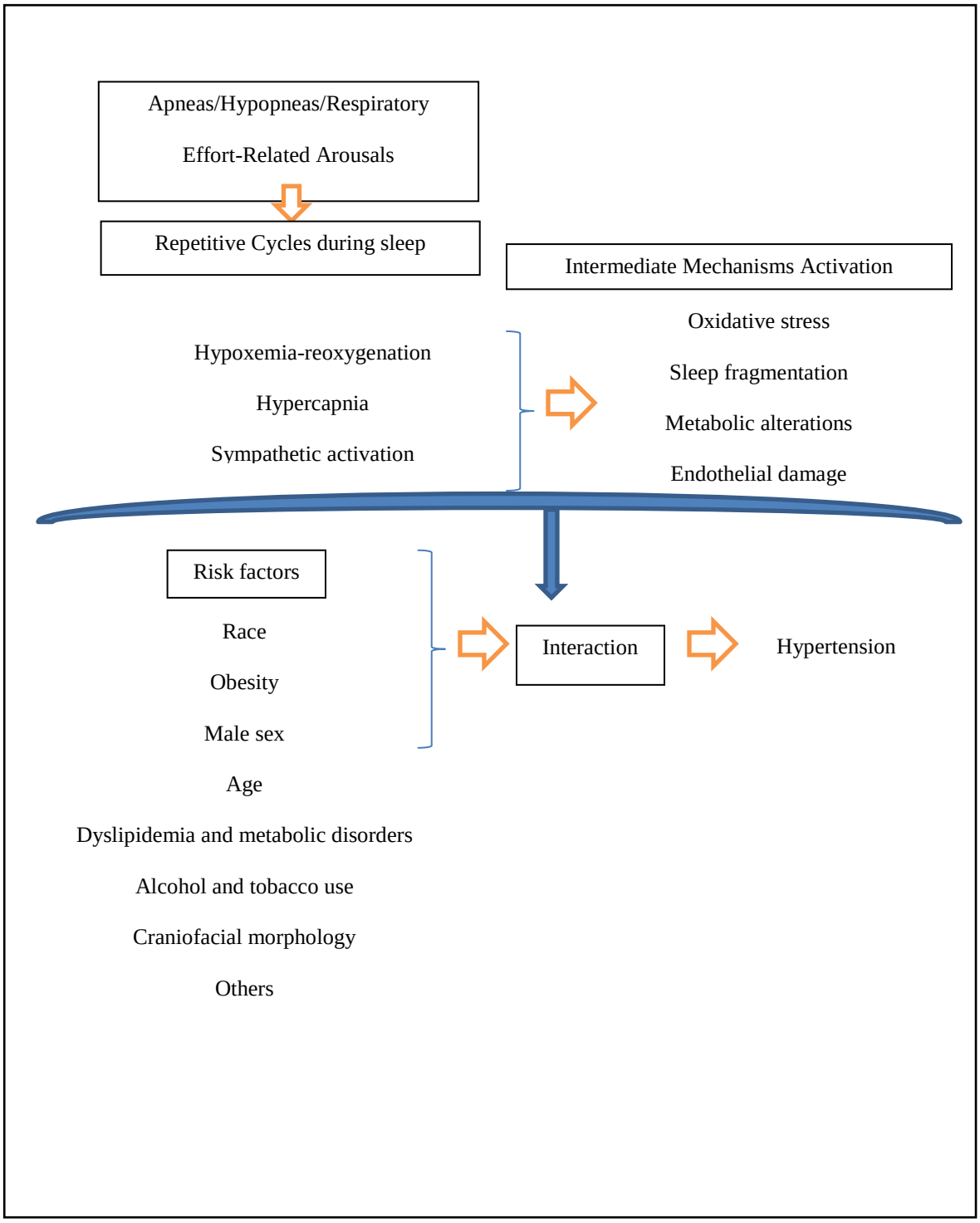
Apneas/Hypopneas/Respiratory
Effort-Related Arousals
Repetitive Cycles during sleep
Intermediate Mechanisms Activation
Hypoxemia-reoxygenation
Hypercapnia
Sympathetic activation
Oxidative stress
Sleep fragmentation
Metabolic alterations
Endothelial damage
Risk factors
Race
Obesity
Male sex
Age
Dyslipidemia and metabolic disorders
Alcohol and tobacco use
Craniofacial morphology
Others
Interaction
Hypertension

Figure 1. Theory of sufficient component cause model. The sufficient component cause model helps explain the relationship between the unique overlapping causal mechanisms that can lead o or affect the pathophysiologic changes involved in the relationship between OSA and hypertension. Adapted from "Obstructive sleep apnea/hypopnea and systemic hypertension" by Cantolla et al., 2009, *Sleep Medicine Reviews.13*, pp.323-331

The distinctive respiratory disturbance associated with OSA is the complete cessation of breathing that leads to apnea or partial cessation of breathing that led to hypoventilation (Krieger, 2005). This disturbance has three pathophysiologic consequences: 1. hypoxemia-reoxygenation leading to arterial blood gas abnormalities; 2. consistent arousals and transformation to light sleep stages; and 3. large dips in intrathoracic pressure (Krieger, 2005, p. 237).

All these pathologic disturbances cause increase in sympathetic neural response. The sympathetic activation originated from the characteristic apneic events associated with OSA which lead to escalation of breathing, high negative intrathoracic pressure, persistent hypoxia, reoxygenation, and oscillations in autonomic activity (Krieger, 2005, p.238). The pronounced and severe apneic events eventually impact the hemodynamic reflex changes and sustained sympathetic activation (Krieger et al., 2005, p. 238). The elevation in sympathetic response causes activation of vascular smooth muscle to vasoconstriction which eventually leads to elevation of blood pressure (Fletcher et al., 2002). These heightened sympathetic activities stimulate production of angiotensin II, and renin in the kidneys (Fletcher et al., 2002. p. 627). The sustained sympathoexcitation as the likely mechanism of the OSA-hypertension relationship had been observed among OSA patients (Bao & Fletcher, 1997; Carlson et al., 1993; Waradeker et al., 1996).

Oxidative Stress

The marked oxidative stress associated with OSA comes from the marked decreased in arterial oxygen saturation (Adegunsoye & Ramachandran, 2011, p. 5). The arterial oxygen desaturation causes similar effects brought about by recurrent episodes of ischemia-reperfusion injury (Yamauchi et al., 2005). This type of injury causes damage to the heart attributed to production of reactive oxygen species (ROS) during reoxygenation (Yamauchi et al., 2005, p. 1674). A number of studies had shown that oxidative stress associated with OSA, including increases in ROC production were seen among OSA patients (Dyugovskaya et. al., 2002; Schulz et. al., 2000). Yamauchi et al., (2005) similarly showed that urinary 8-OHdG excretion, a marker of oxidative stress, were higher among OSA patients.

Vascular Endothelial Dysfunction

Repetitive hypoxia associated OSA syndrome can lead to vascular endothelial dysfunction, (Ip et al., 2004; Ip et al., 2000). This effect is caused by reduction in endothelial nitric oxide production at the transcriptional and posttranscriptional levels as well as the rise of reactive oxygen species (ROS; Liao, et al., 1995; McQuillan, et al., 1994). The increased production of ROS causes oxidative stress, destabilization of eNOS messenger RNA to limit production of cofactors necessary for NO production (Laursen et al., 2001; Takemoto et al., 2002). The short and long term effects of this oxidative stress lead to decline in eNOS activity thru subdual of phosphorylation (Takemoto et al., 2002, p.57). This reduction in NO production affects OSA patients to develop vascular

diseases, (Takemoto et al., 2002, p. 60). The repetitive arousals commonly associated with OSA also lead to endothelial damage (Atkenson et al., 2009). The Nurses' Health Study involving 71, 617 female participants aged 45-65 years showed that self-reported sleep reduction was associated with increased incidence of coronary heart disease (993 coronary events; Ayas et al., 2003). The study participants who had fewer than five, six, or seven hours of sleep reported age adjusted relative risks of coronary heart disease of 1.82 [1.34-2.41], 1.30 [1.08-1.57], and 1.06 [0.89-1.26] 95% Cis (Ayas et al., 2003, p. 205).

Metabolic Dysregulation

Metabolic dysregulation plays a pivotal role in the association between OSA and various cardiovascular diseases (Butt et al., 2010). The main drivers that impact the associated role of these factors are also driven by elevated sympathetic activity, changes in neuroendocrine function, and release of proinflammatory cytokines (e.g. interleukin-6, tumor necrosis factor, and adipocyte derived factors (Aurora & Punjabi, 2007). Five observational studies that looked at patients aged 40-75 years of age with symptoms of snoring or apneas were associated independently with increase in glucose, insulin resistance, or increase in risk for incident diabetes (Al-Delaimy et al., 2002; Elmasry et al., 2000; Enright et al., 1996; Grunstein et al., 1995; Jennum et al., 1993).

Inflammation

There are various markers of inflammation that posed as significant risk factors for cardiovascular disease that are associated with OSA (Nadeem et al., 2013). These

markers of inflammation include tumor necrosis factor alpha (TNF-α), acute phase factor C-reactive protein (CRP), interleukin 6 (IL-6), etc. (Gozal & Gozal, 2008). These inflammatory markers acutely affect cardiac function leading to alterations in cardiac function such as hypertension and atrial fibrillation (Almendros et al., 2011). Oxidation of low density lipoprotein (LDL) due to endothelial injury had been observed among hypoxic OSA patients compared to normal controls (Walli, et al., 1998). Additionally, Carlson et al., (1993) significantly observed that among OSA patients there were more vessel resistance compared to controls. Blunted vasodilator response in the forearm to acetylcholine, as a measure of endothelial injury, were also more apparent among OSA patients compared to carefully match obese subjects without OSA (Kato et al., 2000).

Studies of the Relationship Between OSA and Hypertension

OSA is an independent risk factor for the development of hypertension (National Sleep Foundation, 2005). The association between OSA and hypertension has been established by the scientific literature since 1908s (Santos et al., 2006). The earlier findings were mixed and possibly flawed due to the presence of confounders (e.g., alcohol consumption, caffeine intake, and family history; Sadikot et al., 2008). Subsequently, many published studies considered the flaws in earlier reports of the association between OSA and hypertension. In the past few years, extensive evidence obtained from cross-sectional, longitudinal and treatment studies later reported significant associations between OSA and hypertension (Sadikot et al., 2008, p. 65). In a cross sectional study of 147 men and women, aged 30-60 years old from the Wisconsin Sleep

Cohort Study, the results of the study revealed that mean blood pressure were higher among patients with sleep apnea (AHI ≥ 5) versus patients without sleep apnea (131/80 ±.7/1.1 mmHg versus 122/75 ±.9/1.2 mmHg, $p < 0.05$; Hla et al., 2008). The investigators determined the odds ratio of OSA to hypertension after adjusting for confounders such as blood pressure status at baseline, obesity, neck, waist circumference, age, sex, weekly alcohol, and cigarette use (Hla et al., 2008, p. 795). The investigators also found a significantly higher proportion of patients with sleep apnea, or a history of snoring that experienced higher variability in blood pressure compared to control subjects ($p < 0.05$; Hla et al., 2008, p. 795). Sleep apnea patients also showed higher odds ratio of hypertension in a dose response fashion (Hla et al., 2008, p. 795). Grote et al., (1999) also, cross sectionally analyzed the relationship between OSA and hypertension among 1087 males and 103 females aged 25 to 85 years old in a sleep study clinic. The study analysis revealed that as adjusted by age, BMI, tobacco, alcohol, and cholesterol, an AHI value of ≥40 versus AHI value of ≤ 5 was an independent predictor of systemic hypertension [ORs 4.1] (95% CIs, 2.7-6.5; Grote et al., 1999, p. 1875). The largest cross sectional study to provide the evidence to support OSA-hypertension relationship came from the Sleep Heart Health Study (Nieto et al., 2000). 6132 patients, aged 40 years or older were recruited to participate in a cross-sectional study conducted between the period of November 1995 to January 1998 (Nieto et al., 2000, p. 1829). The main parameters were AHI index, arousal index, percentage of sleep below 90% oxygen saturation, and history of snoring (Nieto et al., 2000, p. 1829). The study results

determined that the prevalence of hypertension were higher among 6132 subjects exposed to AHI and other sleep parameters (Nieto et al., 2000, p. 1820). Despite the possibility that the results could be influenced by body mass index; the study showed that odds ratio for hypertension were highest among patients with AHI ≥ 30 compared to AHI ≤ 1.5 (1.37, versus [1.03-1.83], 95% CIs, $p = 0.005$; Nieto et al., 2000, p. 1831). The OSA and hypertension association was seen regardless of sex, age, ethnic groups, and weight (Nieto et al., 2000, p. 1832). Moreover, Hass et al., (2005) in a cross sectional study of OSA patients obtained from the Sleep Heart Cohort Study showed that when patients' ages were stratified by 40-59 years old, to ≥ 60 years old, the association between OSA and hypertension were more pronounced among younger patients compared to patients ≥ 60 years old, (AHI was significantly associated with higher odds ratio of hypertension , (AHI =15 to 29.9, ORs 2.38 [95% CIs, 1.30 - 4.38]; AHI = 30, ORs 2.24 [95% CIs 1.10 - 4.54]; Haas et al., 2005).

Of particular importance is the first longitudinal studies conducted by Peppard et al., (2000) which analyzed the relationship between OSA and hypertension. The Wisconsin Sleep Cohort Study (2000) looked at subgroup of state employees from four Wisconsin state agencies that had overnight sleep studies at four year intervals (Peppard et al., 2000, p. 1378). After adjusting for systemic hypertension, BMI, neck circumference, waist, and hip perimeter, age, gender, tobacco, and alcohol status, the odds ratio for the presence of hypertension was 1.42 (95% CIs, 1.13-1.78; Peppard, et al., 2000, p. 1378). Patients had an AHI index of 0.1 – 4.9 events per hour [95% CIs, 1.29-

3.17] at baseline as compared to none, AHI index of 5.0-14.9 events per hour, and 2.89 with AHI ≥ 15, (95% CIs, 1.46-5.64; Peppard et al., 2000, p. 1378). In another longitudinal analysis of the relationship between OSA and hypertension, the first National Health and Nutrition Examination Survey (n = 4810) measured patients aged 32 -59 years old using Cox proportional hazards models (Gangwisch, 2006). Patients were followed-up between 1982 and 1992 to determine the incidence of hypertension (defined by physician diagnosis, hospital record, or cause of death over 8-10 year follow-up) among healthy sleep deprived subjects. The results of the study revealed that among patients who had sleep durations of ≤ 5 hours/night were highly associated with increased risk of hypertension (HRs, 2.10; 95% CIs, 1.58-2.79; Gangwisch et al., 2006, p. 833).

There were also a number of open label studies conducted to determine the effect of treatment with CPAP on blood pressure levels of patients with OSA (Cantolla et al., 2009). Since 2009, there were already 28 of these open label studies. The majority of these open label studies on the effect of CPAP on blood pressure among patients with OSA with or without hypertension syndrome showed that patients who were treated with CPAP therapy had significantly reduced blood pressure (p = 0.05; Akashiba et al., 1999; Borgel et al., 2004; Doherty et al., 2005; Heitmann et al., 2004; Hla et al., 2002; Huang & Chen, 1996; Martinez-Garcia et al., 2007; Robinson et al., 2008; Tun et al., 2003; Wilcox et al., 1993). There were also a number of cross-over and parallel group studies that had looked at the relationship between OSA and hypertension. One of these cross-over, parallel group studies shown that the effect of CPAP on blood pressure among patients

with OSA similarly showed dropping of systolic blood pressure of 2.00 (-5,07-9.07), and diastolic blood pressure of 2.00 (-2.38-6.38) among patients treated with 29 weeks of CPAP (Barbe et al., 2004).

The overall results of these studies strongly suggested that dose response association between OSA and hypertension were independent of confounding factors. The sample sizes of the majority of studies were performed in large enough sample sizes to obtain statistical significance. The majority of the studies however were performed among white Caucasian men. So the lack of knowledge of associations, much less the causality between OSA and hypertension among women, men and specific races are enormous. Additionally, obesity is typically related with the association between OSA and hypertension among White populations (Wolk et al., 2003). The interaction between obesity and OSA stemmed from involvement of similar multiple pathophysiological mechanisms and consequences (Davy et al., 2004). However, obesity is not a common problem among Asians (Ip et al., 2001). The lack of knowledge of the association between OSA and hypertension among Asians and the effects of other risk factors presents additional research opportunity

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Table 2

Summary of Epidemiological Studies Evaluating Patients With OSA and Hypertension

Authors/ Year of Publication/ Publication	Population	Design	Subject (*n*) age	Age	Sleep evaluation	Results hypertension (BP>140/90 mmHg) or hypertension (BP> 160/100 mmHg)	Parameters
Grote et., al/1999/ *Journal of Hypertension*	Sleep study patients	Cross-sectional	6120 men and women	60	Polysomnography	Respiratory disturbance index higher among patients with BP 160/95 mmHg, un controlled hyper tension increased significantly as SRBD activity increased (X^2, $p <$ 0.05)	Age, body mass index, alcohol, smoking, and daytime blood gases
Grote et., al/2000/ *Archives of Internal* Medicine	Household of two counties of southern Pennsylvania (Dauphin and Lebanon)	Cross-sectional	4364 men and 12,219 women	20-100	Polysomnography	Prevalence of moderate to severe sleep disordered breathing men -59.3 (44.4,	Age, BMI, sex, menopause status, use of HRT, alcohol use, and smoking

						73.1), women - 51 (27.1, 74.6). Odds ratio moderate to severe 6.85 (2.02-26.36). Mild 2.29 (1.43-3.61)	
Nieto et.,al/2000 /*Journal of American Medical Association*	Population based cohort studies	Cross-sectional	11,053 men and women	>40	Polysomnography	Odds ratio1.25 (1.08-1.44) for AHI (1.5-4.9),1.57 (1.35-1.81) AHI (5-14.9),1.73 (1.43-2.10) AHI (15-29.9),2.27 (1.76-2.92) AHI >30	Age, ethnicity (No Asians), smoking, alcohol use, body weight, BMI, neck circumference, waist to hip ratio
Bixler et.,al /2000/ *Archives of Internal Medicine*	Household of two counties of southern Pennsylvania (Dauphin and Lebanon)	Cross-sectional	4364 men and 12,219 women	20-100	Polysomnography	Prevalence of moderate to severe sleep disordered breathing men -59.3 (44.4, 73.1).Women – 51 (27.1,74.6). Odds ratio moderate to severe 6.85	Age, BMI, sex, menopause status, use of HRT, alcohol use, and smoking

						(2.02-26.36) Mild 2.29 (1.43-3.61)	
Peppard, et., al/2000/*New England Journal of Medicine*	State employees	Longitudinal	1189 men and women	>40	Polysomnography	Odds ratio 1.66 (1.35-2.03) AHI 0.1-4.9,2.74 (1.82-4.12) AHI 5.0-14.9,4.54 (2.46-8.36) AHI >15	Age, sex, BMI
Lavie, et., al/2000/ *BMJ*	Patients from sleep laboratory	Cross-sectional	2677	20-85	Polysomnography	Multiple regression analysis *ß* (95% CI) AHI >1,0.10 (0.07-0.13) p = 0.0001	Age, sex, BMI, neck circumference, waist to hip ratio, smoking, hypertensive
Hass, et., al/2005/ *Circulation*	Sleep Heart Study participants	Cross-sectional	6120	40-60	Polysomnography	Odds ratio 1.41 (0.98–2.03) AHI 1.5-4.9 1.49 (1.02–2.17) AHI 5.0-14.9 1.66 (1.03–2.67) AHI 15-29.9 1.09 (0.58–2.06) AHI >30	Age (No Asians) ,race, gender, BMI, smoking history, waist to hip ratio
Hla, et., al/ 2008/*Sleep*	State employees (Wiscon	Cross-sectional	147 men and women	30-60	Polysomnography	Odds ratio 2.0 (1.2-3.2)	Age, sex, BMI, waist, hip

sin)		moderate vs. none 2.9 (1.5-5.6) severe to none	girth, health, BP, smoking, and alcohol

Risk Factors Associated with OSA and Hypertension:

Review of Current Literature

Age

Age is an important risk factor in the development of both OSA and hypertension. Age related changes in arterial structure and function lead to decreased distensability of the large vessels (Franklin et al., 1997). The enlargement of the vessels contributes to increase pulse wave activity, increase myocardial demand, and late systolic blood pressure augmentation (Franklin et al., 1997, p. 308). The Nurses' Health Study I, a large cohort of 83,882 non- hypertensive women aged 27 to 44 years, determined that older age, aside from other four risk factors (e.g., BMI, physical activity, frequency of aspirin use, and alcohol consumption) increased the incident hypertension (Forman et al., 2009). Participants aged 50 and younger had the lowest risk for all the five factors associated with hypertension, while women aged 61 and older had a hazard ratio of 0.62 (95% CIs, 0-.51-0.75; Forman et al., 2009, p. 401). Cordero et al., (2011) in a multicenter, cross-sectional and observatory registry of 10,743 patients with hypertension from cardiology and primary care clinics showed that 55.4% of patients had controlled blood pressure and slighter higher mean age of 66 years old. The STRONG Heart Study (2006) a longitudinal study of 4549 American Indian showed that hypertension incidence was

>38% (p= 0.051) higher among >65 years of age compared to patients aged 45-54 years of age (Wang et al., 2006).

Large epidemiological studies have been conducted exclusively to look at the effects of controlling hypertension on the aging population. One of these studies, Systolic Hypertension in the Elderly (SHEP) study screened 447,921 and enrolled 2,365 subjects assigned to active treatment (chlorthalidone 12.5 or 25 mg/day, and as needed, addition of atenolol 25 or 50 mg/day or reserpine, 0.05 or 0.10 mg/day), and 2, 371 to placebo, (SHEP Cooperative Research Group, 1991). The average blood pressure 170 mmHg/77 mmHg, with participants mean age of 72 years. The main outcome measures were nonfatal and fatal (total) stroke, while the secondary measures included cardiovascular and coronary morbidity and mortality, all-cause mortality, and quality of life measures. The results of the study showed that after an average follow-up of 4.5, the average blood pressure among the placebo group was 155 mmHg/72 mmHg, while the average blood pressure for the treated group was 143 mmHg/68 mmHg, (SHEP Cooperative Research Group, p. 3244, 1991). The 5-year incidence of total stroke was 5.2 per 100 participants for active treatment and 8.2 per 100 for placebo. Additionally, the relative risk by proportional hazards regression analysis was 0.64 (p = .0003) for the secondary end point of clinical nonfatal myocardial infarction plus coronary death, while the relative risk was 0.73 for major cardiovascular events (relative risk, 0.68) and the relative risk was 0.87 for death from all causes.

Bixler et al., (1998) and other several studies have shown that OSA prevalence increases with age. The study also showed that among men, OSA based on AHI ≥ 10 events/h was 3.2%, 11.3%, and 18.1% among 20- to 44-year, 45- to 64-year, and 61- to 100-year age groups, respectively (Bixler et al., 1998, p. 2289).

With advancing aging, pathologically it affects hypertension by contributing to increase in large arterial stiffness (Benetos et al., 2002). While, symptomatically in a majority of men and women aged 45 and older, manifestations of sleep related difficulties are highly common (Bixler et al., 2001).

Indeed it has been shown in several researches that age increased the prevalence of OSA associated to hypertension; however, whether it increases the risk of prevalence of OSA association to hypertension among middle aged Asians is uncertain.

Craniofacial features

Craniofacial features play a significant effect on the occurrence of OSA among Asians (Aihara et al., 2012). Davidson et al., (2005) postulated that evolutionary changes in the upper respiratory tract inclined men to OSA. The study revealed that among 133 male with OSA who underwent unattended multi-channel home sleep studies had positive correlation between AHI, klinorchy, laryngeal descent, and craniobase angulation (Davidson et al., 2005, p. 497). Numerous studies involving the use of various measures including radiography, computerized tomography, and magnetic resonance imaging showed that craniofacial abnormalities associated with OSA include retrognathia, tonsillar hypertrophy, enlarged tongue or soft palate, inferiorly positioned

hyoid bone, maxillary and mandibular retro position, and decreased posterior airway space can narrow upper airway dimensions (Cistulli et al., 1996). Aihara et al., (2012) in a cross sectional study of 134 Japanese male patients revealed from multiple regression analysis that age, BMI, position of hyoid bone, and proximal airway resistance were significantly related to AHI ($p < 0.05$). Chang et al., (2008) in a cross-sectional study of 84 males and 15 female Chinese patients from sleep centers in Taipei Veterans General Hospital from July 2002 to June 2006 craniofacial measurements of gnathion-gonion, anterior superior hyoid mandibular plane, posterior nasal spine to the velum tip, and widest point of the soft palate were positively correlated to AHI.

Regardless of the absence of craniofacial abnormalities, slight difference in the maxillary or mandibular size can be a risk factor to the development of OSA (Punjabi et al., 2008). A qualitative and meta-analysis of the literature explained that mandibular body length best predicted the increased risk of OSA (Miles et al., 1996).

However, differences in craniofacial morphology can explain the variability of risk among certain ethnic groups (Punjabi et al., 2008, p. 139). A study conducted among Chinese patients revealed that the crowded upper airway and relative retrognathia compared to Whites contributed to OSA risk (Lam et al., 2005). The craniofacial features, like shorter cranial base and acute cranial base flexure affected the incidence of OSA of other Asians (Li et al., 2000). Based from these evidences, clearly it showed that given the differences among Asians groups, studying the effects of these craniofacial

differences in the risk of OSA and its relationship to hypertension is of paramount importance.

Obesity

The Wisconsin Sleep Study, the Sleep Heart Study, Cleveland Family Study and others have shown that obesity is not only a significant risk factor for OSA but for hypertension as well (Punjabi, 2008). Moreover, the Wisconsin Sleep Study described a one standard deviation in BMI was associated with four-fold intensification OSA prevalence (Young et al., 1993). Epidemiological evidence among various White, Korean, and Chinese populations had also described excess body weight as highly correlated with increased in OSA prevalence (Duran et al., 2001; Ip et al., 2001; Ip et al., 2004; Kim et al., 2004; Peppard et al., 2000; Young et al., 1993). Epidemiological evidence among hypertension studies had also shown that obesity was also associated with inducing and accelerating renal complications in essential hypertension (Narkiewicz, 2006). However, an interesting observation made by studies conducted abroad showed that while Asians were less obese than Whites, the disease prevalence for a given sex, age, and BMI was higher compared to Whites (Li, et al., 2000; Ong & Clerk, 1998).

Despite the vast amount of evidence to support increased prevalence of obesity to OSA and hypertension, controversy still remains as to whether this risk factor reflect an increase risk of OSA and hypertension among middle-aged Asians in the United States.

Summary

Both OSA and hypertension are pervasive disorders that affect significant proportion of the United States population. The sufficient component cause theory supports the ideology of multifactorial etiology in the association between OSA and hypertension. Asians are underrepresented in OSA and hypertension studies, even as their great number in the US population is steadily increasing. There have been significant amount of studies that had shown the association between OSA and hypertension. Again these studies do not significantly represent Asians, thus these observed OSA and hypertension relationships have not been fully recognized. A better understanding of the factors contributing to the observed OSA and hypertension association among Asians is warranted. Knowledge of other mitigating risk factors like craniofacial features might inform the development of specific management, treatment and prevention strategies that can confer optimization of treatment of these diseases.

Chapter 3: Research Method

Introduction

OSA-hypertension epidemiology has been well researched among predominantly White populations; whereas data for middle-aged Asians are limited. The compelling evidence of the association of OSA and hypertension has mostly been based on White populations specifically those residing in North America, Europe, and Australia and may not be applicable to Asians (Villanueva et al., 2005). Studies done in Asia indicate that the prevalence rate of OSA among Asians is probably comparable to or even higher than the rate among U.S and European Whites (Ip et al., 2001; Kim, et al., 2004). However, these rates could be different from the actual rates among Asians living in the United States. The difference in rates seen in various studies can be attributed to a number of factors that may confound the results, including differences in sleep study techniques, clinical outcomes, genetic factors, and diet and lifestyle (Villanueva et al., 2005, p. 419). The difference in rates can also be attributed to differences in fundamental characteristics such as age, sex, person, place, time, and race (Labarthe, 2011). Although a number of epidemiological studies linking OSA with increased risk of hypertension have been performed, few studies using similar methods have observed these relationships among middle-aged Asians in the United States. It is also uncertain whether in the United States OSA is common among Asians and if OSA is also associated with hypertension.

This section of the study addresses the research design and rationale, methodology, and threats to validity.

Research Design and Rationale

A cross-sectional study design was used to determine (a) the prevalence rate of OSA among middle-aged Asian patients (Chinese, Filipino, Vietnamese, Asian Indian, Korean, Taiwanese, Japanese, and Singaporean) in San Jose, CA; (b) the association between OSA and hypertension, and (c) the association of other risk factors--body mass index (BMI); Mallampati score (MS); the Epworth Sleepiness Scale (ESS), and Apnea-Hypopnea Index (AHI) with hypertension as the outcome. The cross-sectional design of this study was the suitable study design to describe the burden and distribution of OSA in association with hypertension among this population of interest (Babbie, 2010). This study design also allowed me to make observations about the prevalence and characteristics of this disease in a distinct population during a certain period of time (Gordis, 2004, p. 195). The general design of a cross-sectional study consist of looking at a slice of the population to examine characteristics associated with a disease by comparing cases to noncases and performing predefined measurements or ascertainments (Gordis, 2004, p.196). This can be accomplished by examining a population of *n* persons for the study, then identifying the presence or absence of the disease for each subject (Gordis, 2004, p. 197). This study design allows the determination of prevalent cases at a fixed point in time. One constraint of this study design is that although association may be obtained for the possible risk factor(s), temporal association cannot be highly determined (Gordis, 2004, p. 198). This type of study design is appropriate for determining the prevalence of OSA with hypertension (Gordis, 2004, p. 195). The other

limitation of a using cross-sectional study design is that the confounding factors may not be equally distributed between groups (Babbie, 2010, p. 106). This unequal distribution of confounding factors can lead to bias and misinterpretation (Babbie, 2010, p, 106). Biases include selection, recall, length, and biased sampling. Selection bias can be addressed by ensuring that the study is powered enough to represent the target population. Recall bias can be addressed by clearly describing the problem and gaining a thorough understanding of the available evidence before data collection (Varkevisser et al., 2003). A clearly defined problem can enable the investigator to formulate specific objective(s) and sample the right population of interest (Varkevisser et al., 2003, p.195). Length biased sampling can be eliminated by knowing the duration of the disease of interest to avoid overrepresentation or underrepresentation of the said disease (Varkevisser et al., 2003, p. 195). The other variables of interest were age, gender, smoking consumption, body mass index (BMI), Epworth Sleepiness Scale (ESS), Mallampati score (MSS), and Apnea and Hypopnea (AHI).

Methodology

Population

The data that were generated for this study originated from patients living in San Jose, CA. The target populations for this study were Asians (Chinese, Filipino, Vietnamese, Asian Indian, Korean, Taiwanese, Japanese, and Singaporean) residing on southern side of San Jose, CA who had visited the sleep clinics between January 1, 2008 to December 31, 2011. A total of 462 middle-aged Asian patients were needed to

perform this study and were randomly selected from three major sleep study clinics in San Jose, CA. The recruitment and selection of the eligible patients were accomplished by random sampling. The inclusion criteria for these patients were the following: (a) men and women between 35 and 60+ years of age who had observed apneas, daytime fatigue, daytime sleepiness, or snoring who were referred to sleep study clinics; (b) diagnosis of OSA verified by overnight polysomnograms, and (c) a systolic blood pressure [SBP] level of 140mmHg, and a diastolic blood pressure [DBP] level of 90 mm Hg). Eligible patients needed to have a completed physical examination. The exclusion criteria for the study included patients with physical or psychological incapacity, no self-reported history of hypertension, no current or self-reported treatment for OSA, no previous treatment for snoring or any previous CV event (myocardial infraction, unstable angina, transient ischemic stroke, or attack, myocardial revascularization), chronic disease, and drug or alcohol addiction. Patients were also excluded if they had severe congestive heart failure (NYHA class IIIb or IV), known cardiomyopathy, valvular disease, coronary artery disease, diabetes mellitus, current active liver disease, unexplained elevated serum creatine kinase (CK > 3XULN), cancer, uncontrolled hyperthyroidism, or other important comorbidities.

Sampling and sampling procedures

The sample population for the study was independently and randomly selected from three sleep study clinics in San Jose, CA. The sample size needed was calculated and a third of the sample was collected from each clinic.

A simple random sampling procedure was used to select the study participants. The research study of interest involved widely dispersed large populations of patients. The use of simple random sampling allowed equal opportunity for all sets within the population to be sampled (Anderson & Finn, 1997). In cross-sectional studies, the power is estimated by factoring in the sample size among the exposed and nonexposed with the desired confidence interval (Portney & Watkins, 1993, p. 236). In order to determine a sample size that would be sufficient to power the study, the following considerations were used: margin of error -- 5%; confidence level --95%; estimated prevalence of OSA based on limited studies among Asians outside of the United States -- 4%, (Cantolla, et al., 2009; Kamil, et al., 2007; Kim, et al., 2004; Punjabi, 2008; Vozoris, 2012). The sample calculation based on the following equation:

$$N = \frac{t^2 \times p(1-p)}{m^2}$$

Where *n* is the sample size, *t* is confidence level at 95% (standard value of 1.96), *p* is the estimated prevalence, and *m* is the margin of error at 5% (standard value of 0.05) Kadam & Bhalerao, 2012).

$$n = \frac{1.96^2 \times .4\ (1-.4)}{0.05^2}$$

$$n = \frac{3.8416 \times .4\ (.6)}{}$$

$$n = \frac{0.0025}{.9219}$$

$$n = \frac{0.0025}{460}$$

460 divided by three clinics is 153.333. The number of subgroups in each of the three clinics to be sampled is an important consideration in the study. Because an equal number of male and females subjects in each of the three clinics was considered, *n*=153.33 will be rounded to whole persons to154.

Based from this calculation, the number of subjects needed for the analysis is 462 (Kadam & Bhalerao, 2010). The total patients (*n*) equals' 462 subjects will be divided among the three sleep clinics. The total patient (*n*) for each sleep clinics is 154. A schematic representation of the sampling strategy is presented in the figure below.

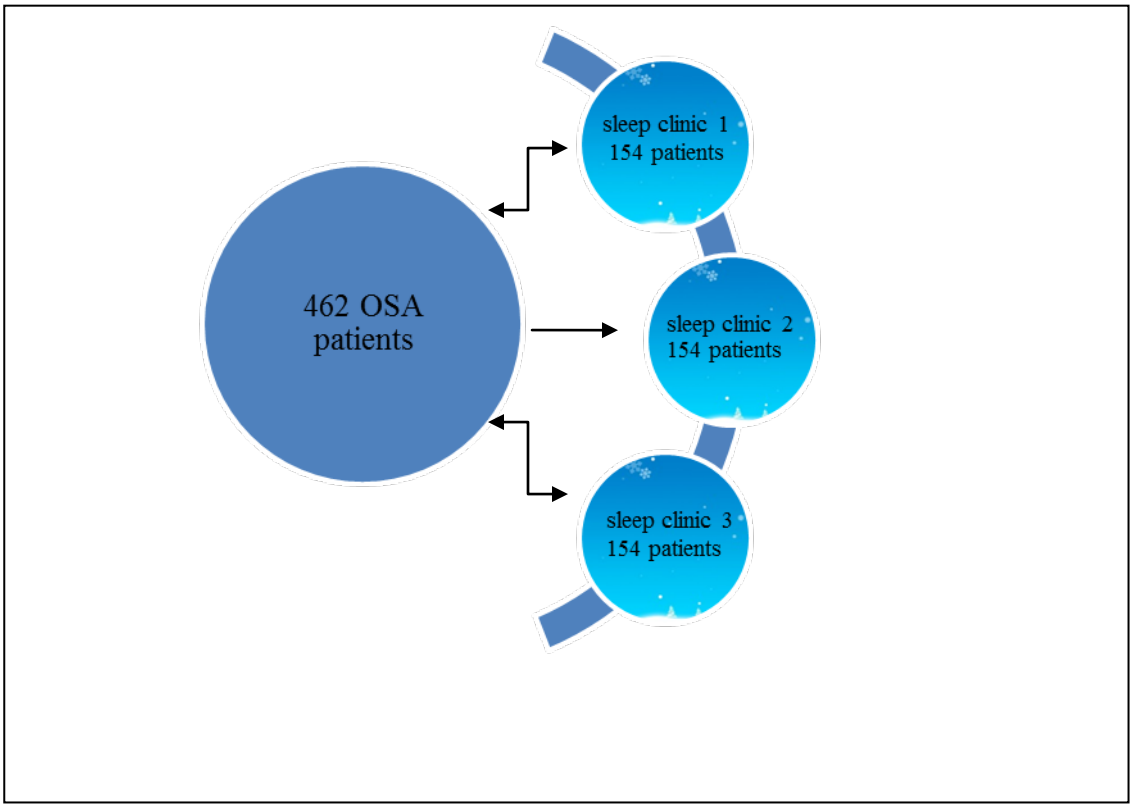

Figure 2. Sampling design

Procedures for Recruitment, Participation, and Data Collection

All the study subjects who were recruited were approved by the Human and Research Committee of Walden University (Institutional Review Board approval 03-25-14-0153639). The study was also conducted in accordance to the principles of human research protections as specified by the Declaration of Helsinki. All study subjects who qualified for the study had to meet the study inclusion, and exclusion criteria. The data that were collected for the study were obtained with the use of paper and electronic medical records (EHR). Since, this study only used secondary data; all data collected were subjected to confidentiality. The data regarding patient demographics, patient's history, anthropometric measurements, physician diagnoses, and laboratory results were extracted from paper and electronic health records. In order to ensure data confidentiality, I obtained sample confidentiality agreement from each of the sleep study clinics. The data collected were extracted from patient records that were identified by the medical staff as Chinese, Filipino, Vietnamese, Asian Indian, Korean, Taiwanese, Japanese, and Singaporean. The cross-sectional nature of the study, as well as the use of paper and electronic health records does not require debriefing patients, or any need for follow-ups. The physician in charge in each of the three sleep study centers in San Jose, CA provided permission to use data obtained from the paper and electronic health record.

Sample data use agreements were obtained to ensure that data obtained were limited to the prevalence rate of OSA in association with hypertension among Asian Americans in San Jose, CA.

Clinical Definition of OSA

The clinical definition of *OSA* was in accordance with the Adult OSA Task Force of the American Academy of Sleep Medicine (2009) as "occurrence of daytime sleepiness, loud snoring, witnessed breathing interruptions or awakenings due to gasping or choking in the presence of at least five obstructive respiratory events (apneas, hypopneas or respiratory effort related arousals) per hour of sleep". OSA was also clinically defined by the presence of 15 or more of observed respiratory events per hour of sleep in the absence of sleep related symptoms (AASM, 2009, p. 263). The categories of OSA were defined according to the AHI groups, as follows; group 1 (AHI < 5); group 2 ($5 \leq$ AHI < 15); group 3 ($15 \leq$ AHI < 30); and group 4 (AHI $\geq$ 30; AASM, 2009, p, 263-264).

Clinical Definition of Hypertension

Hypertension was defined as *high blood pressure*, in which the arteries have persistent high arterial pressure. Based from the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), the categories of hypertension will be; *group 1* (pre-hypertension, SBP, 120-139 mmHg, DSP, 80-89 mmHg); *group 2* (stage 1 hypertension, SBP, 140-159 mmHg,

DSP, 90-99 mmHg), and *group 3* (stage 2 hypertension, SBP ≥ 160 mmHg, DSP, ≥ 100 mmHg).

Polysomnography

All patients were qualified if they did at least one overnight polysomnographic study at a sleep center in San Jose, CA. The polysomnographic study will include the following measurements: electroencephalogram (EEG, C3 and C4), electro-oculogram (EOG), chin, and leg electromyogram (EMG), and electrocardiography, (ECG, modified V2 lead). Oronasal flow, thoracic, and abdominal measurements by inductive plethysmography and oxygen saturation will be used to measure respiration. Sleep disruption and EEG arousals will be detected by PSG recordings from skin surface electrodes per current AASM criteria for sleep/wake and cortical arousal determination, (Chang, et al., 2008). All the records were scored according to scoring criteria established by Rechtschaffen and Kales (1968), the American Sleep Disorders Association (Thornton et al., 2012). This scoring criterion, used in various populations, including Asians based from studies conducted outside the U.S, was validated to be fairly accurate in the diagnosis of OSA (Thornton et al., 2012, p. 425). This scoring criterion has been the standard scoring system used by physicians to diagnose OSA.

Sleepiness

The study used the definition of sleepiness using the Epworth Sleepiness Scale (ESS). This is an eight item questionnaire, with scores ranging from 0 (the least sleepy)

to 24 (the most sleepy) Chung et al., 2000). The ESS total score is the sum of the eight scores with points ranging from 0 to 24 (Gonzales et al., 2011).

BP Measurements

A non-invasive blood pressure measurement in office for at least two measurements was used to determine diagnosis of hypertension.

Neck Circumference

The study used neck circumference measurement as placing the tape at the level of the cricothyroid membrane the night before the polysomnography.

Body Mass Index (BMI)

The subjects BMI were calculated by dividing a person's weight in kilograms (kg) by the person's height in meters squared. BMI measurement was also be calculated by multiplying weight in pounds (lbs.) by 705 and then dividing by height in inches (in.) twice. A healthy BMI is in the range of 18.5 to 24.9, while BMI over 30 is considered obese.

Mallampati Score

The Mallampati Scoring System (MSS) was used to assess the patients' oropharyngeal region. The healthcare professional needed to identify the four anatomical landmarks in the oropharyngeal region. MSS was classified according to four groups: group 1, Class I (all anatomical structures can be visualized); group 2, Class II (soft palate, hard palate and upper portions of the uvula and tonsils can be visualized); group 3, Class III (only soft, hard palate and base of the uvula can be visualized); and group 4,

Class IV (only the hard palate can be visualized), (Gonzales, et al., 2011, p. 3).

Table 3

Summary of Variables

Type of variable	Description of variable	SPSS Variable Name	Coding instructions
Categorical			
a. Nominal	Identification number	ID	
	Sex	Sex	0-Female 1-Male
	Race	Race	1-Chinese 2-Filipino 3-Vietnamese 4-Asian Indian 5-Korean 6-Taiwanese 7-Japanese 8-Singaporean
	Smoking status	Smoking status	0-No 1-Yes
	Hypertension	Hypertension status	0-No 1-Yes
	Mallampati score	MS score	1-Class1 2-Class II 3-Class III 4-Class IV
	OSA status	OSA status	0-No 1-Yes
	Snoring	Snoring	0-No 1-Yes
Numeric			
a. Discrete	ESS score	ESS score	Total ESS score (range from 0=low to 24=high daytime sleepiness)
	AHI score	AHI score	AHI score (range from 5 and above)
b. Continuous			
	Age	Age (years)	
	BMI	BMI	
	Neck circumference	Neck circumference (inches)	
	BP measurements	BP measurements (systolic/diastolic pressure)	

Procedures for Archival Data

In order to address data integrity, the data was accessed only by qualified users, audit trails on all changes will be logged and specific controls over identification codes and passwords will be instituted. Only data pertinent to the study protocol was collected and no extra data was collected. If it is appropriate, cross checks were imposed to ensure inclusion/exclusion criteria and procedures are appropriately collected. Examples of cross-checks are age, blood pressure ranges, AHI, etc. Cross checks of procedure sequence were also followed. For example, the study required that polysomnography should be done before the determination of OSA; MSS scores were done prior to determination of MSS scores, etc. The study ensured that specific designs for collecting analyzable data were followed. For example, numeric analysis required numeric data, and categorical analysis required categorical data. Standard units for each of the measureable data were followed to ensure data collected were reliable and valid. Laboratory data collected were reconciled, which mean that each subject have matching information, laboratory values were consistent and laboratory ranges were not different. The data should also be cleaned. I avoided duplication errors, eliminated ambiguous responses from subjects, and checked missing responses (Prokscha, 2012). I also obtained permission to collect and use data by ensuring that proper forms and requirements as per Walden University's Office of Research Ethics and Compliance (IRB) were duly met and submitted prior to data collection.

Data Analysis Plan

The latest version of SPSS, version 21 was used for data analysis. The analysis of patients included in the study was obtained from paper and electronic medical records (EMR). EMRs are paperless or digital versions of patients' charts. The cleaning and screening in patients for data analysis only involved analyzing patient demographics. The patient demographics in paper and EHR included gender, age, race, smoking status, hypertension status, systolic diastolic blood pressure readings, neck circumference, body mass index (BMI), snoring status, Epworth Sleepiness Scale (ESS), Mallampati score (MS), Apnea, and Hypopnea Index (AHI). The other items that were included in the paper and EHR database for analysis included medical history, family history, diagnosis codes, laboratory data, and prescription data.

The analysis determined the estimated unadjusted age, BMI, smoking, alcohol status, and neck circumference effect on OSA, and its association with hypertension. Mean and frequency of distribution were calculated for gender, age, ethnicity, smoking status, hypertension status, snoring and OSA status. Mean, mean standard deviation, standard deviation, and variance were also calculated for gender, age, ethnicity, smoking status, systolic, diastolic, neck circumference, BMI, snoring, Epworth Sleepiness Scale, Mallampati score, Apnea Hypopnea Index, OSA status and AHI groups. The continuous variables were expressed as means ± standard deviation (SD). The subjects' age, BMI and Mallampati scores were considered independent confounding variables. The variables of interest (BMI, MSS, ESS and AHI) were not adjusted by age. These

variables were analyzed in the study because other epidemiologic evidence conducted among predominantly White populations showed that these factors affected the prevalence of OSA among Caucasians. The associations of different variables to hypertension were analyzed by logistic regression analysis. The odds ratios (ORs) of OSA association with hypertension were calculated for ethnicity, age, gender, smoking, BMI, MSS, ESS, and AHI.

Descriptive statistics were performed in the defined categorical variables in the study. Frequencies tabulations were utilized for gender, sex, race, smoking, and alcohol history, elevated blood pressure, and history of hypertension. Descriptive statistics for continuous variables (e.g., age) which enlisted the summary statistics included *n*, mean, mean standard deviation, standard deviation, and variance. The study also included the use of tables to describe and explore the data.

The specific hypotheses of the study expressed in the null form were statistical analyzed by the following

Null Hypothesis1. There was no association between OSA and hypertension among a sample of middle-aged Asians living in San Jose, CA.

In order to determine the association between OSA and hypertension, the study conducted logistic regression analysis. OSA and hypertension were evaluated first as a binary response, denoted as either yes or no. SPSS coding was denoted as 0- No and 1- Yes. Binary response variables described the proportion of the population specified in the

analysis (Grobee & Hoes, 2009). The binary response variable was calculated using the following formulary:

$$ln \left[Y / (1-Y) \right] = b_0 + b_1 X_1$$ which calculated the odds. Where *Y* is representative of the proportion of the subjects with the outcome, the probability of the disease is represented by *(1-Y)*, and the probability of the study subjects who do not have the disease is represented by *ln [Y/ (1-Y)]* is the odds of the disease. Additionally, *b0* is the intercept for the odds of the disease and X_1 is the intercept for the independent variable (Grobbee & Hoes, 2009, p. 345).

The measure of association between the outcome of interest and predictor variable was measured using odds ratio. The level of significance was evaluated at 0.05.

Null hypothesis 2. There was no association between age and hypertension among a sample of middle-aged Asians living in San Jose, CA.

In order to determine the association between age (continuous variable), and hypertension (categorical variable) among a sample of middle aged Asians living in San Jose, CA, the study conducted logistic regression analysis. This type of analysis can better explain the functional relationship of OSA and other variables (Wassertheil-Smoller, 1990).

The absolute probability or the risk of the outcome for each of the subjects was also be calculate using logistic regression by substituting the coefficients for each determinants with the use of the formula:

$$P = 1/ 1+ e^{-(ß0+ß1x1+ß2x2+\ldots.)}$$

The measure of association between the outcome of interest and predictor variable was measured using odds ratio. The level of significance was evaluated at 0.05.

Null hypothesis 3. There was no association between gender and hypertension among a sample of middle-aged Asians living in San Jose, CA.

In order to determine the association between gender and hypertension (categorical variables) among a sample of middle-aged Asians living in San Jose, CA, the study conducted logistic regression analysis. This type of analysis can better explain the functional relationship of OSA and other variables (Wassertheil-Smoller, 1990). The absolute probability or the odds of the outcome for each of the subjects was also calculated using logistic regression by substituting the coefficients for each determinant with the use of the formula:

$$P = 1/\ 1+ e^{-(ß0+ß1x1+ß2x2+\ldots..)}$$

The measure of association between the outcome of interest and predictor variable was measured using odds ratio. The level of significance will be evaluated at 0.05.

Null hypothesis 4. There was no association between smoking consumption and hypertension among a sample of middle-aged Asians living in San Jose, CA.

In order to determine the association between smoking and hypertension (categorical variables) among a sample of middle-aged Asians living in San Jose, CA. the study conducted logistic regression analysis. This type of analysis can better explain the functional relationship of OSA and other variables (Wassertheil-Smoller, 1990). The absolute probability or the odds of the outcome for each of the subjects was also be

calculated using logistic regression by substituting the coefficients for each determinant with the use of the formula:

$$P = 1/\ 1+ e^{-(ß0+ß1x1+ß2x2+\ldots..)}$$

The measure of association between the outcome of interest and predictor variable was measured by using odds ratio. The level of significance was evaluated at 0.05 level of significance.

Null hypothesis 5. There was no association between body mass index (BMI) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

In order to determine the association between body mass index (BMI) (continuous variable) and hypertension (categorical variables) as the outcome among a sample of middle aged Asians living in San Jose, CA, the study conducted logistic regression analysis. The binary response variable was calculated using the following formulary:

$lnY/ (1-Y)= b_0 + b_1X_1$ which will calculate the odds. Where *Y* is representative of the proportion of the subjects with the outcome, the probability of the disease is represented by *(1-Y),* and the probability of the study subjects who do not have the disease is represented by *ln [Y/ (1-Y)]* is the odds of the disease. Additionally, b_0 is the intercept for the odds of the disease andX_1 is the intercept for the independent variable, (Grobbee & Hoes, 2009, p. 345).

Null hypothesis 6. There was no association between Mallampati Score (MS) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

In order to determine the association between Mallampati score (MS) and hypertension (categorical variables) among a sample of middle aged Asians living in San Jose, CA, the study conducted logistic regression analysis. This type of analysis can better explain the functional relationship of OSA and other variables (Wassertheil-Smoller, 1990). The absolute probability or the risk of the outcome for each of the subjects was also calculated using logistic regression by substituting the coefficients for each determinant with the use of the formula:

$$P = 1/\ 1+ e^{-(ß0+ß1x1+ß2x2+\ldots..)}$$

The measure of association between the outcome of interest and predictor variable was measured using odds ratio. The level of significance was evaluated at 0.05.

Null hypothesis 7. There was no association between Epworth Sleepiness Scale (ESS) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

In order to determine the association between ESS and hypertension (categorical variables) among a sample of middle-aged Asians living in San Jose, CA, the study will conduct logistic regression analysis. This type of analysis can better explain the functional relationship of OSA and other variables (Wassertheil-Smoller, 1990). The absolute probability or the odds of the outcome for each of the subjects was also calculated using logistic regression by substituting the coefficients for each determinant with the use of the formula:

$$P = 1/\ 1+ e^{-(ß0+ß1x1+ß2x2+\ldots..)}$$

The measure of association between the outcome of interest and predictor variable was measured using odds ratio. The level of significance was evaluated at 0.05.

Null hypothesis 8. There was no association between Apnea-Hypopnea index (AHI) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

In order to determine the association between Apnea-Hypopnea Index (AHI) and hypertension (categorical variables) among a sample of middle aged Asians living in San Jose, CA, the study conducted logistic regression analysis. This type of analysis can better explain the functional relationship of OSA and other variables (Wassertheil-Smoller, 1990). The absolute probability or the odds of the outcome for each of the subjects was also calculated using logistic regression by substituting the coefficients for each determinant with the use of the formula:

$$P = 1/\ 1+ e^{-(ß0+ß1x1+ß2x2+\ldots..)}$$

The measure of association between the outcome of interest and predictor variable was measured using odds ratio. The level of significance was evaluated at 0.05.

Each of the specified hypotheses included this table in a similar format

Table 4

Sample table of results

							95% CI for exp (B)	
Step		SE	Wald	*f*	Sig	Exp(B)	Lower	Upper
	Presence of HTN							
	Constant							

Threats to Validity

Threats to validity can be external or internal (Groves et al, 2009). The external validity addressed the question of how the results of the study could be generalized to the population (Groves et al., 2009, p. 373). In order to address the external validity of the study, the study strictly adhered to the study's inclusion and exclusion criteria. The study also clearly defined the variables; provided detailed description of the study methodology; clearly explained the instrumentation, and measurements used in the study and openly provided the protocol for data collection (Groves et al, 2009, p. 373). There are various types of internal validity associated with cross-sectional studies. Construct validity as such is one of them. Construct validity assures that possible causal relationships exists between a variable to another. In this particular study, numerous epidemiological studies have shown such relationships among predominantly White populations. Thus, this study postulated that such relationship can also be seen among Asian patients. There other internal validity issue for the study. Face validity being one of them, was addressed by ensuring that the appropriate statistical measurement for the

various variables to be used was appropriate for study analysis. This was established by consulting statistical references and literatures with similar study design, methods, and patient population. The other internal validity issue was selection of study subjects. Although, I did a careful analysis of the existing literature, and considered all known variables that may affect the study results, other confounders can still influence the results of the study. These include other existing medical conditions, and other risk factors that may affect the disease. Selection maturation, an internal validity issue, can occur when study subjects mature at different speeds (Asmundson et al., 2002). In cross - sectional studies such as this one, although subjects maybe of the same age, other factors may affect outcomes, and thus the study may not be able to differentiate between maturation and cohort differences (Olsen & St. George, 2004). The study tried to address this issue by ensuring that age is factored into the analysis.

Ethical Concerns

The study strictly adhered to the widely accepted standards for ethical, professional and scientific conduct of the study from study design and implementation. The study adhered to the principles as set forth by Walden University's IRB, which included confidentiality agreement, data use agreement, and authorization to disclose private health information (PHI). In order to do this, the study strictly viewed all patient data as highly confidential, and respected the study subject's cultural and social differences (Groves et al., 2009). The investigator also observed the highest level of professional integrity in the conduct of all the stages of the study (Groves et al., 2009, p.

373). The investigator also made sure that the findings was reported accurately (Groves et al., 2009, p.375). The study also advocated following appropriate quality control procedures (Groves et al, 2009, p. 375). All materials were documented in relation to the ethical conduct of the study (Groves et al., 2009, p. 375). All data procured abided by the standards set forth by Walden University's IRB process that included: obtaining consent forms, confidentiality agreements, letter of cooperation, data collection request, data use agreement, and authorization to disclose PHI. If participants refuse to grant such request; the investigator will comply, and obtain information from subjects who would consent to the use of PHI.

Summary

In order to determine the prevalence of OSA in association with hypertension, the study conducted a cross-sectional survey of middle-aged Asians living in San Jose, CA. The study analyzed paper and electronic medical records of 462 patients randomly selected at three sleep study centers in San Jose, CA. The study employed random sampling to eliminate bias in participant selection and limited the possibility of confounders affecting the results of the study. The study also employed frequencies tabulations and logistic regression analysis to determine the prevalence rate of OSA in association with hypertension together with other risk factors including age, gender, smoking status, ESS, BMI, MSS, and AHI. All data that I collected for the study, including the processing of data collection, management, and data analysis abided with the rules and regulations as set forth by Walden University's Office of Research Ethics

and Compliance (IRB). This guaranteed that all data obtained and all outcomes presented were all under the pretext of highest standards of integrity and ethical procedures.

The next chapter will discuss the data collection and results.

Chapter 4: Results

Introduction

The main purpose of this quantitative cross sectional study was to determine (a) the prevalence rate of OSA among middle-aged Asian patients (Chinese, Filipino, Vietnamese, Asian Indian, Korean, Taiwanese, Japanese, and Singaporean) in San Jose, CA.; (b) the association between OSA and hypertension; and (c) the association of other risk factors --age, gender, smoking, body mass index (BMI); Mallampati score (MS), the Epworth Sleepiness Scale (ESS) and Apnea-Hypopnea Index (AHI) --with hypertension as the outcome.

This section addresses the results of the study.

Results

Research Questions and Hypotheses

The overarching research question involved determining the association of OSA and other risk factors as related to hypertension among middle-aged (40-60+ years old) Asians living in San Jose, CA. To answer the above research question, the following sub questions were examined.

Research Question 1. What was the association between OSA and hypertension among a sample of middle-aged-Asians living in San Jose, CA?

Null Hypothesis 1. There was no association between OSA and hypertension among a sample of middle-aged-Asians living in San Jose, CA.

Alternative Hypothesis 1. There was an association between OSA and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Research Question 2. What was the association between age and hypertension among a sample of middle-aged-Asians living in San Jose, CA?

Null Hypothesis 2. There was no association between age and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Alternative Hypothesis 2. There was an association between age and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Research Question 3. What was the association between gender and hypertension among a sample of middle-aged Asians living in San Jose, CA?

Null Hypothesis 3. There was no association between gender and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Alternative Hypothesis 3. There was an association between gender and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Research Question 4. What was the association between smoking status and hypertension among a sample of middle-aged Asians living in San Jose, CA?

Null Hypothesis 4. There was no association between smoking status and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Alternative Hypothesis 4. There was an association between smoking status and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Research Question 5. What was the association between body mass index (BMI) and hypertension among a sample of middle-aged Asians living in San Jose, CA?

Null Hypothesis 5. There was no association between body mass index (BMI) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Alternative Hypothesis 5. There was an association between body mass index (BMI) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Research Question 6. What was the association between Mallampati score (MS) and hypertension among a sample of middle-aged Asians living in San Jose, CA?

Null Hypothesis 6. There was no association between Mallampati score (MS) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Alternative Hypothesis 6. There was an association between Mallampati score (MS) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Research Question 7. What was the association between Epworth Sleepiness Scale (ESS) and hypertension among a sample of middle-aged Asians living in San Jose, CA?

Null Hypothesis 7. There was no association between Epworth Sleepiness Scale (ESS) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Alternative Hypothesis 7. There was an association between Epworth Sleepiness Scale (ESS) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Research Question 8. What was the association between Apnea-Hypopnea Index (AHI) and hypertension among a sample of middle-aged Asians living in San Jose, CA?

Null Hypothesis 8. There was no association between Apnea-Hypopnea Index (AHI) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

Alternative Hypothesis 8. There was an association between Apnea-Hypopnea Index (AHI) and hypertension among a sample of middle-aged Asians living in San Jose, CA.

The analysis determined the association between OSA, age, gender, smoking status, body mass index, Mallampati score, Epworth Sleepiness Scale, and apnea-hypopnea index to hypertension. Means, standard deviation, and frequency of distribution were calculated for continuous independent variables such as age, gender, ethnicity, sex, and BMI.

The purpose of this chapter is to provide the précis of the collected data, the statistical analyses and mechanics of the analysis.

Data collection

This study used cross sectional design. After obtaining Institutional Review Board approval (03-25-14-0153639), data were collected among Asian men and women patients between the ages of 35 and 60+ years of age who had observed obstructive sleep apneas living in San Jose, CA or Santa Clara County. For this study, eligible patients were randomly selected from each of the three identified sleep study clinics located in San Jose, CA who were seen from January 1, 2008 to December 31, 2011. Inclusion

criteria were the following: a. men and women 35- 60+ years of age who had observed apneas, daytime fatigue, daytime sleepiness, or snoring who were referred to sleep study clinics; b. diagnosis of OSA verified by overnight polysomnograms; and c. a systolic blood pressure [SBP] level of 140mmHg and a diastolic blood pressure [DBP] level of 90 mm Hg). All eligible patients completed a physical examination. Consequently, exclusion criteria were applied to patients with physical or psychological incapacity, no self-reported history of hypertension, no current or self-reported treatment for OSA, no previous treatment for snoring or any previous CV event (myocardial infraction, unstable angina, transient ischemic stroke, or attack, myocardial revascularization), chronic disease, and drug or alcohol addiction. Patients were also excluded if they had severe congestive heart failure (NYHA class IIIb or IV), known cardiomyopathy, valvular disease, coronary artery disease, diabetes mellitus, current active liver disease, unexplained elevated serum creatine kinase (CK > 3XULN), cancer, uncontrolled hyperthyroidism, or other important comorbidities. Personnel at all three sites provided consent by signing the data collection request form and data use agreement forms. All sites were furnished with a copy of the approved dissertation proposal.

Data collection started in July 2014 and ended in October 2014. The polysomnographic information of patients was obtained by randomly choosing the appointment days that fall between January 1, 2008 and December 31, 2011. Eligible patients were drawn from a list of patients that each physician at each site identified. The list contained no patient names, but did contain dates. A medical assistant then retrieved

the patient records and provided the data needed for analysis. The following data were collected from the medical records of eligible patients: age, gender, ethnicity, smoking status, history of hypertension, systolic blood pressure, diastolic blood pressure, neck circumference, Body Mass Index (BMI), snoring (yes or no), Epworth scale (ESS), Mallampati score, and Apnea Hypopnea Index (AHI). A total of 462 middle-aged Asian patients (Chinese, Filipino, Vietnamese, Asian Indians, Korean, Taiwanese, Japanese, and Singaporean) were randomly selected among the three sleep study clinics. From Sites 1 and 2, data were collected on a totaled of 308 patients; however, Site 3 only had 80 eligible patient's data. In order to meet the requirement 154 from each site, additional data were collected from Site 1. Table 5 summarizes the demographic information of the study sample

Table 5

Demographic Characteristics of the Study Sample

Characteristics	*N*	%
Gender		
Male	278	60.2
Female	184	39.8
Age bracket		
35-40	49	10.5
40-50	75	16.1
50-60	80	17.2
60-70	107	23.0
70-80	114	24.5
80 and above	36	7.7
Ethnicity		
Chinese	220	47.6
Filipino	139	30.1
Vietnamese	37	8.0
Asian Indian	48	10.4
Korean	5	1.1
Taiwanese	4	0.865
Japanese	8	1.7
Singaporean	1	0.216
Smoking status		
Yes	96	20.8
No	366	79.2
Hypertension		
Yes	319	69.0
No	143	31.0
Snoring		
Yes	454	98.3
No	8	1.7
OSA		
Yes	416	90.0
No	46	10.0

More than half of the sampled populations were males, about 60.2%, and only 39.8% were females. A larger proportion of the population falls between the ages of 70 and 80 years of age (24.5%), while there were few participants that were 80 years and

above (7.7%). The mean age of the sampled population is 61 years old. The percentages of the sampled population were as follows: Chinese (47.6%), Filipinos (30.1%), Asian Indians (10.4%), Vietnamese (8.0%), Japanese (1.7%), and Korean (1.1%). There were very few Taiwanese (0.865%) and Singaporeans (0.216%). Table 6 provides the demographic characteristics of the sampled population.

Table 5

Demographic Characteristics of the Sampled Population

Variables	*n*	Sum	Statistic	Mean SE	*SD*	Variance
Gender	462	278	.60	0.023	.490	.240
Age	462	28355.00	61.3745	.69522	14.94315	223.298
Ethnicity	457	882	1.93	0.58	1.232	1.517
Smoking status	462	96	.21	0.019	.406	.165
Systolic	462	57802	125.11	.679	14.598	213.098
Diastolic	462	34657	75.02	.469	10.080	101.616
Neck circumference	462	6739.3	14.587	.0932	2.0028	4.011
BMI	462	12300.53	26.6245	.24190	5.19939	27.034
Snoring	462	454	.98	.006	.131	.017
Epworth scale	462	5618	12.16	.206	4.432	19.640
Mallampati score	462	1714	3.71	.028	.606	.367
AHI	462	14504.2	31.394	1.1910	25.600	655.362
OSA	462	416	.90	.014	.300	.090
AHI GROUPS	462	1024	2.22	.061	1.303	1.697
Valid N(list wise)	457					

Note. BMI= body mass index; AHI = *Apnea-Hypopnea Index*

There were 366 non-smokers compared to 96 smokers. 319 patients were hypertensives compared to 143 non hypertensive patients. The mean systolic blood pressure of the sampled patients is 125 mmHg and mean diastolic blood pressure is 75 mmHg. The subjects had a mean neck circumference of 14.58 cm; body mass index

average of 26.62; Epworth Sleepiness Scale average of 12.16; average Mallampati score of 3.71, and mean Apnea-Hypopnea Index of 31.39. The majorities of the participants were snorers (98.3%) and diagnosed with obstructive sleep apnea (90%). Table 7 below provides the descriptive summary of the Apnea Hypopnea Index (AHI) groups of the study.

Table 6

Apnea Hypopnea Index (AHI) Groups

AHI	Frequency	%	Valid %	Cumulative %
Under 5.999	60	13.0	13.0	13.0
6-14.999	76	16.5	16.5	29.4
15-29.999	126	27.3	27.3	56.7
30-49.999	104	22.5	22.5	79.2
Over 50	96	20.8	20.8	100.0
Total	462	100.0	100.0	100.0

Note. AHI = *Apnea-Hypopnea Index*

Research question 1. What was the association between OSA and hypertension among a sample of middle aged Asians living in San Jose, CA?

A binary logistic regression analysis was conducted to determine the association between OSA and hypertension among a sample of middle aged Asians living in San Jose, CA. There were 462 cases included in the analysis.

Table 8 below illustrates the logistic coefficient, Wald test and odds ratio for the predictor variable which is hypertension. Using a .05 criterion for statistical significance, in a sample of middle aged Asians living in San Jose, CA, hypertension had no significant association with OSA, x^2 (1, N = 462) = .065. p =.799.

Table 7

Logistic Regression Analysis to Determine Association Between OSA and Hypertension

Variables in equation									
		B	S.E	Wald	*df*	Sig	Exp(B)	95% C.I. for EXP(B) Lower	Upper
Step 1a	OSA(1)	.085	.332	.066	1	.798	1.089	.568	2.087
	Constant	.726	.315	5.327	1	.021	2.067		

Note. S.E. = standard error; *df* = degrees of freedom; Sig = significance; C.I. = confidence interval. a.Variable (s) entered on Step 1:OSA

In this analysis, the confidence interval for the variable hypertension (OR = .919) ranges from .568 to 2.087. Based from this analysis, I failed to reject the null hypothesis. There was no association between OSA and hypertension among a sample of middle aged Asian living in San Jose, CA.

Research question 2. What is the association between age and hypertension among a sample of middle aged Asians living in San Jose, CA?

A binary logistic regression analysis was conducted to determine the association between age and hypertension among a sample of middle aged Asian living in San Jose, CA. There were 462 cases included in the analysis. Table 9 showed the logistic coefficient, Wald test and odds ratio of the predictor.

Table 8

Logistic Regression Analysis Between Age and Hypertension

Variables in equation									
		B	S.E	Wald	*df*	Sig.	Exp(B)	95% C.I. for EXP (B) Lower	Upper
Step 1a	Age	.089	.009	93.792	1	.000	1.093	1.093	1.112
	Constant	-4.362	.524	69.205	1	.000	.013		

Note. S.E. = standard error; *df* = degrees of freedom; Sig = significance; C.I. = confidence interval. a.Variable (s) entered on Step 1: Age

Using a .05 criterion for statistical significance, in a sample of middle aged Asians living in San Jose, CA, age had significant association with hypertension, x^2 (1, N = 462) = 127.932, p < .000. Age recorded an odds ratio of 1.093. This indicated that older middle age Asians living in San Jose, CA were 1 time more likely to be hypertensive compared to younger middle age Asians.

Based from this analysis, I rejected the null hypothesis and therefore accepted the alternative hypothesis. There was an association between age and hypertension among a sample of middle aged Asians living in San Jose, CA.

Research question 3. What is the association between gender and hypertension among a sample of middle aged Asians living in San Jose, CA?

A binary logistic regression analysis was conducted to determine the association between gender and hypertension among a sample of middle aged Asians living in San Jose, CA. There were 462 cases included in the analysis.

Table 10 showed the logistic coefficient, Wald test and odds ratio of the predictor.

Table 9

Logistic Regression Analysis Between Gender and Hypertension

Variables in equation									
		B	S.E	Wald	*df*	Sig	Exp(B)	95%C.I for EXP (B) Lower	Upper
Step 1a	Gender	-.430	.211	4.160	1	.041	.650	.430	.983
	Constant	1.070	.169	40.053	1	.000	2.915		

Note. S.E. = standard error; *df* = degrees of freedom; Sig = significance; C.I. = confidence interval. a.Variable(s) entered on Step 1: Gender

Using a .05 criterion for statistical significance, in a sample of middle aged Asians living in San Jose, CA, gender had no significant association with hypertension, x^2 (1, N = 462) = 4.245, p = .039. Gender recorded an odds ratio of .650. Based from this analysis, I failed to reject the null hypothesis.

Research question 4. What is the association between smoking status and hypertension among a sample of middle aged Asians living in San Jose, CA?

A binary logistic regression analysis was conducted to determine the association between smoking status and hypertension among a sample of middle aged Asians living in San Jose, CA. There were 462 cases included in the analysis.

Table 11 showed the logistic coefficient, Wald test and odds ratio of the predictor.

Table 10

Logistic Regression Analysis Between Smoking Status and Hypertension

Variables in equation									
		B	S.E	Wald	*df*	Sig	Exp(B)	95% C.I for EXP (B)	
								Lower	Upper
Step 1a	Smoking Status	-.139	.245	.321	1	.571	.871	.539	1.406
	Constant	.832	.114	53.500	1	.000	2.297		

Note. S.E. = standard error; *df* = degrees of freedom; Sig = significance; C.I. = confidence interval. a.Variable (s) entered on Step 1:Smoking status

Using a .05 criterion for statistical significance, in a sample of middle aged Asians living in San Jose, CA, smoking status had no significant association with hypertension, x^2 (1, N = 462) = 3.18, p = .573. Smoking status recorded an odds ratio of .871. Based from this analysis, I failed to reject the null hypothesis.

Research question 5. What is the association between body mass index (BMI) and hypertension among a sample of middle aged Asians living in San Jose, CA?

A binary logistic regression analysis was conducted to determine the association between body mass index (BMI) and hypertension among a sample of middle aged Asians living in San Jose, CA. There were 462 cases included in the analysis.

Table 12 showed the logistic coefficient, Wald test and odds ratio of the predictor.

Table 11

Logistic Regression Analysis Between BMI and Hypertension

Variables in equation									
		B	S.E.	Wald	*df*	Sig.	Exp(B)	95% C.I for EXP (B) Lower	Upper
Step 1a	BMI	-.025	.019	1.775	1	.183	.975	.939	1.012
	Constant	1.480	.520	8.085	1	.004	4.392		

Note. BMI= body mass index; S.E. = standard error; *df* = degrees of freedom; Sig = significance; C.I. = confidence interval. a.Variable(s) entered on Step 1:BMI

Using a .05 criterion for statistical significance, in a sample of middle aged Asians living in San Jose, CA, BMI had no significant association with hypertension, x^2 (1, N = 462) = 1.768, p = .184. BMI recorded an odds ratio of .975. Based from this analysis, I failed to reject the null hypothesis.

Research question 6. What is the association between Mallampati Score (MS) and hypertension among a sample of middle aged Asians living in San Jose, CA?

A binary logistic regression analysis was conducted to determine the association between Mallampati Score (MS) and hypertension among a sample of middle aged Asians living in San Jose, CA. There were 462 cases included in the analysis.

Table 13 showed the logistic coefficient, Wald test and odds ratio of the predictor.

Table 12

Logistic Regression Analysis Between Mallampati Score and Hypertension

Variables in equation									
		B	S.E.	Wald	*df*	Sig.	Exp(B)	95% C.I. for EXP (B) Lower	Upper
Step 1a	Mallampati	.251	.159	2.479	1	.115	1.285	.940	1.757
	Constant	-.125	.595	.044	1	.834	.882		

Note. S.E. = standard error; *df* = degrees of freedom; Sig = significance; C.I. = confidence interval. a.Variable(s) entered on Step 1:Mallampati

Using a .05 criterion for statistical significance, in a sample of middle aged Asians living in San Jose, CA, Mallampati Score had no significant association with hypertension, x^2 (1, N = 462) = 1.768, p = .184. Mallampati Score recorded an odds ratio of 1.285. Based from this analysis, I failed to reject the null hypothesis.

Research question 7. What is the association between Epworth Sleepiness Scale (ESS) and hypertension among a sample of middle aged Asian living in San Jose, CA?

A binary logistic regression analysis was conducted to determine the association between Epworth Sleepiness Scale (ESS) and hypertension among a sample of middle aged Asian living in San Jose, CA. There were 462 cases included in the analysis.

Table 14 showed the logistic coefficient, Wald test and odds ratio of the predictor.

Table 13

Logistic Regression Analysis Between Epworth Sleepiness Scale

Variables in equation									
		B	S.E.	Wald	*df*	Sig.	Exp (B)	95% C.I. for EXP (B) Lower	Upper
Step 1a	Epworth	-.039	.023	2.821	1	.093	.962	.919	1.007
	Constant	1.282	.306	17.534	1	.000	3.604		

Note: S.E. = standard error; *df* = degrees of freedom; Sig = significance; C.I. = confidence interval. a.Variable(s) entered on Step 1:Epworth

Using a .05 criterion for statistical significance, in a sample of middle aged Asians living in San Jose, CA, Epworth Sleepiness Scale had no significant association with hypertension, x^2 (1, N = 462) = 2.870. p = .090. Epworth Sleepiness Scale recorded an odds ratio of .962. Based from this analysis, I failed to reject the null hypothesis.

Research question 8. What is the association between Apnea-Hypopnea Index (AHI) and hypertension among a sample of middle aged Asians living in San Jose, CA?

A binary logistic regression analysis was conducted to determine the association between Apnea-Hypopnea Index (AHI) and hypertension among a sample of middle aged Asians living in San Jose, CA. There were 462 cases included in the analysis.

Table 15 showed the logistic coefficient, Wald test and odds ratio of the predictor.

Table 14

Logistic Regression Analysis Between Apnea-Hypopnea Index (AHI) and Hypertension

Variables in equation									
		B	S.E	Wald	*df*	Sig	Exp(B)	95%C.I for EXP(B) Lower	Upper
Step 1a	AHI	-.001	.004	.071	1	.789	.999	.991	1.007
	Constant	.835	.159	27.491	1	.000	2.305		

Note: AHI = Apnea-Hypopnea Index; S.E. = standard error; *df* = degrees of freedom; Sig = significance; C.I. = confidence interval. a.Variable (s) entered on Step 1:AHI

Using a .05 criterion for statistical significance, in a sample of middle aged Asians living in San Jose, CA, Apnea Hypopnea Index had no significant association with hypertension, x^2 (1, N = 462) = 6.974. p = .790. Apnea Hypopnea Index recorded an odds ratio of .999. Based from this analysis, I failed to reject the null hypothesis.

A multiple regression analysis was conducted to determine the association of OSA and other risk factors as related to hypertension among middle-aged (40-60+ years old) Asians living in San Jose, CA. There were 462 cases included in the analysis. Table 16 showed the logistic coefficient, Wald test and odds ratio of the predictors. Table 16 below summarizes the results of the multiple logistic regression analysis.

Table 15

Summary of Results of the Logistic Regression Analysis

		Variables in equation							
		B	S.E.	Wald	*df*	Sig	Exp(B)	95% C.I.for EXP(B) Lower	Upper
	OSA(1)	-.541	.457	1.400	1	.237	.582	.237	1.427
	Age	.099	.011	87.808	1	.000	1.104	1.082	1.128
	Gender	.396	.282	1.972	1	.160	1.486	.855	2.581
	Smoking status	-.245	.302	.660	1	.417	.783	.433	1.414
Step 1a	BMI	.043	.024	3.232	1	.072	1.044	.996	1.095
	Mallampati	.481	.204	5.541	1	.019	1.618	1.084	2.414
	Epworth Scale	-.025	.027	.866	1	.352	.975	.926	1.028
	AHI	-.005	.005	.733	1	.392	.995	.985	1.006
	Constant	7.166	1.320	29.490	1	.000	.001		

Note. OSA= obstructive sleep apnea; AHI = *Apnea-Hypopnea Index*; BMI= body mass index; S.E. = standard error; *df* = degrees of freedom; Sig = significance; C.I. = confidence interval. a.Variable(s) entered on Step 1: OSA, Age, Gender, Smoking status, BMI , Mallampati score, Epworth Scale, AHI

Using a .05 criterion for statistical significance, in a sample of middle-aged Asians living in San Jose, CA, age had significant association with hypertension, p = .000. Age recorded an odds ratio of 1.104. Mallampati score had also a significant association with hypertension, p = .019. Mallampati score recorded an odds ratio of 1.618. Based from this analysis, age and Mallampati score had significant association to OSA in relation to hypertension.

Summary

This quantitative cross sectional study showed that OSA is associated with hypertension among middle aged Asians living in San Jose, CA. This result were based from the analysis of electronic and paper medical records of 462 patients randomly selected from three sleep study centers in San Jose, CA. The logistic regression analysis also determined the prevalence rate of OSA in association with hypertension together with other risk factors including age, gender, smoking status, ESS, BMI, MSS, and AHI. The model containing the eight variables (OSA, age, gender, smoking status, BMI, Mallampati score, Epworth Sleepiness Scale, and Apnea-Hypopnea Index) were statistically significant, x^2 (8, N = 462) = 139.549, p < .000. The model as a whole explained 26.1% (Cox and Snell R square) and 36.7% (Nagelkerke R squared) of the variance in OSA association with hypertension and correctly classified 79.2% of the cases. Age was the strongest predictor. Based from the results of the multiple logistic regression analysis, age and Mallampati score had significant association to OSA in relation to hypertension among middle-aged Asians living in San Jose, CA.

The next chapter will provide the discussion, conclusion and recommendations

Chapter 5: Discussion, Conclusions, and Recommendations

Introduction

The goal of this study was to understand the prevalence of OSA and hypertension among Asians. There are no published scientific reports on the general prevalence of OSA among Asians. OSA poses significant CVD burden. This imposes an important health crisis in a county of Santa Clara, where out of the 18 million residents 33.7% are Asians (U.S Census Data, 2012). In order to understand the burden of these diseases, there is a need to understand what the prevalence of OSA and hypertension among Asians is. Hence, the purpose of the study was to address this gap and to determine the role of other risk factors, such as age, gender, smoking, body mass index (BMI), Mallampati score (MS), Epworth Sleepiness Scale (ESS), and Apnea-Hypopnea Index (AHI), that influence the prevalence rate of OSA and its association with hypertension among middle aged Asians residing in San Jose, CA.

This chapter provides the summation of the findings, conclusions, and recommendations based on the results on the quantitative cross-sectional study of the prevalence of OSA among middle aged Asians in Santa Clara County using paper and electronic medical records. Data collection started in July 2014 and ended in October 2014. In order to ensure that data interpretation and analysis were impartial, I used logistic regression analysis to determine the prevalence of OSA and the association of

different variables. The odds ratios (ORs) of OSA association with hypertension were calculated for ethnicity, age, gender, smoking, BMI, MSS, ESS, and AHI.

Descriptive statistics were performed in the defined categorical variables in the study. Frequency tabulation was used for gender, sex, race, smoking, and alcohol history, elevated blood pressure, and history of hypertension. Descriptive statistics for continuous variables (e.g., age) which enlisted the summary statistics included *n*, mean, median, standard deviation, and range. The study also included the use of tables to describe and explore the data.

Statement of the Problem

The main purpose of this quantitative cross-sectional study was to determine (a) the prevalence rate of OSA among middle-aged Asian patients (Chinese, Filipino, Vietnamese, Asian Indians, Korean, Taiwanese, Japanese, and Singaporean) in San Jose, CA.; (b) the association between OSA and hypertension, and (c) the association of other risk factors: age, gender, smoking, body mass index (BMI); Mallampati score (MS), the Epworth Sleepiness Scale (ESS), and Apnea-Hypopnea Index (AHI) with hypertension as the outcome.

This quantitative cross-sectional study showed that OSA is associated with hypertension among middle-aged Asians living in San Jose, CA. This result were based from the analysis of paper and electronic medical records of 462 patients randomly selected from three sleep study centers in San Jose, CA. The logistic regression analysis also determined the prevalence rate of OSA in association with hypertension together

with other risk factors including age, gender, smoking status, ESS, BMI, MSS, and AHI. The model containing the eight variables (OSA, age, gender, smoking status, BMI, Mallampati score, Epworth Sleepiness Scale, Apnea-Hypopnea Index) was statistically significant, x^2 (8, N = 462) = 139.549, p < .000. The model as a whole explained 26.1% (Cox and Snell *R* square) and 36.7% (Nagelkerke *R* squared) of the variance in OSA association with hypertension and correctly classified 79.2% of the cases. Age was the strongest predictor.

Interpretation of Findings

The results of this study established verifications from other studies that OSA is common and associated with hypertension among Asian patients. Similarly, this study also showed that among Asian patients with OSA, the association with hypertension is significantly increased with advancing age (Bixler et al., 2000; Drager et al., 2010; Young et al., 2004). This study also adds further proof that weight as measured by body mass index (BMI) is not highly associated among OSA Asian patients with hypertension compared to other OSA Caucasian patients with hypertension (Kim et al., 2013; Hla et al., 1994, Yoon, et al., 2009). This particular finding was a stark contrast to the findings by Min et al., (2014). Min et al., 2014 found that among men with moderate to severe OSA, age was not associated with hypertension while neck circumference was positively correlated with OSA associated hypertension (Hla et al., 1994, p. 1310). Additionally, gender, smoking status, Mallampati score, Epworth Sleepiness Scale, and Apnea-Hypopnea Index had no significant association among OSA Asian patients with

hypertension. However, Mallampati Score (MS) showed a trend towards suggesting that this particular risk factor could be considered as an important diagnostic tool in evaluating Asian patients with OSA and hypertension. This particular finding supported the research findings by Li et al., (2000). According to that study, the shorter anterior cranial base and acute cranial base flexure are more common among Far East Asian men compared to Caucasian men contributed to the high degree of association between OSA with hypertension (Li et al., 2000, p. 1691).

The findings from this study supported the evidence that OSA is prevalent among Asians. The study also showed that there is an association of OSA with hypertension. Given such association between OSA and hypertension among Asians, Asian patients should be screened, diagnosed, and treated appropriately to reduce the significant cardiovascular burden of this disease in the community.

Limitations of the Study

A limitation of the current study was that subjects were only sampled in Santa Clara County. Additionally, the sample size was small. Due to time and financial constraints, the study had to employ data obtained from paper and electronic medical records that were basically designed for clinical care and not research. EMR was used because it provided easy access to patient data, large cohorts, patient level diagnosis, treatment data, billing and laboratory information. However, limitations in the use of electronic medical records include information entered being decided by the provider, information entered in free text, scanned images, flexibility in terminology, a minimal

number of required fields, and unimportant data irrelevant to clinical care is missing (Terry et al., 2010). Another limitation of the use of secondary data is the lack of clinical detail (Gallin & Ognibene, 2012). This is especially true because certain EMR data sets contained clinical data relevant to physician payments (Gallin & Ognibene, 2012, p. 375). Another limitation of cross-sectional studies similar to this one is the inability of the researcher to provide a temporal sequence of the exposure and the outcome (Ho et al., 2008). The limitations associated with this data analysis also included variation in software platforms used by each clinic for their EMR systems, medical terminology, and clinical data, i.e., laboratory results, and units of measurements (Dean et al., 2009). However, the potential bias in the use of EMR as a source of secondary data was minimized by the random sampling of the subjects and the rigorous adherence to study protocol. Additionally, this study did not include participants' medical information such as medication use, patients' medical history, sleep time, and other factors that might affect the association of OSA with hypertension. The homogeneousness of the study population, the sample size, and the sampling convenience overall limited the generalizability of this study.

Recommendations

Prospective studies involving bigger cohorts should be conducted to determine accurately the prevalence of OSA among Asian patients compared to White populations. Ideally, future research should include analysis of the association of OSA and hypertension should be conducted among Asian and Caucasian patients while controlling

for age, gender, smoking status, body mass index (BMI), Mallampati score (MS), Epworth Sleepiness Scale (ESS), and Apnea Hypopnea Index (AHI).

Social Change

This study fostered to the epidemiologic understanding of OSA as the independent variable and hypertension as an outcome among middle aged Asians in San Jose, CA. This study conducted a research on a disease that can generate valuable public health insight to the consequence of this disease to cardiovascular health among high risk middle-aged Asians. This is critically important especially when studies involving OSA does not adequately synthesized or provide clarity into the health differences among Asian Americans. Because there are still a great number of underdiagnosed and undertreated Asian patients in San Jose, CA, the results generated from this research can lead to successful physician identification, screening, treatment, and management of OSA and hypertension especially among high risks middle-aged Asians, thus creating positive social change for those individuals, their families, and their communities. This study can advance social change by providing more justification for the need to conduct prospective large scale OSA studies among this vulnerable patient population who are definitely at risk for OSA and its health consequence. This study can also advance social change by empowering this ethnic group to advocate for themselves and collectively challenge service providers, government agencies and other institutions to ensure equal access to healthcare, and available services. Additionally, the results of this study would also

encourage positive social change by improving the health outcomes and the lives of Asians who have been suffering from OSA and hypertension for a long time.

Conclusions

OSA is common among middle aged Asians. OSA does increase the risk for hypertension among middle aged Asians in Santa Clara County. This quantitative cross-sectional study showed that OSA is associated with hypertension among middle aged Asians living in San Jose, CA. This particular research is very meaningful especially knowing that there are a number of Asians living in Santa Clara County that remains undiagnosed and untreated. The question that remains, that possibly could be answered by other research, is what else aside from age that one should consider as an important risk factor for this disease.

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Appendix A: IRB Approval Letter

Dear Ms. Benin,

This email is to notify you that the Institutional Review Board (IRB) has approved your application for the study entitled, "The Severity of Obstructive Sleep Apnea and Hypertension among Middle-aged Asians." conditional upon the approval of the community research partners, which will need to be documented in signed data use agreements. Walden's IRB approval only goes into effect once the Walden IRB confirms receipt of those data use agreements.

Your approval # is 03-25-14-0153639. You will need to reference this number in your dissertation and in any future funding or publication submissions.

Your IRB approval expires on March 24, 2015. One month before this expiration date, you will be sent a Continuing Review Form, which must be submitted if you wish to collect data beyond the approval expiration date.

Please note that this letter indicates that the IRB has approved your research. You may NOT begin the research phase of your doctoral study, however, until you have received the **Notification of Approval to Conduct Research** e-mail. Once you have

received this notification by email, you may begin your data collection. Your IRB approval is contingent upon your adherence to the exact procedures described in the final version of the IRB application materials that have been submitted as of this date. This includes maintaining your current status with the university. Your IRB approval is only valid while you are an actively enrolled student at Walden University. If you need to take a leave of absence or are otherwise unable to remain actively enrolled, your IRB approval is suspended. Absolutely NO participant recruitment or data collection may occur while a student is not actively enrolled.

Your IRB approval is contingent upon your adherence to the exact procedures described in the final version of the IRB application materials that have been submitted as of this date. If you need to make any changes to your research staff or procedures, you must obtain IRB approval by submitting the IRB Request for Change in Procedures Form. You will receive confirmation with a status update of the request within 1 week of submitting the change request form and are not permitted to implement changes prior to receiving approval. Please note that Walden University does not accept responsibility or liability for research activities conducted without the IRB's approval, and the University

will not accept or grant credit for student work that fails to comply with the policies and procedures related to ethical standards in research.

When you submitted your IRB application, you a made commitment to communicate both discrete adverse events and general problems to the IRB within 1 week of their occurrence/realization. Failure to do so may result in invalidation of data, loss of academic credit, and/or loss of legal protections otherwise available to the researcher.

Both the Adverse Event Reporting form and Request for Change in Procedures form can be obtained at the IRB section of the Walden web site or by emailing irb@waldenu.edu: http://inside.waldenu.edu/c/Student_Faculty/StudentFaculty_4274.htm.

Researchers are expected to keep detailed records of their research activities (i.e., participant log sheets, completed consent forms, etc.) for the same period of time they retain the original data. If, in the future, you require copies of the originally submitted IRB materials, you may request them from Institutional Review Board.

Both students and faculty are invited to provide feedback on this IRB experience at the link below:

http://www.surveymonkey.com/s.aspx?sm=qHBJzkJMUx43pZegKlmdiQ_3d_3d

Sincerely,

Jenny Sherer, M.Ed., CIP

Associate Director

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