A STUDY ON THE EFFECTS OF ACUTE SLEEP DEPRIVATION ON PULSE PRESSURE

A RESEARCH THESIS SUBMITTED AS PARTIAL FULFILLMENT OF THE MASTERS OF SCIENCE DEGREE IN MEDICAL PHYSIOLOGY

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MARTIN KURIA MUNGAI

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DEPARTMENT OF MEDICAL PHYSIOLOGY

UNIVERSITY OF NAIROBI

DECLARATION

CANDIDATE

This thesis is my original work and has not been presented for a Master Degree in any other University.

Signed **Date**

…… ……..

Martin Kuria Mungai.

APPROVAL

SUPERVISORS

This thesis has been submitted with the approval of my supervisors:

1. **Dr. Frederick Bukachi, PhD**

   Head of Department,

   Medical Physiology,

   University of Nairobi.

   Signature ……

   Date ……

2. **Dr. Jeswinder Sian, PhD**
   Lecturer,
   Department of Medical Physiology,
   University of Nairobi .

   Signature …….

   Date ……

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ABBREVIATIONS

SBP- Systolic blood pressure

DBP- Diastolic blood pressure

PP- Pulse pressure

PPf - Fractional pulse pressure

PVR- Peripheral vascular resistance

NREMS- Non-rapid eye movement sleep

SNA- Sympathetic nervous activity

ABD- Arterial blood pressure

PCI- Percutaneous coronary intervention

MAP- Mean Arterial blood pressure

ANOVA- Analysis of variance

MSNA- Muscle sympathetic nervous activity

ABR- Arterial baro-reflex.

df- Degrees of freedom

Sig.- Value of significance

N- Sample size

Std. deviation- Standard deviation

ABSTRACT

Currently a great proportion of our population experiences sleep deprivation. There has been research carried out previously and depicted an increase in diastolic blood pressure due to sleep deprivation. This leads to greater risk for diseases and even death in sleep deprived individuals. For any given level of mean arterial blood pressure, a high or low pulse pressure is by itself an accurate indicator of an individual's risk for cardiovascular diseases and even death. Low and high pulse pressure have been separately linked to increased mortality rates. There is no available data on any physiological influence of lack of sleep on an individual's pulse pressure. Thus this study set out to determine effects of chronic sleep deprivation on pulse pressure as an independent physiological variable of blood pressure in healthy adults between ages 20 and 40 years.

This study set out to assess any relationship between chronic sleep deprivation and pulse pressure in healthy subjects aged between 20 and 40 years. It was a randomized control trial done at The Karen Hospital involving healthy human subjects working at the hospital aged between 20 and 40 years.

All subjects who volunteered for the study underwent physical examination. Socio-demographic characteristics, medical history and sleeping pattern were obtained using the study questionnaire. A sample size of 56 human subjects was used. An inclusion and exclusion criteria was used to form a test group of 28 subjects and a control group of 28 subjects. Test group comprised fourteen males and fourteen females who were sleep deprived. The control group comprised fourteen males and fourteen females who were non- sleep deprived. The study was conducted over a period of one month.

On a daily basis, at 7.30 a.m every day, blood pressure readings were taken using a manual sphygmomanometer for both the test group and the control group. A sleep deprived subject must have had less than four hours of sleep for the last 24 hours whereas a non- sleep

deprived subject must have had more than 6 hrs of sleep in the last 24 hrs. Data was collected by the principal investigator using predesigned data collection sheets. Pulse pressure and fractional pulse pressure were derived using their respective formulae. Data was then entered into Microsoft Excel sheets and data cleaning was done before analysis. These were coded then analysis done using IBM SPSS software.

All the fifty six subjects who had been recruited were studied. The mean pulse pressure at recruitment of the control group was 48.09 mmHg while that of the test group was 47.22 mmHg. Both groups at recruitment had an equal mean fractional pulse pressure of 0.54 with mean age of control group at 28.42 years and that of test group at 27.86 years. By the fourth week of the study, the control group had a mean 50.0 mmHg and a mean fractional pulse pressure of 0.58; the test group had a mean pulse pressure of 44.43 mmHg and a mean fractional pulse pressure of 0.54. A person chi-square test revealed no relationship between pulse pressure and number of hours slept (Chi square value =165.99 df= 190 p= 0.895). There was also no relationship between fractional pulse pressure and number of hours slept (Chi-square value=- 454.98, df= 460, p=0.557). Pearson's correlation analysis between pulse pressure and number of hours slept in both groups revealed a non-significant and positive relationship (p= 0.686). The correlation was weak in strength(r= 0.055). There was an association between sleeping more hours and having an increased pulse pressure. Correlation analysis between fractional pulse pressure and number of hours slept revealed a non-significant and negative relationship (r=-0.046 p=0.739). Multiple regression was also conducted on overall effect of gender, both the two groups and number of hours slept on predictors had no relationship with pulse pressure. It was deducted from the study that the relationship between sleep deprivation and pulse pressure or fractional pulse pressure in healthy young adults aged between 20 and 40 years is not statistically significant. This was observed in both the test group and control group throughout the period of the study.

CHAPTER ONE

1.1 INTRODUCTION

Sleep deprivation is a common phenomenon in the present society. Currently 20 % of the population is sleep deprived. This is especially due to the pressures of modern living in which most people have to work overtime or during night shifts. On the other hand cardiovascular diseases have been on an upward trend for the last two decades and there has been a close relationship between their high incidences with modern changes in lifestyle.

Sleep physiology underlines the importance of sleep not only for the nervous system but also for the overall health of the individual. Research has shown various deleterious effects of sleep deprivation on many body systems. Of particular importance is that sleep deprivation causes alteration of the baro-reflex mechanism in the brain which increases diastolic blood pressure and an increase in sympathetic nervous system.

Pulse pressure is calculated by subtracting diastolic blood pressure from Systolic blood pressure. It is normally about one third of the Systolic blood pressure. If the Blood pressure is 120/80 mmHg, the pulse pressure is 40. Known factors that increase systolic blood pressure thus increasing pulse pressure include exercise and atherosclerosis. Patients with heart failure and low blood volume causes low pulse pressure.

Fractional pulse pressure (PPf) directly reflects large artery function and stiffness. It is calculated by dividing pulse pressure with the mean arterial blood pressure. Studies done have shown that impaired coronary circulation is associated with an ascending fractional pulse pressure. The inelasticity of arteries is affected more by fractional pulse pressure than the arterial pulse pressure.

During a study to evaluate the relationship between coronary flow reserve (CFR) and fractional pulse pressure (PPf) in known patients with hypertension with normal coronary arteries, one-hundred and six consecutive hypertensive patients (aged 52.8 + 9.4 years), with indications of myocardial ischaemia with exercise electrocardiogram (EECG) and normal coronary arteries in coronary angiography.

Hypertensive patients who had a low coronary blood flow were shown to have high fractional pulse pressure compared with those with normal Coronary flow rate who had normal flow rate.

In the same study; for hypertensives with low coronary flow rate, it was shown that coronary flow rate was negatively correlated to fractional pulse pressure. They then applied multivariate linear regression analysis where fractional pulse pressure, age of the patient and left ventricular mass index were shown to be independent indicators of Coronary Flow rate. (Ragab A , 2013).

Estimation of PPf by using simple sphygmomanometer blood pressure measurement is a simple non-invasive index for assessment of coronary microcirculation in essential hypertensive patients with indications of myocardial ischaemia and normal coronary arteries.

The two main risk factors for coronary heart disease are increased pulse pressure and fractional pulse pressure. Previous studies have shown a very strong association between increased fractional pulse pressure and pulse pressure with coronary artery disease. (Serkan Cay et al, 2006).

Well-known correlates of conduit vessel stiffness hence pulse pressure, include age (Bramwell et al, 1923 and Franklin *, 1997)* family history of diabetes mellitus (Salomaa et al, 1995) or hypertension (Avolio et al, 1985). These three factors were found to be related to pulse pressure and have been strictly controlled for in the present study.

1.2 LITERATURE REVIEW

Researchers have used different approaches to try and give answers to questions pertaining to sleep; any diseases associated with lack of sleep and for how long a human adult should sleep. Previous research has not been conclusive on these. Sleep deprivation has complex behavioral, nervous and also broader physiological effects. Studies have also shown that lack of sleep also has economical and social effects on a country.

Studies have concluded that normal require 8 hours of sleep per night for optimal functioning (National sleep foundation, 2002). However, the modern way life and occupational factors including increased use of technology in the evening, all decrease sleep duration and can cause chronic sleep deprivation. (Colton & Altevogt, 2006).

The first study published on sleep deprivation was over a century ago. (Patrick & Gilbert, 1896) and since then many studies have examined the impact of sleep deprivation on healthy physiologic functioning. A study done in 1996 (Pilcher & Huffcutt, 1996) highlighted the impact of sleep deprivation. Their results showed that mental performance and self-rated mood of the sleep deprived individuals below the 9th percentile of non-sleep-deprived subjects.

In another study (Dawson & Reid, 1997), the negative effect of sleep deprivation on performance was illustrated by use of alcohol. They found out that cognitive performance after seventeen hours of continuous wakefulness was equal to that of a person with a blood alcohol concentration of 0.05 %. On further analysis, mental performance of an individual after a day of wakefulness was equal to that of an individual with a 0.10% blood concentration of alcohol (Dawson & Reid,1997).

Sleep deprivation is common in many occupations especially those requiring full day operation such as nursing, medicine, and the transport industry and in many cases chronic sleep deprivation has caused tragic accidents and dangerous incidences in factories and mines. (Mitler et al, 1988)

Early experiments on sleep deprivation illustrated few alterations in waking performance associated with sleep deprivation, but more significant effects following late sleep deprivation. This observation led to the formulation of the core sleep hypothesis (Horne, 1988). It describes that only a sleep period of 4–5 hours per night is physiologically required to maintain healthy functioning.

However, afterwards experiments on controlled sleep restriction have depicted significant functional alterations after sleep is decreased to less than7 hours per night. (Dongen et al, 2003). Moreover, tests on sleep fragmentation in which total sleep time has been minimally reduced have showed significant cognitive deficits when awake. This is similar to cognitive deficits after partial or total sleep deprivation (Belenky G et al, 2003).----------

There is a decrease in arterial blood pressure in 95% of normo-tensive individuals (Staessen et al, 1997). However, there is no similar change of arterial blood pressure in individuals on total bed rest and total sleep deprivation (Kerkhof et al, 1998). This means that the change in arterial blood pressure is affected by level of activity and state of rest and sleep. A decrease in blood pressure during sleep (Brush & Fayer, 1901) is related to the fact that during sleep an individual is in as state of inactivity.

There is still no unanimous conclusion from earlier researchers on effect of sleep deprivation on the sympathetic nervous system and the cardiovascular system. Some researchers have reported increases in blood pressure, heart rate, and urine catecholamine level; (Lusardi et al,

1999) non- alterations in blood pressure (Gonzalez-Ortiz et al, 2000) or no change in heart rate (Tofler et al, 1987) after total sleep deprivation compared with after controlled sleep.

According to an experiment done in 2003 (Ogawa et al, 2003) human subjects after total sleep deprivation were found to have a significantly high diastolic blood pressure than after controlled sleep. Other than the change in diastolic blood pressure, there was concomitant decrease in the burst rate and burst incidence of muscle sympathetic nervous activity after total sleep deprivation. It was inferred from the study that the resetting of the Arterial baro-reflex after total sleep deprivation was towards a high blood pressure.

Both a decreased cardiac output and an increase in blood vessel vascular conduction, seen during Non-rapid eye movement sleep, do not follow normal functioning of the arterial baro-reflex during wakefulness. Thus, after the arterial Baro-reflex is pharmacologically reduced to the level of Non-rapid eye movement sleep, there will be increases in the sympathetic nervous activity of muscles and the heart rate. (Somers et al, 1993).

It can be interpreted from the results demonstrates that the arterial baro-reflex either is altered with respect to its sensitivity or during periods of wakefulness there is a re-setting (Somers et al, 1993). Animal experiments have provided evidence that supports the fact that there is a resetting of the baro-reflex during wakefulness. These has been done on lambs (Horne et al, 1991, cats and even rats(Nagura et al, 2004). All the experiments show that there is no major difference in the baro-reflex gain between periods of wakefulness and Non-rapid eye movement sleep.

Smyth et al, in 1969 showed an increase in cardiac baro-receptor reflex while another researcher (Bristow, 1969) described no change in the cardiac baro-reflex gain when drugs were used to stimulate blood pressure during Non-rapid eye movement sleep.

Subsequent studies have provided different results on changes in cardic baro-reflex based on the index which the researcher uses for baro-reflex gain. The gain in cardiac baro-reflex with respect to spontaneous blood pressure changes was shown to be higher during NREMS (Legramante et al, 2003) especially in the presence of cyclic alternating pattern (Lellamo et al, 2004). A gain with respect to spontaneous decrease in blood pressure appears not to change with respect to wakefulness (Nakazato et al).

Similarly, Monti et al, 2002, has shown that serial calculations of the magnitude of gain in cardiac baro-reflex during NREMS may be greater in the high frequency range but remains unchanged in the lower range of frequency.

1.2.1 PHYSIOLOGY AND PATHOPHYSIOLOGY OF PULSE PRESSURE

Pulse pressure increases with increase in age as part of the normal physiological changes. This is due to a corresponding increase in stroke volume of the heart and peripheral vascular resistance. As cumulative effect, there is marked increase in systolic blood pressure and a decrease in diastolic blood pressure resulting in a notable increase in pulse pressure by the age of sixty. (Dart & Kingwell , 2001).

Pulse pressure and the velocity of the pulse wave important have been used as important diagnostic markers of cardiovascular pathology (Safar, 2001).An increased age of an individual put him or her at higher risk of cardiovascular diseases. This is associated mainly with higher incidences of increased pulse pressure and a high systolic pressure (Hozawa A et al, 2000).

More recent studies on pulse pressure have found that a wide or high pulse pressure is a stronger marker for poor cardiovascular prognosis, especially deaths related to coronary vessels. This is mainly due to the fact that a wide pulse pressure indicates inelasticity of the great vessels. A study done by Athanase et al in 199 where he used male subjects aged between 40 and 69 years illustrated that a high pulse pressure was the main risk factor for cardiovascular deaths and specifically those related to coronary arteries.

Research related to pulse pressure has increased as more evidence points at a strong correlation between it and poor cardiovascular prognosis (Tozawa et al, 2002). A gradual increase in pulse pressure with increased age is mainly due to a decrease in diastolic blood pressure, increase in systolic blood pressure or a combination of both factors (Franklin , 1999).

A wide pulse pressure physiologically results in an increase preload which is an important determinant of the left ventricular anatomy and physiology. On the other hand decreased diastolic blood pressure may cause a reduced blood flow through the coronary arteries.

These two parameters and their physiologic effects can thus explain the increased cardiovascular morbidity and mortality associated with an increased pulse pressure (Verdecchia et al, 2001). More over an increase in peripheral vascular resistance is the main basis of arterial hypertension and is associated with wide pulse pressure.

A wide pulse pressure, however, is a result of both increased systolic blood pressure that causes dilation of blood vessels and stiffness of arteries that are to accommodate the ejected blood (Haider et al, 2003). In the pathophysiology of hypertension, atherosclerosis causes an increased pulse pressure. A wide pulse pressure may thus be due to changes in the structure of blood vessels, especially those that cause hardening or stiffening. A high pulse pressure therefore suggests a more severe pathology than increase in peripheral vascular resistance.

Thus, in the time course of cardiovascular disease, high pulse pressure may indicate preclinical vascular disease, whereas arterial hypertension is the risk factor for the development of such preclinical disease (Devereux & Alderman, 1993)

Franklin et al, 1999 showed that brachial pulse pressure, compared systolic blood pressure, was a better index for assessing coronary heart disease. For any given value of systolic blood pressure, the individual has a higher risk of cardiovascular disease if the diastolic blood pressure is decreased. This was due to the greater arterial stiffness with the wide pulse pressure. The concept of high pulse pressures and a corresponding high risk of cardiovascular diseases has been replicated in human studies (Van Bortel et al, 2001). Other studies have shown a strong association of brachial pulse pressure with anatomical alterations of large blood vessels (Van Dijk et al, 2001). Moreover, pulse pressure and other risk factors for arterial stiffness have a similar pathophysiologic pattern in causing cardiovascular diseases . (Viazzi et al, 2002) and (Wilkinson et al, 2002).

In a study, (Madhavan et al, found that patients with high blood pressures, above 63 mmHg, that were not on treatment subjects with a pulse pressure were more likely to develop cardiovascular complications. In the same study, they also found that the same subjects were more at risk of were at greater risk of myocardial infarction once treated if the diastolic blood pressure was greatly reduced. Different researchers did a study with a bigger sample of hypertensive subjects, some on treatment and others not on of treatment. They found out that the only parameter during the course of treatment that was positively related to myocardial infarction was pulse pressure. (Fang et al, 1995).

The link between pulse pressure and cardiovascular complications has also been documented in patients with myocardial infarction who has left ventricular dysfunction (Mitchelle et al, 1997). They found out that the daily measurements of pulse pressure between three and sixteen days after myocardial infarction was a good prognostic marker of refractory cardiovascular diseases . In another study, Athanase et al, 1998 showed that the most significant marker cardiovascular mortality is pulse pressure. Their study was done among males aged between 40 and 69 years. Their study also showed that assessment of pulse pressure is of importance even among individuals with normal values of both systolic blood pressure and diastolic blood pressure.

Research has shown that in individuals with normal blood pressure, pulse pressure is a better patho-physiologic marker of cardiovascular disease. An increase of 10 mm Hg of pulse pressure among normotensives has a higher index of cardiovascular disease than a corresponding increase among hypertensive . There was no such difference noted in the study between the hypertensive subjects and those with normal blood pressure; this was due to a bigger difference in pulse pressure levels among those in the hypertensive group.

As expected, hypertensive individuals globally show higher mortality levels than normotensive individuals. However, cardiovascular, especially coronary, death rates were similar in normotensive men with a PP >50 mm Hg and in hypertensive men with PP <45 mm Hg. They also did a multivariate Cox regression analysis where they adjusted for age and other risk factors but the results were unchanged.

In their study, individuals who has normal blood pressure but a high pulse pressure (Mean systolic blood pressure of 131 mm Hg; Mean diastolic blood pressure of 73 mm Hg and a mean pulse pressure of 58 mm Hg) had a 40% higher risk of cardiovascular pathology when compared to individuals with normal blood pressure but a normal pulse pressure (Mean systolic blood pressure of 120 mm Hg , mean diastolic blood pressure of 78 mmHg and a mean pulse pressure of 42 mmHg). On the further analysis, the first group with high pulse pressure but normal blood pressure had an equal cardiovascular risk as the subjects who were hypertensive but had a low pulse pressure (Mean Systolic blood pressure of 145 mm Hg, Mean diastolic blood pressure of 105 mm Hg and a mean pulse pressure of 40 mm Hg).

Mortality from coronary artery disease was strongly associated with an increased pulse pressure. A physiologic explanation of pulse pressure is the oscillation around the mean arterial pressure is physiologically affected by distinct mechanisms that differ from those controlling the mean arterial blood pressure .Physiologically, mean arterial blood pressure is defined as that pressure in the aorta and major arteries during a given cardiac cycle especially if the cardiac output is not pulsatile (Nicholas & O'Rourke, 1990).

Pulse pressure normally increases significantly as you move from the central arteries to the peripheral arteries. Mean arterial blood pressure however remains constant from the central arteries to the peripheral arteries. The increased pulse pressure is due to a corresponding increase in systolic blood pressure and a decrease in diastolic blood pressure down the vascular tree.

The factors that affect pulse pressure in an individual at a given stroke at a giPP are mainly the elastic properties and the timing of pressure waves from the arterial walls . Research has shown that an increase in stiffness and formation of early pressure wave reflections (Kelly et al, 1992) result in increased pulse pressure. An increase in left ventricular ejection rate(LVER) coupled with an increase in stroke volume(SV) would cause an increase in systolic blood pressure but no change in the diastolic blood pressure .Wanatabe et al reported the highest pulse pressure to be as a result of high systolic blood pressures and low diastolic blood pressures (Watanabe et al, 1993).

It can then be postulated that pulse pressure is an independent indicator of stiffness of arteries, thus subsequently determining cardiovascular mortality of coronary origin. (Hoffman, 1987). Studies done have shown that an increased pulse pressure among elderly patients who have essential hypertension is a strong marker for poor prognosis and even death (Franklin et al, 1997 & Franklin et al 199

As systolic blood pressure increases there is an increased workload on the heart after systole. This is a fundamental mechanism underlying development of ventricular hypertrophy and a higher demand of oxygen by the cardiac muscles (Pannier et al, 1989). Consequently there will be impaired coronary perfusion (Watanabe et al, 1993).This cascade of events illustrate why an increased pulse pressure will mainly affect coronary and not cerebrovascular circulation.

Interest in pulse pressure has now extended to the young population (*Benetos* et al 1997 & Benetos et al 1998) and those with normal blood pressures (Fang et al, 2000).

1.2.1.1 Low (Narrow) Pulse Pressure

Pulse pressure is considered low if its calculated value is less than a quarter of the systolic blood pressure. According to the American college of Surgeons atlas, 2008, a decreases stroke volume is the leading cause of low pulse pressure. Within the clinical set-up, a narrow pulse pressure may indicate excessive hemorrhage , or decreased intravascular fluid which compromises cardiac output. Cardiovascular morbidities like aortic valve stenosis, heart failure, hemorrhagic shock and cardiac tamponade can result in significantly low pulse pressures.

High (Wide) Pulse Pressure

a) High values during or shortly after exercise

A healthy individual should have a pulse pressure of between 30mm Hg and 40 mmHg at rest. During exercise, there is an increase in stroke volume that increases pulse pressure(Farida et al, 2007),However , the pulse pressure normalizes within approximately 10 minutes. Pulse pressure can rise to as high as 100 mmHg due to the sustained fall in peripheral vascular resistance as the systolic blood pressure increases.

Systolic blood pressure increases during exercise while the diastolic blood pressure does not change. Long distance athletes have been noted to have a decreasing diastolic blood pressure as the systolic blood pressure increases. This enhances an increase of both cardiac output and stroke volume at a much lower mean arterial blood pressure. This allows for better physical performance and greater aerobic capacity.

Decrease peripheral vascular resistance is the basis for decreased diastolic pressure during exercise. High body mass index in individuals with an increased muscle mass like weight lifters separately been shown cause lower diastolic pressures and wide pulse pressures (Bertovic et al, 2008).

b) Consistently high values of pulse pressure

Cases of chronically high or wide pulse pressures are most likely due to inelasticity of the major arteries, arterio-venous malformation , regurgitation at the aortic valve, known cases of hyperthyroidism or multiple effects . Persistenytly high stroke volume in some cases can also be a causative factor (Haider et al, 2003).

Studies have shown that Angiotensin –converting enzyme inhibitors lower pulse pressure. Conversely a large number of anti-hypertensive drugs cause a persistently high pulse pressure. Normal aging process of body organs, especially heart, the brain and kidneys is faster in individuals with chronically high pulse pressure readings. This indicates a deleterious effect of pulse pressure on organ integrity (Dart & Kingwell, 2001).

Irregular breathing pattern, very low blood pressure and an increased pulse pressure is a strong predictor of raised intracranial pressure (ICP). It should be treated as a medical emergency. This is mainly seen in patients who have sustained head trauma resulting in intracranial bleeding or cerebral oedema (Pannier et al, 1989) .

Therefore, as a specific marker, pulse pressure has been used clinically to assess prognosis of cardiovascular health and diseases. It is a more specific marker of cardiovascular health. Increase in pulse pressure with normal blood pressures has been associated with many cardiovascular diseases and a higher morbidity and mortality rate.

Fractional pulse pressure is an equally specific marker of cardiovascular health. No study at present has assessed the effect of sleep deprivation on these parameters.

This study was aimed at assessing whether chronic sleep deprivation has any significant effect on pulse pressure and fractional pulse pressure. This would aid in assessing the effect of sleep deprivation on cardiovascular health, if any. The results of this study would contribute to the growing field of sleep physiology and provide more insight in management of cardiovascular diseases.

Importantly, this would highlight the role of daily sleep requirement in general health which would be considered by relevant authorities in policy making.

1.3 JUSTIFICATION

Chronic sleep deprivation has been found to increase the diastolic blood pressure and mean arterial blood pressure by resetting the baro-reflex mechanism. Pulse pressure as a component of blood pressure can be is a specific marker of cardiovascular function. Two derivatives of pulse pressure, the fractional pulse pressure and pulse pressure variation index are important physiologic parameters in determining cardiovascular health and prognosis of cardiovascular diseases

To our knowledge, no research study has been performed to show the relationship between chronic sleep deprivation and pulse pressure or its derivatives. This is important in view of the pressures of modern living that have made sleep deprivation very common as people engage in a myriad of activities for many hours in a day. As much as one in five adults are sleep deprived. Moreover, many chronic diseases nowadays have lifestyle as a prime risk factor.

This study aimed at probing on whether there is a significant effect of sleep deprivation on pulse pressure or any of its derivatives. This will aid us have more insight on the physiology of sleep and its relation, if any, to cardiovascular physiology and patho-physiology. Furthermore, the results will help us in management of hypertension and cardiovascular health in general.

1.4 OBJECTIVES

The broad objective of the present study is:

1. To establish any significant relationship between acute sleep deprivation and pulse pressure.

The specific objectives of the study are:

1. To determine the effects of acute sleep deprivation on pulse pressure.
2. To determine the effect of acute sleep deprivation on fractional pulse pressure.
3. To determine the effects of acute sleep deprivation on pulse pressure and fractional pulse pressure.

1.5 HYPOTHESIS

H_0 : Acute sleep deprivation has no correlation with changes in pulse pressure .

H_1: Acute sleep deprivation has a correlation with changes in pulse pressure

CHAPTER TWO

METHODS AND MATERIALS

2.1 Study Design

The study was a randomized control study.

2.2 Study Setting

The study was done at The Karen Hospital located at Karen, Nairobi.

2.3 Ethical Consideration

Approval from Kenyattta National Hospital/ University of Nairobi Ethics and research committee was obtained prior to commencement of study. Further approval was sought from the Karen Hospital research and Ethics Committee. Informed consent was obtained from each of the subjects who agreed to participate in the study

(See appendix II)

2.4 Sampling Methods:

All eligible subjects were recruited randomly in the study. Questionnaires were then used to assign them to either the test group or the control group

2.5 Sample size determination

This is a randomized controlled study whose objective is to establish if there is any relationship between chronic sleep deprivation and changes in pulse pressure. The alpha was taken at 0.05, which means that there was a desired <5% chance of drawing a false-positive conclusion. The power of the study (complement of beta: 1-beta of 0.20) was 0.80 or 80%.

The primary outcome of the study was pulse pressure changes which is a continuous outcome variable. The normal range for the pulse pressure is between 30 to 50 mmHg. Diagnostic thresholds for clinical Pulse Pressure (> or =65 mm Hg) determined either by adding 2 SD to the means or from the 95th percentiles are in close agreement with clinic Pulse pressure

values previously reported to be associated with increased cardiovascular morbidity and mortality. The minimum clinically relevant difference was taken to be 10 mmHg. The standard deviation of pulse pressure in the population was taken to be 20mm Hg.

Formulae and calculation:

n = the sample size in each of the groups

$\mu_1 - \mu_2$ = the difference the investigator wishes to detect. In this case, the significance of interest is a change of 15 mmHg in pulse pressure

σ^2 = population variance (SD). The normal standard deviation of pulse pressure is 20 mmHg.

a = conventional multiplier for alpha = 0.05 which is 1.96

b = conventional multiplier for power = 0.80 which is 0.842

$$n = \frac{2\left[(a+b)^2\sigma^2\right]}{(\mu_1-\mu_2)^2}$$

$$N = \frac{2[(1.96+0.842)^2 \times 20^2]}{15^2}$$

N = 27. 914

N = 28 subjects on each group

2.6 Inclusion criteria

Both the control group and test group will be screened by use of questionnaires

a) Control group
   - ✓ Healthy
   - ✓ Between 20 and 40 years old.
   - ✓ Having a healthy sleeping pattern of not less than 7 hours of sleep

b) Test group
   - ✓ Healthy
   - ✓ Between 20 and 40 years old.
   - ✓ Having a sleeping pattern of less than 4 hours of sleep

2.7 Exclusion criteria

a. Control group
   - ✓ Sick/ unhealthy
   - ✓ Known diabetic or hypertensive
   - ✓ Drug abuser
   - ✓ Currently on any medication that disturbs sleeping pattern
   - ✓ Pregnant

b. Test group
   - ✓ Sick/ unhealthy
   - ✓ Known diabetic or hypertensive
   - ✓ Drug abuser
   - ✓ Currently on any medication that disturbs sleeping pattern
   - ✓ Pregnant

2.8 Study Population

The study involved a total of 56 Subjects who were divided into two equal arms; a control group of 28 subjects(14 male and 14 female) and a test group of 28 subjects (14 male and 14 female).

2.8.1 Control group:

The control group was defined as the non-sleep deprived subjects. It constituted twenty eight subjects who met the inclusion criteria for non- sleep deprived individuals. Each subject had to have sleep duration of more than seven hours in a night .It comprised of an equal number of males (14) and females (14). On each day during the study period, blood pressure measurements by use of a manual sphygmomanometer were done at 8.00 a.m.

Each subject had to report the number of hours they had slept over the night and for the last 24 hours. The first Korotkoff sound was taken as systolic blood pressure while the last korotkoff sound as the diastolic blood pressure. The readings were recorded in the data collection sheets and pulse pressure and fractional pulse pressure derived from their specific formulae. All blood pressure measurements were taken by the principal investigator for consistency.

2.8.2 Test Group:

The test group was defined as subjects who were sleep deprived. This group was selected by use of the questionnaire. It constituted subjects who reported to have had sleep duration less than four hours. It comprised of an equal number of males (14) and females (14).Upon selection each subject was assigned a number. Every morning at 7.30 a.m blood pressure measurement was done to subjects in the test group. Before blood pressure measurement each of the subjects had to report the number of hours they slept over the night and the whole 24 hours.

Blood pressure measurements were taken in a sitted position, after a five minute relation time. The first Korotkoff sound was taken as systolic blood pressure while the last korotkoff sound as the diastolic blood pressure. The readings were recorded in the data collection sheets and pulse pressure and fractional pulse pressure derived from their specific formulae. All blood pressure measurements were taken by the principal investigator for consistency.

2.9 Data collection

The study was conducted over a period of one month. On a daily basis, at each time every day, blood pressure readings were taken for both the test group and the control group. A sleep deprived subject must have had less than four hours of sleep for the last 24 hours whereas a non- sleep deprived subject must have had more than 7 hours of sleep in the last 24 hrs. This was done using the manual sphygmomanometer. The American Heart Association guidelines on taking manual blood pressure readings with a sphygmomanometer were followed. The systolic blood pressure and the diastolic blood pressure readings were taken.

All the readings were taken manually daily and later analysed and interpreted as discussed below.

For each subject, their respective Mean Arterial blood pressure, Pulse pressure and fractional pulse pressure were derived using the following formulae:

1. ***Mean Arterial Blood Pressure***

One- third of the difference between systolic and diastolic blood pressure added to the diastolic blood pressure.

- ✓ **MAP = 1/3 (SBP – DBP) + DBP**

2. *Pulse Pressure*

Systolic blood pressure minus diastolic blood pressure

- ✓ **Pulse Pressure= SBP- DBP**

3. *Fractional Pulse Pressure*

Pulse pressure divided by mean arterial pressure

- ✓ (SBP-DBP/MAP)

Pulse pressure increases with age and also most hemodymanic parameters change with age. After 50 years of age pulse pressure has been found to increase. Thus an age group of between 20 and 40 years was considered most appropriate. Diabetes and hypertension both have a direct effect on pulse pressure through their thickening of blood vessels and effect on the heart muscles respectively. Various disease states, drugs like alcohol and smoking and physiologic states like pregnancy also remarkably affect blood pressure and pulse pressure.

2.9.1 Interpretation of mean arterial pressure

Physiologically, mean arterial pressure represents the mean arterial blood pressure during a cardiac cycle. The counter-resistance to flow of blood is very low in the large arteries, therefore mean arterial pressure in the aorta and that of the big arteries is almost equal. Thus commonly, the brachial artery at the ante-cubital fossa is used to for measuring blood pressure. A lower threshold of 60 mm Hg mean arterial blood pressure is required to maintain blood flow through the arteries. The normal physiological ranges of Mean arterial pressure are between 65 mmHg – 110 mmHg. Mean arterial blood pressures above 120 mmHg were considered abnormally high and those below 60mmHg were considered low.

2.9.2 Interpretation of Pulse pressure:

Physiologically, pulse pressure is calculated as the difference between the systolic and diastolic blood pressure. It is measured in millimeters of mercury. A millimeter is the metric unit that represents 1/1000th of a meter. It is considered to be within the normal ranges between 30 to 50 mmHg. High pulse pressure in this study was considered to be pressure above 65 mmHg while low pulse pressure was considered to be pressure below 20 mmHg.

2.9.3 Interpretation of fractional pulse pressure

Estimation of fractional pulse pressure (PPf) by using simple sphygmomanometer blood pressure measurement is a simple non-invasive index for assessment of coronary microcirculation. Moreover, PPf reflects arterial stiffness more accurately than pulse pressure, because dividing the pulse pressure by mean arterial pressure theoretically cancels out the influence of cardiac output and peripheral vascular resistance.

Fractional pulse pressure values were calculated by dividing values of pulse pressure by the the corresponding values of mean arterial blood pressure.

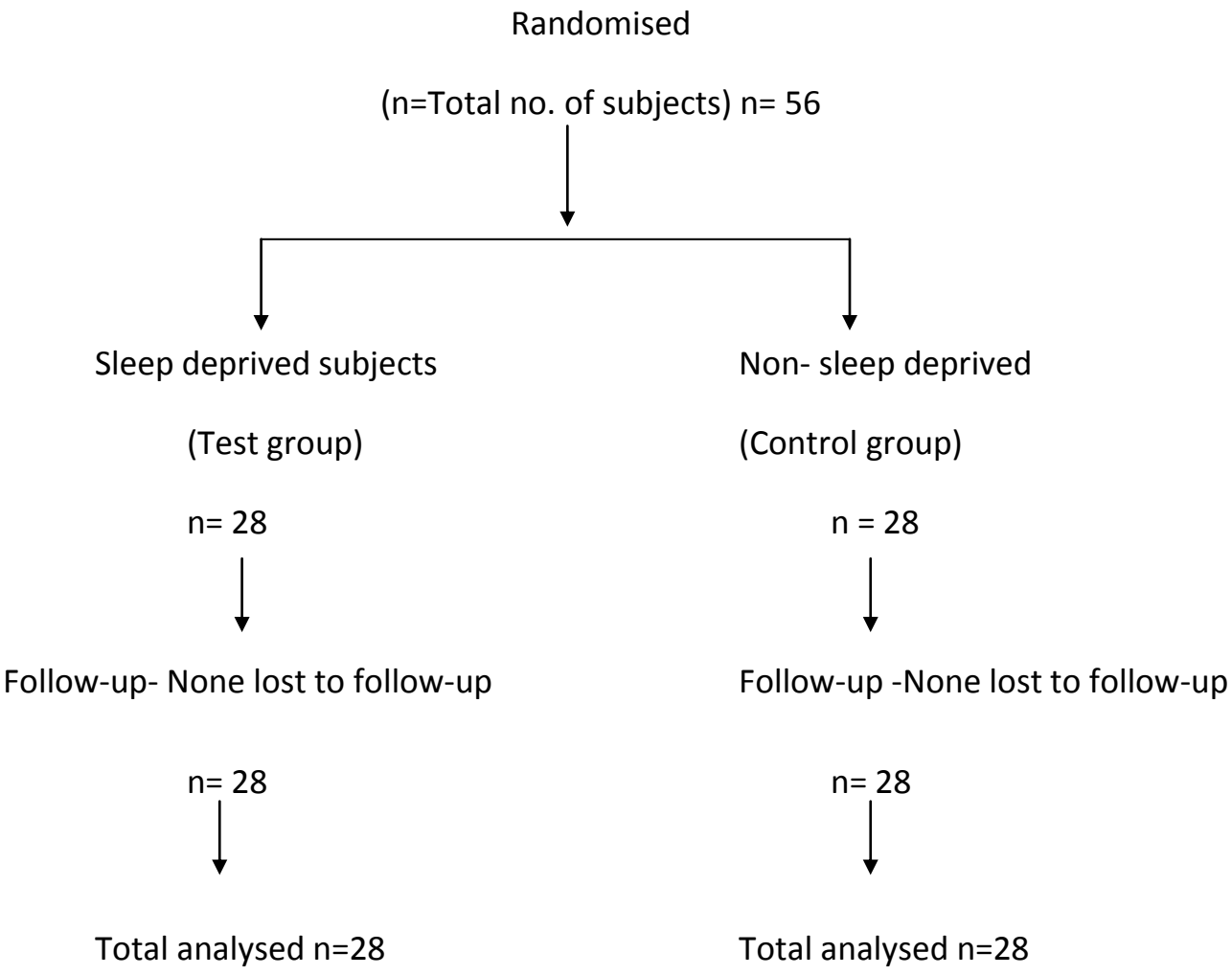
Increased fractional pulse pressure is associated with impaired coronary flow reserve (CFR) and subclinical diastolic dysfunction as shown by Mahfouz, 2013.

An ascending fractional pulse pressure was thus considered abnormal.

CHAPTER THREE

3.1 RESULTS AND ANALYSIS

Fifty six (56) subjects who met the inclusion criteria for either group were recruited into the study. No subject dropped out of the study after first contact and also throughout the period of study thus data from all the subjects; 28 in the test group and 28 in the control group was analysed.



Study flow diagram

Table 1: Summarised selected Pre-study characteristics of subjects in the two groups

Characteristic	*Control group(n=28)*	*Test group (n=28)*
Gender	Males =14	Males = 14
	Females=14	Females =14
Age	Range= 20-40	Range= 22- 36yrs
	Mean= 28.42	Mean= 27.86
Weight	Range=52-74 kg	Range=56-78kg
	Mean= 66.48	Mean =64.62
BMI	Range= 19.4- 29.7	Range= 18.5- 28.8
	Mean=23.8	Mean= 23.2
Mean Blood pressure	Systolic- 121.77	Systolic- 118.62
	Diastolic-73.68	Diastolic-71.74
Mean Pulse pressure	48.09	47.22
Mean arterial Pressure	82.71	78.48
Fractional pulse pressure	0.54	0.54

Data exploration showed that there was no significant difference in average weight in kilograms between the two groups; Test group (64.62) and control group (66.48) at the time of recruitment. Therefore weight and BMI were not controlled for in models for pulse pressure and fractional pulse pressure. There was also no significant difference in average BMI between the two groups; test group (23. 2) and control group (23 .8) at the time of recruitment. Only one female subject in the test group had a BMI of 28.8; overweight. Two females in the control group had a BMI greater than 24.9; one with 25.2 and 29.7.

There was also no significant difference in both systolic and diastolic blood pressure measurements between the control and the test group. None of the subjects both in the test group and the control group had blood pressure readings above 140 mmHg systolic and 90 mmHg diastolic. The mean pulse pressure of the test group at the time of recruitment was 47.22 while that of the control group was 48.09. These were within the normal ranges of 30 to 50 mm Hg. None of the subjects at recruitment had a pulse pressure greater than 50 or less

than 30. There was an equal measurement of fractional pulse pressure of 0.54 both of the control group and test group at the point of recruitment. There was also no significant difference in mean arterial blood pressure between the test group (78.48) and the control group (82.71). All parameters at the point of recruitment were normal.

Further exploration of data at recruitment time revealed no significant gender differences between all the three outcomes as shown in the table below.

Table 2: Pre-study gender characteristics of the control group and the test group

Characteristic	*Control group(n=28)*		*Test group (n=28)*	
Gender	*Males (n=14)*	*Females (n=14)*	*Males (n=14)*	*Females (n=14)*
Age	Range=20-36yrs	24-40yrs	Range= 28-36yrs	22-32 yrs
	Mean= 27.62	Mean=29.22	Mean= 26.52	Mean=28.36
Weight	Range=56-74kg	52-70 kg	Range=56-74kg	60-78kg
	Mean= 67.10kg	Mean=65.86 kg	Mean =63.93	Mean=65.31
BMI	Range= 19.8-24.1	19.4-29.7	Range= 18.5- 22.7	18.8-28.8
	Mean=22.8	Mean= 24.1	Mean= 22.4.	Mean= 23.6
Mean Blood pressure	Systolic= 121.44	Mean=122.10	Systolic- 116.21	Systolic=120.03
	Diastolic=72.90	Mean=74.46	Diastolic-70.64	Diastolic=72.84
Mean Pulse pressure	47.94	48.24	47.10	47.34
Mean arterial Pressure	80.54	84.88	77.62	79.64
Fractional pulse pressure	0.56	0.52	0.56	0.52

The two main outcome data in terms of pulse pressure and fractional pulse pressure were analysed using multivariate repeated measurements controlling for age and sex. The data was then analysed using IBM Statistics software .Data exploration showed that there was no significant difference in average weight between the two groups.

Table 3: Means, Ranges and standard deviation of Mean Arterial blood pressure, pulse pressure and fractional pulse pressure of subjects

	CONTROL GROUP			TEST GROUP		
	Mean	*Range*	*Standard deviation*	*Mean*	*Range*	*Standard deviation*
Pulse pressure						
Initial	48.09	32.0-74.0	10.33	47.22	31.0-77.0	10.65
1st week	48.75	30.0-76.0	10.46	42.93	30.0-76.0	11.07
2nd Week	47.93	30.0-76.0	10.08	44.32	38.0-66.0	7.11
3rd Week	48.42	32.0-78.0	12.97	48.25	19.0-80.0	12.45
4th Week	50.0	32.0-78.0	10.52	44.43	19.0-82.0	14.0
Fractional Pulse Pressure						
Initial	0.54	0.35-0.84	0.096	0.54	0.34-0.76	0.094
1st week	0.56	0.38-0.87	0.104	0.58	0.37-0.76	0.091
2nd Week	0.58	0.38-0.87	0.099	0.55	0.45-0.79	0.084
3rd Week	0.56	0.38-0.87	0.127	0.59	0.21-0.73	0.115
4th Week	0.58	0.36-0.85	0.097	0.54	0.21-0.87	0.097
Mean Arterial blood pressure						
Initial	82.71	68.24- 93.34	7.76	78.48	53.33-93.09	8.84
1st week	86.34	71.33-106.67	8..31	82.76	70.67-104.0	8.37
2nd Week	83.08	66.67-106.67	9.39	79.92	71.33-92.67	6.12
3rd Week	81.20	66.67-98.0	7.81	79.94	44.0-107.33	12.42
4th Week	79.38	30.0-88.67	10.66	76.81	42.0-92.67	10.85

Data shown in the table above depict various outcome variables that were collected and calculated over the four weeks of the study period. Analysis was done on a weekly basis as explained below.

END OF FIRST WEEK ANALYSIS

Table 4: Means, Ranges and Standard deviation of Mean Arterial blood pressure, pulse pressure and fractional pulse pressure of subjects during the first week

		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
Pulse pressure	Test	28	47.82	10.456	1.976	43.77	51.88	30	76
	Control	28	48.75	11.071	2.092	44.46	53.04	30	76
	Total	56	48.29	10.680	1.427	45.43	51.15	30	76
Fractional pulse pressure	Test	28	.5759	.10404	.01966	.5356	.6163	.38	.87
	Control	28	.5606	.09066	.01713	.5254	.5957	.39	.76
	Total	56	.5683	.09700	.01296	.5423	.5942	.38	.87
Mean Arterial blood pressure	Test	28	82.7679	8.31521	1.57143	79.5436	85.9922	71.33	106.67
	Control	28	86.3393	8.37526	1.58278	83.0917	89.5869	70.67	104.00
	Total	56	84.5536	8.46312	1.13093	82.2871	86.8200	70.67	106.67

Test = Test group

Control = Control group

After the first week of analysis, the two main outcome data in terms of pulse pressure and fractional pulse pressure were analysed by use of IBM SPSSS statistics 20 by use of chi-square, Pearsons correlation and multi-linear regression. Analysis was done for both groups. The above table is a frequency table of the various variables for both groups during the first week of the study.

Analysis of data from the test group indicated that subjects had a mean sleeping time of 2.2 hours and a mean pulse pressure of 47.8 mm Hg and a mean fractional pulse pressure of 0.57 as indicated in table 2 below. Both outcome data were within the normal range. In contrast the control group had a mean no. of 7.99 sleeping hours and a mean pulse pressure of 48.8 mm Hg and a mean fractional pressure of 0.56. Further analysis by one way- ANOVA between the test group and control group in the first week indicated a non –significant variation of pulse pressure between the groups (p=0.748). Similarly, the variation of fractional

pulse pressure between the test group and control group was non- significant (p= 0.558). This is illustrated in table 5 below.

Table 5: One-way ANOVA table on variation of pulse pressure and fractional pulse pressure between the test and control groups during the first week

		Sum of Squares	df	Mean Square	F	P
Pulse pressure	Between Groups	12.071	1	12.071	0.104	**0.748**
	Within Groups	6261.357	54	115.951		
	Total	6273.429	55			
Fractional pulse pressure	Between Groups	.003	1	.003	0.347	**0.558**
	Within Groups	.514	54	.010		
	Total	.517	55			

Groups refer to the test group and control group.
Df= degrees of freedom
p= p value of significance

Further analysis by use of Pearson chi-square illustrated a non - significant relationship between number of hours slept and pulse pressure (p=0.895). This is illustrated in table six (6) below. The same analysis illustrated a non-significant relationship between fractional pulse pressure and number of hours slept (p= 0.557)

Table 6: Chi-square test on relationship between number of hours slept and fractional pulse pressure and pulse pressure during the first week

	FRACTIONAL PULSE PRESSURE				**PULSE PRESSURE**		
	Value	df	P		Value	Df	p
Pearson Chi-Square	454.978	460	**0.557**		165.995	190	**0.895**
Likelihood Ratio	233.603	460	**1.000**		125.852	190	**1.000**
Linear-by-Linear Association	.114	1	**0.735**		.168	1	**0.682**
N	56				56		

Pearson correlation analysis showed a non significant positive correlation between number of hours slept and pulse pressure (r= 0.055, p=0.686). This is illustrated in table seven (7) below. Moreover a non-significant negative correlation was depicted between number of hours slept and fractional pulse pressure (r= -0.46 p= 0.739).

Table 7: Pearson's correlation between number of hours slept and pulse pressure and fractional pulse pressure in the first week

		PULSE PRESSURE		**FRACTIONAL PULSE PRESSURE**	
		Number of hours slept		Number of hours slept	
NO. of hours slept	Pearson Correlation (r value)	1	**0.055**	1	**-0.046**
	p value		**0.686**		**0.739**
	N	56	**56**	56	**56**

On multiple linear regression analysis; with gender, the two groups and number of hours slept as the predictors, none was found to have a significant effect on pulse pressure. All the three predictors had a cumulative non- significant effect (p= 0.744). Similarly, on multiple linear regression, gender, the two groups and number of hours slept had a cumulative non-significant effect (p=0.502) on fractional pulse pressure.

Table 8: Multiple linear regression of gender, number of hours slept and the groups on pulse pressure

Model	Sum of Squares	Df	Mean Square	F	P
Regression	146.077	3	48.692	0.413	**0.744**[b]
Residual	6127.352	52	117.834		
Total	6273.429	55			

a. Dependent Variable: Pulse pressure

b. Predictors: (Constant), Male& Female, Test group & control group, Number of hours slept

Table 9: Multiple linear regression on gender, number of hours slept and the groups on fractional pulse pressure

Model		Sum of Squares	df	Mean Square	F	P
	Regression	.023	3	.008	0.795	**0.502**[b]
	Residual	.495	52	.010		
	Total	.517	55			

Dependent Variable: Fractional pulse pressure

b. Predictors: (Constant), Male &Female, Test group & control group, Number of hours slept

Table 10: Various co-efficients of significance on multiple linear regression during the first week

Model		Unstandardized Coefficients		Standardized Coefficients	t	p	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	.526	.047		11.276	.000	.433	.620
	NO. of hours slept	.009	.013	.299	.720	.475	-.017	.035
	Test group and control group	-.001	.001	-.362	-.873	.387	-.003	.001

Table 11: Descriptive statistics of various outcome variables on week 2

		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
No. of hours slept	Test	28	1.5357	1.03574	.19574	1.1341	1.9373	.00	3.00
	Control	28	8.1071	.84280	.15927	7.7803	8.4339	7.00	10.00
	Total	56	4.8214	3.44493	.46035	3.8989	5.7440	.00	10.00
Mean Arterial blood pressure	Test	28	79.9167	9.38593	1.77377	76.2772	83.5562	66.67	106.67
	Control	28	83.0833	6.11725	1.15605	80.7113	85.4554	71.33	92.67
	Total	56	81.5000	8.01060	1.07046	79.3547	83.6453	66.67	106.67
Pulse pressure	Test	28	44.32	10.078	1.905	40.41	48.23	30	76
	Control	28	47.93	7.107	1.343	45.17	50.68	38	66
	Total	56	46.13	8.830	1.180	43.76	48.49	30	76
Fractional pulse pressure	Test	28	.5535	.09909	.01873	.5151	.5920	.38	.87
	Control	28	.5783	.08400	.01587	.5457	.6109	.45	.79
	Total	56	.5659	.09187	.01228	.5413	.5905	.38	.87

Table 12: Descriptive statistics of various outcome variables on week 3

		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
No. of hours slept	Test	28	1.7143	.80999	.15307	1.4002	2.0284	.00	3.00
	Control	28	8.4286	.67651	.12785	8.1662	8.6909	7.50	10.00
	Total	56	5.0714	3.46729	.46334	4.1429	6.0000	.00	10.00
Mean Arterial blood pressure	Test	28	79.9405	7.80738	1.47546	76.9131	82.9679	66.67	98.00
	Control	28	81.2143	12.42731	2.34854	76.3955	86.0331	44.00	107.33
	Total	56	80.5774	10.30298	1.37679	77.8182	83.3365	44.00	107.33
Pulse pressure	Test	28	48.2500	12.96612	2.45037	43.2223	53.2777	30.00	76.00
	Control	28	48.4524	12.34091	2.33221	43.6671	53.2377	18.00	80.00
	Total	56	48.3512	12.54220	1.67602	44.9924	51.7100	18.00	80.00
Fractional pulse pressure	Test	28	.5990	.12712	.02402	.5497	.6483	.38	.87
	Control	28	.5565	.11542	.02181	.5117	.6013	.21	.73
	Total	56	.5778	.12220	.01633	.5450	.6105	.21	.87

Table 13: Descriptive statistics of various outcome variables on week 4

		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
No. of hours slept	Test	28	1.7679	1.50605	.28462	1.1839	2.3518	.00	8.00
	Control	28	8.1607	.62440	.11800	7.9186	8.4028	7.00	10.00
	Total	56	4.9643	3.42167	.45724	4.0480	5.8806	.00	10.00
Pulse pressure	Test	28	44.4286	10.51781	1.98768	40.3502	48.5070	32.00	78.00
	Control	28	50.0000	14.00529	2.64675	44.5693	55.4307	18.00	82.00
	Total	56	47.2143	12.58963	1.68236	43.8428	50.5858	18.00	82.00
Mean Arterial blood pressure	Test	28	76.8095	10.66413	2.01533	72.6744	80.9446	30.00	88.67
	Control	28	79.3810	10.84561	2.04963	75.1755	83.5864	42.00	92.67
	Total	56	78.0952	10.73571	1.43462	75.2202	80.9703	30.00	92.67
Fractional pulse pressure	Test	28	.5440	.09733	.01839	.5062	.5817	.38	.87
	Control	28	.5830	.12255	.02316	.5354	.6305	.21	.87
	Total	56	.5635	.11140	.01489	.5336	.5933	.21	.87

Analysis of the means of the two main outcome variables in the second, third and fourth week indicated that mean pulse pressure of the test group was 42.93mm Hg, 48.3 mmHg and 44.42mmHg respectively while that for the control group was 47.8 mmHg, 48.4 mmHg and 50.0 mmHg. In all the three weeks the pulse pressure for the control group was higher. There was a decrease in mean pulse pressure of the test group compared to the control group by 4.87 mmHg in the second week. A decrease of 0.1 mmHg in the third week was found while a decrease of 4.42mmHg in the fourth week was recorded.

Analysis of mean fractional pulse pressure depicted a mean of 0.55, 0.56 and 0.54 in the second, third and fourth weeks respectively for the test group. The control group had a mean of 0.57, 0.58 and 0.57 respectively. This shows a marginal decrease in fractional pulse pressure of 0.02, 0.02 and 0.03 for the test group in comparison with the control group for the second, third and fourth weeks respectively.

Further analysis by one way ANOVA indicated a non-significant variation of pulse pressure between the test group and the control group during the three weeks. On the second week p= 0.128; third week p=0.953 and fourth week p= 0.098. Similarly, there was a non-significant variation of fractional pulse pressure between the test group and the control group. The p values during for the three weeks were 0.318, 0.196 and 0.193 respectively.

A Pearson chi-square test was done to assess the relationship between pulse pressure and number of hours slept over the second, third and fourth week. On all the tests, a non-significant relationship was found with p values of 0.592 for the 2^{nd} week, p= 0.246 for third week and p=0.237 for the fourth week.

Pearson's correlation between pulse pressure and number of hours slept indicated a positive non-significant correlation on the 2^{nd} week(r=0.237 p=0.079). The third week a positive non-

significant correlation was also found(r= 0.037 p=0.786). On the fourth week a similar positive non-significant correlation between pulse pressure and hours slept was depicted (r=0.132, p=0.334).

A multiple linear regression analysis was done on effect of gender, group (test or control) and mean arterial pressure on pulse pressure during the second week. The results showed that the three predictors had a cumulative non-significant effect (p=0.326). Each of the three predictors had a non significant effect on pulse pressure. Number of hours slept (p= 0.309); gender (p= 0.799) and groups (p= 0.566).

Similar results were found on the third and fourth week of the study on multiple regression where all the three predictors had a cumulative non-significant effect (p=0.596) on the third week. Specific p values for the predictors during the third week; gender (p=0.35), number of hours slept (p=0.267) and groups (p=0.286). On the fourth week a non-significant cumulative effect was found (p=0.770). None of the three specific predictors had a significant effect; number of hours slept (p=0.631), groups (p=0.883) and gender (p=0.665). Thus throughout the period of the study no significant relationship, correlation or effect was found of sleep deprivation or number of hours slept on pulse pressure either in the control group or the test group. Moreover, there was also no significant variation in mean pulse pressure between the two groups throughout the study period. Gender differences were also found to have no significant effect on pulse pressure in the control and test group.

Throughout the study period the mean pulse pressure was within the normal ranges of between 30 and 50 mm Hg for both the control and the test groups at the first, second, third and fourth week. This is even as the mean numbers of hours slept by both the test and control group were significantly different. In all the four weeks the test group had a mean number of

hours slept of less than two hours while the control group had a mean number of sleeping hours more than seven hours.

Table 14: One way ANOVA analysis of the control and test group during the second week

		Sum of Squares	df	Mean Square	F	p
No. of hours slept	Between Groups	604.571	1	604.571	678.125	**0.000**
	Within Groups	48.143	54	.892		
	Total	652.714	55			
Mean Arterial bloold pressure	Between Groups	140.389	1	140.389	2.237	**0.141**
	Within Groups	3388.944	54	62.758		
	Total	3529.333	55			
Pulse pressure	Between Groups	182.161	1	182.161	2.396	**0.128**
	Within Groups	4105.964	54	76.036		
	Total	4288.125	55			
Fractional pulse pressure	Between Groups	.009	1	.009	1.015	**0.318**
	Within Groups	.456	54	.008		
	Total	.464	55			

Table 15: One way ANOVA analysis during the third week

		Sum of Squares	Df	Mean Square	F	p
No. of hour slept	Between Groups	631.143	1	631.143	1133.359	**0.000**
	Within Groups	30.071	54	.557		
	Total	661.214	55			
Mean Arterial blood pressure	Between Groups	22.716	1	22.716	.211	**0.648**
	Within Groups	5815.615	54	107.697		
	Total	5838.331	55			
Pulse pressure	Between Groups	.573	1	.573	.004	**0.953**
	Within Groups	8651.298	54	160.209		
	Total	8651.871	55			
Fractional pulse pressure	Between Groups	.025	1	.025	1.717	**0.196**
	Within Groups	.796	54	.015		
	Total	.821	55			

Table 16: One way ANOVA analysis during the fourth week

		Sum of Squares	df	Mean Square	F	p
No. of hours slept	Between Groups	572.161	1	572.161	430.509	**0.000**
	Within Groups	71.768	54	1.329		
	Total	643.929	55			
Pulse pressure	Between Groups	434.571	1	434.571	2.833	**0.098**
	Within Groups	8282.857	54	153.386		
	Total	8717.429	55			
Mean Arterial pulse pressure	Between Groups	92.571	1	92.571	.800	**0.375**
	Within Groups	6246.476	54	115.675		
	Total	6339.048	55			
Fractional pulse pressure	Between Groups	.021	1	.021	1.740	**0.193**
	Within Groups	.661	54	.012		
	Total	.683	55			

Table 17: Pearson chi-square relationship between pulse pressure and number of hour slept in the second third and fourth week

	SECOND WEEK			**THIRD WEEK**			**FOURTH WEEK**		
	Value	df	**p**	Value	df	p	Value	df	**P**
Pearson Chi-Square	148.316[a]	153	**0.592**	192.689[a]	180	**0.246**	272.796[a]	204	**0.237**
Likelihood Ratio	102.182	153	**0.999**	125.852	180	**0.999**	140.250	204	**1.000**
Linear-by-Linear Association	3.085	1	**0.079**	.076	1	**0.783**	.952	1	**.329**
N of Valid Cases	56			56			56		

Table 18: Pearson correlation between pulse pressure and number of hours slept in the second, third and fourth week

		SECOND WEEK		THIRD WEEK		FOURTH WEEK	
		No. of hours slept	Pulse pressure	No. of hours slept	Pulse pressure	No. of hours slept	Pulse pressure
No. of hours slept	Pearson Correlation	1	**.237**	1	**.037**	1	**.132**
	Sig. (2tailed)		**.079**		**.786**		**.334**
	N	56	**56**	56	**56**	56	**56**
	Pearson Correlation	.237	**1**	.037	**1**	.132	**1**
	Sig. (2-tailed)	.079		.786		.334	
	N	56	**56**	56	**56**	56	**56**

Table 19: Multiple regression analysis on effects of gender, groups and number of hours slept on pulse pressure(cumulative effect)

		SECOND WEEK			THIRD WEEK			FOURTH WEEK		
		Sum of Squares	F	**p**	Sum of Squares	F	**p**	Sum of Squares	F	**P**
Model	Regression	273.350	1.180	**0.326**[b]	305.647	.635	**.596**[b]	134.748	.377	**0.770**[b]
1	Residual	4014.775			8346.224			6202.091		
	Total	4288.125			8651.871			6336.839		

Dependent Variable: Pulse pressure

b. Predictors: (Constant), Male & Female, Test group and control group, No. of hours slept

Table 20: Multiple regression analysis on effects of groups, gender and number of hours slept on pulse pressure (specific effects)

	SECOND WEEK		**THIRD WEEK**		**FOURTH WEEK**	
Model	*t*	*p*	t	p	T	p
(Constant)	*10.202*	**0.000**	7.147	.000	9.145	**0.000**
No. of hours slept	*1.028*	**0.309**	.942	.350	0.483	**0.631**
Male and Female	*0.256*	**0.799**	1.122	.267	-0.148	**0.883**
Test group=T Control group= C	*-0.577*	**0.566**	-1.078	.286	-0.435	**0.665**

3.1.1 ANALYSIS OF FRACTIONAL PULSE PRESSURE DURING THE SECOND, THIRD AND FOURTH WEEK.

Analysis of fractional pulse pressure between the test and control group showed no significant variances during the second (p=0.318), third (p=0.196) and fourth (p=0.193) weeks. The mean fractional pressures for the test group during the second (0.5659), third (0.5778) and fourth (0.5635) weeks were all within the normal ranges.

A Pearson chi-square was used to assess the relationship between fractional pulse pressure and number of hours slept. During the second week a non-significant relationship (p=0.643) was observed. Similarly the third week (p=0.075) and fourth week (p=0.00) were non-significant. To assess the correlation between fractional pulse pressure and number of hours slept during the second week, Pearson correlation test depicted a positive non-significant correlation(r=0.129 p= 0.344).

During the third week the same test depicted a negative non-significant correlation (r= -0.16 , p= 0.238). During the fourth week a positive non-significant correlation(r=0.092, p= 0.5) was found.

Multiple linear regression was used to assess the effects of three predictors; gender, group and number of hours slept on fractional pulse pressure. For the second week, the three predictors had a cumulative non-significant effect (p=0.79). None of the three specific predictors; gender (p=0.80), hours slept (p=0.938) and group (p=0.736) had a significant effect.

During the third week the three predictors had a non-significant cumulative effect (p=0.471). None of the three predictors; gender (p=0.619), hours slept (p=0.397) and group (0.453) had a significant effect on fractional pulse pressure.

During the fourth week, the three predictors had a non-significant cumulative effect

(p=0.814). None of the three predictors; gender (p=0.520), number of hours slept (p=0.992) and group (p=0.792) had a significant effect on fractional pulse pressure.

Table 21: Pearson Chi-square relationship between fractional pulse pressure and number of hours slept in the second, third and fourth week

	SECOND WEEK			THIRD WEEK			FOURTH WEEK		
	Value	df	**p**	Value	df	p	Value	df	**p**
Pearson Chi-Square	340.711[a]	351	**0.643**	408.767[a]	369	**.075**	514.861[a]	408	**0.000**
Likelihood Ratio	189.844	351	**1.000**	197.868	369	**1.000**	206.167	408	**1.000**
Linear-by-Linear Association	.912	1	**0.340**	1.412	1	**.235**	.465	1	**0.495**
N of Valid Cases	56			56			56		

Table 22: Pearson correlation between fractional pulse pressure and number of hours slept in the second, third and fourth week

		SECOND WEEK		THIRD WEEK		FOURTH WEEK	
		No. of hours slept	Fractional pulse pressure	No. of hours slept	Fractional pulse pressure	No. of hours slept	Fractional pulse pressure
No. of hours slept	Pearson correlation r value	1	**.129**	1	**- 0.160**	1	**0.092**
	p value		**0.344**		**0.238**		**0.500**
	N	56	**56**	56	**56**	56	**56**

Table 23: Multiple linear regression analysis on effects of gender, groups and number of hours slept on fractional pulse pressure (Cumulative effect)

		SECOND WEEK			THIRD WEEK			FOURTH WEEK		
		Sum of Squares	F	**p**	Sum of Squares	F	Sig.	Sum of Squares	F	**p**
Model	Regression	.009	.349	**0.790**[b]	.039	.854	**0.471**[b]	.006	.315	**0.814**[b]
1	Residual	.455			.783			.324		
	Total	.464			.821			.330		
								Sum of Squares		

Dependent Variable: Fractional pulse pressure

b. Predictors: (Constant); Test group and Control group, Male and Female, Number of hours slept

Table 24: Multiple linear regression analysis on effects of groups, gender and number of hours slept on the second, third and fourth week (specific effects)

	SECOND WEEK		THIRD WEEK		FOURTH WEEK	
Model	*t*	*p*	t	p	t	p
(Constant)	12.004	**0.000**	9.612	**0.000**	15.224	**0.000**
No. of hours slept	-.077	**0.939**	.854	**0.397**	-.010	**0.992**
Male = 1 Female =2	.254	**0.800**	.500	**0.619**	.269	**0.789**
Test group= T Control group= C	.340	**0.736**	-.757	**0.453**	-.648	**0.520**

Dependent Variable: Fractional pulse pressure

CHAPTER FOUR

4.1 DISCUSSION

The results of this study suggest that there was no significant difference/variation of the two outcome variables; pulse pressure and fractional pulse pressure between the two groups throughout the period of the study. Even with significant differences in mean number of hours slept between the test group(less than 2) and the control group (more than 8); no significant variation was noted between the two groups on the two variables.

The mean pulse pressure at recruitment of the control group was 48.09 mmHg while that of the test group was 47.22 mmHg. Both groups at recruitment had an equal mean fractional pulse pressure of 0.54 with mean age of control group at 28.42 years and that of test group at 27.86 years. By the fourth week of the study, the control group had a mean 50.0 mmHg and a mean fractional pulse pressure of 0.58; the test group had a mean pulse pressure of 44.43 mmHg and a mean fractional pulse pressure of 0.54. A person chi-square test revealed no relationship between pulse pressure and number of hours slept (Chi square value =165.99 df= 190 p= 0.895).

The correlation was weak in strength(r= 0.055). Higher pulse pressure was associated with higher number of hours slept. Correlation analysis between fractional pulse pressure and number of hours slept revealed a non- significant and negative relationship (r=-0.046 p=0.739). Multiple regression was also conducted on overall effect of gender, both the two groups and number of hours slept on pulse pressure and showed a non-significant combined effect (p= 0.744). Each of the three predictors had no relationship with pulse pressure.

This could be possibly explained partly by the fact that both systolic and diastolic blood pressures are equally affected by sleep deprivation. Thus, even with a significant rise in blood pressure, the pulse pressure remains almost unchanged. This is in tandem with results shown by Army Martin et al, 2013 who tested effects of sleep deprivation on six human subjects over a 24- hr period. Results specifically for blood pressure in their study indicate a slight decrease in both the systolic and diastolic blood pressure.

As noted by Franklin et al, 1999 and Verndecchia et al, 2001 with relation to age, a wide pulse pressure may result from increased systolic blood pressure, decreased diastolic BP, or both. The results of this study showed no significant rise in systolic blood pressure ($p=0.842$) related to sleep deprivation in the test group or a decrease in diastolic blood pressure ($p=0.633$). In the patho-physiology of pulse pressure increase, high systolic pressure increases vascular load while low diastolic pressure may reduce coronary perfusion pressure, both of which provide pathophysiologic explanations for the prognostic value of pulse pressure (Haider et al, 2003).

Michael et al, 2000 showed that each 10 mm Hg increase in baseline pulse pressure was associated with a 5% increase in mortality, whereas a 10 mm Hg decrease in mean arterial pressure was associated with an 11% increase in risk. The effects of both mean arterial pressure and pulse pressure were adjusted for covariates of pulse pressure and other predictors of outcome in patients with ventricular dysfunction. Their study was done on hypertensive patients.

This **s**tudy was done on healthy subjects and with all co-morbidities controlled for and could explain the disparities between the two studies. As shown by Michael et al, 1999, the main indicator of pulse pressure are conduit vessel stiffness, which contributes to increased pulse pressure, resistance vessel activation, which accompanies a fall in mean arterial pressure and adverse cardiovascular events . This is more pronounced in patients with left ventricular

dysfunction rather than healthy subjects as used in the present study. No available study has shown an effect of sleep deprivation on the patho-physiology of blood vessel stiffness. Thus, lack of a direct effect of sleep deprivation on blood vessel stiffness or increased vascular resistance would be a reason for the observed results. Nonetheless, it is not yet clear how increases in other potential determinants of pulse pressure, such as peak ejection rate or stroke volume, would be associated with sleep deprivation and their magnitude effect, if any.

Moreover, pulse pressure values for most subjects in the test group were within the normal ranges. Only 4 subjects in week 1, 3 subjects in week 2, 4 subjects in week 3 and 3 subjects in week 4 had a pulse pressure above 65. This was equally noted in the control group with 2 subjects in week 1, 5 subjects in week 2, 3 in week 3 and 4 subjects in week 4. Thus the random changes in pulse pressure could not be attributed to sleep deprivation. Fractional analysis showed no relationship between sleep deprivation with either an increase or decrease in pulse pressure. This is unlike Kato et al, 2000 who reported that blood pressure elevated and MSNA decreased after total sleep deprivation; however the exact mechanism for such change was not clear.

Fractional pulse pressure is derived by dividing pulse pressure by mean arterial blood pressure. It has also been imputed as a significant parameter in assessing cardiovascular pathology. Serkan et al, 2006 indicated that increased fractional pulse pressure is an independent risk factor for coronary heart disease. Moreover, increased fractional pulse pressure is a better indicator for arterial stiffness than pulse pressure. Mohammed et al depicted that increased fractional pulse pressure was a marker for adverse in-hospital outcomes in patients with S-T elevation myocardial infarction. Compared to the initial pre-study value of 0.54 for both the test group and control group, no significant change or increase in fractional pulse pressure was noted. The highest mean value was 0.59 for the test group in the third week which was within the normal ranges.

Previous studies that have examined the effect of sleep deprivation on cardiovascular function and sympathetic activity have not yet reached a consensus result. Lusardi et al, 1999 reports an increase in blood pressure, heart rate, and urine catecholamine level while Gonzalez-Ortiz et al,2000 reports no change in blood pressure and Tofler et al, 1987 describe minimal or no change in heart rate after total sleep deprivation in human subjects.

However, in all of these studies, the subjects were not healthy. In addition, factors such as aging, sex, obesity, physical activity, and history of diabetes and hypertension were not strictly controlled for unlike in the present study. Therefore, it is difficult to compare the results of the present study with those of the previous studies.

Prior to conducting the present study, we expected that sleep deprivation would affect pulse pressure. This was guided by studies of Ogawa et al, 2003 showing increased diastolic blood pressure significantly after a 24 hour period of sleep deprivation (66.5 ± 1.7 vs 57.4 ± 3.3 mm Hg). His study was done on six young healthy men but only done for one day. They speculated that the increase in blood pressure was caused by a peripheral mechanism such as an activation of the renin - angiotensin system and an enhanced production of the vasoconstrictor endothelin.

However, this study showed that pulse pressure was not related to sleep deprivation in both the control group and test group throughout the study period.

As fractional pulse pressure is a factor of both the pulse pressure and mean arterial blood pressure, the non-significant change could be attributed to lack of any equally significant change in either of the two parameters during the period of the study.

No gender differences were noted on either pulse pressure or fractional pulse pressure on multiple linear regression. This could indicate no specific physiologic responses to sleep deprivation between the male and female subjects in all the outcome variables.

4.2 STUDY LIMITATIONS

1. The study period was short as the study was done for a period of one month.
2. The criterion for sleep deprivation was the verbal response of the subjects rather than a more accurate gauge that is not subjective.
3. There was no blinding to the researcher who knew both the control and the test group and this could introduce subjectivity in collection of data especially hours slept during the study period.
4. Diastolic blood pressure values with a manual sphygmomanometer can be subjective as not all subjects have a clear end- korotkoff sound.
5. A limited number of subjects was analysed. To generalise the results of this study, studies involving a large number of subjects are essential.

4.3 CONCLUSION

This study shows that acute sleep deprivation has no significant effect on pulse pressure changes and fractional pulse pressure. None of the two outcome variables had a significant correlation with sleep deprivation. Both mean pulse pressure and mean fractional pulse pressure for the test group were within the normal ranges throughout the four weeks of the study.

The test group of sleep deprived subjects showed no specific patterns of change in any of the two outcome variables during the period of the study. No gender differences were noted in either of the outcome variables throughout the study period.

4.4 RECOMMENDATIONS

1. Sleep deprivation should be considered to have a non-significant effect on pulse pressure and fractional pulse pressure.

2. Further research with longer follow-up periods to better clarify the effects of chronic sleep deprivation on pulse pressure and fractional pulse pressure

REFERENCES

1. American College of Surgeons (2008). Atls, Advanced Trauma Life Support Program for Doctors. Amer College of Surgeons. p. **58**. ISBN 978-1-880696-31-6.
2. Amy M, Christine D, Young M. Effects of sleep deprivation on basic vital signs and cognitive function in human beings. Sleep. 2003;**2**:6-7.
3. Athanase B, Anne R,Michel S, Louis G. Pulse pressure and cardiovascular mortality in normo-tensive and hypertensive subjects. Hypertension. 1998;**32**;560-564.
4. Avolio AP, Deng FQ, Li WQ, Luo YF, Huang ZD, Xing LF, O'Rourke MF. Effects of aging on arterial distensibility in populations with high and low prevalence of hypertension: comparison between urban and rural communities in China. *Circulation*. *1985*;***71***:*202*–210
5. Belenky G, Wesensten NJ, Thorne DR, et al. Patterns of performance degradation and restoration during sleep restriction and subsequent recovery: a sleep dose–response study. J Sleep Res. 2003;**12**:1–12.
6. Benetos A, Rudnichi A, Safar M, Guize L: Pulse pressure and cardiovascular mortality in normotensive and hypertensive subjects. Hypertension **32**:560–564, 1998.
7. Benetos A, Safar M, Rundnichi A, Smulyan H, Richard JL, Ducimetiere P, Guize L: Pulse pressure: a predictor of long-term cardiovascular mortality in a French male population. Hypertension **30**:1410–1415, 1997.
8. Bertovic et al. Muscular Strength Training Is Associated With Low Arterial Compliance and High Pulse Pressure 2008. **33** (6): 1385 – Hypertension
9. Bramwell JC, Hill AV, McSwiney BA. The velocity of the pulse wave in man in relation to age as measured by the hot-wire sphygmograph. *Heart*. *1923*;***10***:*233*–255
10. Bristow JD, Honour AJ, Pickering TG, Sleight P. Cardiovascular and respiratory changes during sleep in normal and hypertensive subjects. *Cardiovasc. Res*. 1969; **3**: 476–85.
11. Brush CE, Fayerweather R. Observations on the changes in blood pressure during normal sleep. *Am. J. Physiol*. 1901; **5**: 199–210.

clinical relevance.J Am Coll Cardiol. 2001 Mar 15; **37** (4): 975-984.

12. Colton HR, Altevogt BM. Sleep disorders and sleep deprivation: an unmet public health problem. Washington: National Academies Press; 2006.

13. Conway J, Boon N, Jones JV, Sleight P. Involvement of the baro-receptor reflexes in the changes in blood pressure with sleep and mental arousal. *Hypertension* 1983; **5**: 746–8

14. Dart AM, Kingwell BA. Pulse pressure–a review of mechanisms and clinical relevance. *J Am Coll Cardiol*. 2001; **37**: 975–984.

15. Dawson D, Reid K. Fatigue, alcohol and performance impairment. Nature. 1997;**388**:235.

16. Del Bo A, Baccelli G, Cellina G, Fea F, Ferrari A, Zanchetti A. Carotid sinus reflexes during postural changes, naturally elicited fighting behavior and phases of sleep in the cat. *Cardiovasc. Res*. 1985; **19**: 762–9.

17. Demet E, Chicz-Demet A, Fallon JH, Sokolski KN. *Sleep deprivation therapy in depressive illness and Parkinson's disease.* Prog Neuropsychopharmacol Biol Psychiat 1999;**23**:753–84.

18. Devereux RB, Alderman MH. Role of preclinical cardiovascular disease in the evolution from risk factor exposure to development of morbid events. *Circulation*. 1993;**88** (4 Pt 1):1444–1455.

during sleep in normal subjects. *N. Engl. J. Med*. 1993; **328**: 303–7.

19. Fang J, Madhavan S, Alderman MH: Pulse pressure: a predictor of cardiovascular mortality among normotensive subjects. Blood Pressure **9**:260–266, 2000.

20. Fang J, Madhavan S, Cohen H, Alderman MH. Measures of blood pressure and myocardial infarction in treated hypertensive patients. J Hypertens. 1995;**13**:413–419.

21. Farida Munawar, Fareeha, Maryam, Sana, Anushe, Nida. Determination of cardiac output in medical students by pulse pressure method, - Department of Physiology, Fatima Jinnah Medical College, Lahore, Pak J Physiol 2007;3(2)

22. Franklin SS, Gustin IVW, Wong ND, Larson MG, Weber MA, Kannel WB, Levy D: Hemodynamic patterns of age-related changes in blood pressure: the Framingham Heart Study. Circulation **96**: 308–315, 1997.

23. Franklin SS, Gustin W, Wong ND, Larson MG, Weber MA, Kannel WB, Levy D. Hemodynamic patterns of age-related changes in blood pressure: the Framingham heart study. *Circulation*. *1997*;***96***:*308*–315

24. Franklin SS, Khan SA, Wong ND, Larson MG, Levy D. Is pulse pressure useful in predicting risk for coronary heart Disease? The Framingham heart study. *Circulation*. 1999; **100**: 354–360.

25. Franklin SS. Cardiovascular risks related to increased diastolic, systolic and pulse pressure. An epidemiologist's point of view. *Pathol Biol (Paris)*. 1999;**47**: 594–603.

26. Gonzalez-Ortiz M, Martinez-Abundis E, Balcazar-Munoz B, Pascoe-Gonzalez S. Effect of sleep deprivation on insulin sensitivity and cortisol concentration in healthy subjects. Diabetes Nutr Metab 2000;**13**: 80-3.

27. Haider AW, Larson MG, Franklin SS, Levy D. Systolic blood pressure, diastolic blood pressure, and pulse pressure as predictors of risk for congestive heart failure in the Framingham Heart Study. *Ann Intern Med*. 2003; **138**:10–16.
heart rate during the wake–sleep cycle in rat. *Sleep* 2001; **24**: 753–8.

28. Hoffman JIE. A critical view of coronary reserve. *Circulation.* 1987; **75**(suppl I):I-6– I-11.

29. Horne A. Why we sleep: the functions of sleep in humans and other animals. Oxford: Oxford University Press; 1988.

30. Horne RSC, De Preu ND, Berger PJ, Walker AM. Arousal responses to hypertension in lambs: Effect of sinoaortic denervation. *Am. J. Physiol. Heart Circ. Physiol*. 1991; **260**: H1283–9.

31. Hozawa A, Ohkubo T, Nagai K, Kikuya M, Matsubara M, Tsuji I, Ito S, Satoh H, Hisamichi S, Imai Y: Prognosis of isolated systolic and isolated diastolic hypertension as assessed by self-measurement of blood pressure at home: the Ohasama study. Arch Intern Med. 2000 Nov 27; **160** (21): 3301-6.

32. Lellamo F, Placidi F, Marciani MG *et al*. Baroreflex buffering of sympathetic activation during sleep. Evidence from autonomic assessment of sleep macroarchitecture and microarchitecture. *Hypertension* 2004; **43**: 1–6.

33. Kato M, Phillips BG, Sigurdsson G, Narkiewicz K, Pesek CA, Somers VK Effects of sleep deprivation on neural circulatory control. Hypertension 2000; 35(5): 1173-5.

34. Kelly R, Tunin R, Kass D. Effect of reduced aortic compliance on left ventricular contractile function and energetics in vivo. Circ Res. 1992;**71**:490–502.

35. Kerkhof GA, Van Dongen HPA, Bobbert AC. Absence of endogenous circadian rhythmicity in blood pressure? *Am. J. Hypertens*. 1998; **11**: 373–7.

36. Legramante JM, Marciani MG, Placidi F *et al*. Sleep-related changes in baroreflex sensitivity and cardiovascular autonomic modulation. *J. Hypertens*. 2003; **21**: 1555

37. Lusardi P, Zoppi A, Preti P, Pesce R, Piazza E, Fogari R. Effects of insufficient sleep on blood pressure in hypertensive patients. Am J Hypertens 1999;**12**:63-8.

38. Madhavan S, Ooi WL, Cohen H, Alderman MH. Relation of pulse pressure and blood pressure reduction to the incidence of myocardial infarction. Hypertension. 1994;**23**:395–401.

39. Mahfouz RA, Dewedar A, Abdelmoneim A et al. Aortic and pulmonary artery stiffness and cardiac function in children at risk for obesity. Echocardiography, 2013; 29: 984–990.

40. Matthews KA, Owens JF, Kuller LH, Sutton-Tyrrell K, Lassila HC, Wolfson SK. Stress-induced pulse pressure change predicts women's carotid atherosclerosis. *Stroke*. 1998;**29**:1525–1530.

41. Mensink GBM, Hoffmeister H. The relationship between resting heart rate and all-cause, cardiovascular and cancer mortality. Eur Heart J. 1997; **18:1404**–1410.

42. Michael O, Edward D. pulse pressure. Is this a clinically useful risk factor? *Hypertension*.1999;**34**: 372-374

43. Michael F, James B. Isolated systolic hypertension, pulse pressure and arterial stiffness as risk factor for cardiovascular disease. Circulation. 2000; **18**: 1527-1535.

44. Mitchell GF, Moye LA, Braunwald E, Rouleau J-L, Bernstein V, Geltman EM, Flaker GC, Pfeffer M: Sphygmomanometric determined pulse pressure is a powerful independent predictor of recurrent events after myocardial infarction in patients with impaired left ventricular function. Circulation. 1997;**96**: 4254–4260.

45. Mitler M, Carskadon M, Czeisler C, Dement W, Dinges DF, Graeber RC. Catastrophes, sleep and public policy: consensus report. Sleep. 1988; **11**: 100–9.

46. Mohammed ED, Tilak P, Dinesh S. Aortic stiffness as reflected by fractional pulse pressure is a marker of adverse in-hospital outcomes in patients with STEMI. 2014;**63**:150-159.

47. Monk TH. Shift work: basic principles. In: Kryger MH, Roth T, Dement WC, editors. Principles and practice of sleep medicine. 4th ed. Philadelphia: Elsevier/Saunders; 2005.

48. Monti A, Medigue C, Nedelcoux H, Escourrou P. Autonomic control of the cardiovascular system during sleep in normal subjects. *Eur. J. Appl. Physiol*. 2002; **87**: 174–81.

49. Nagura S, Sakagami T, Kakiichi A, Yoshimoto M, Miki K. Acute shifts in baroreflex control of renal sympathetic nerve activity induced by REM sleep and grooming in rats. *J. Physiol*. 2004; **558**: 975–83.

50. Nakazato T, Shikama T, Toma S, Nakajima Y, Masuda Y. Nocturnal variation in human sympathetic baroreflex sensitivity. *J. Auton. Nerv. Syst*. 1998; **70**: 32–7.

51. National Sleep Foundation. Sleep in America poll. Washington: National Sleep Foundation; 2002.

52. Nicholas WV, O'Rourke MF. McDonald's Blood Flow in Arteries: Theoretic, Experimental, and Clinical Principles. 3rd ed. London, UK: E. Arnold; 1990:77–142, 216–269, 398–411.

53. Ogawa Y, Kanbayashi T, Saito Y, *et al*. Total sleep deprivation elevates blood pressure through arterial baroreflex resetting: a study with microneurographic technique. Sleep 2003; 26(8): 986-9.

54. Ogawa Y, Kanbayashi T, Saito Y, Takahashi Y, Kitajima T, Takahashi K, Hishikawa Y, Shimizu T. Total sleep deprivation elevates blood pressure through arterial baroreflex resetting: a study with microneurographic technique. *SLEEP*. 2003;26:986 –989.

55. O'Rourke M. Arterial stiffness, systolic blood pressure, and logical treatment of arterial hypertension. *Hypertension*. 1990; **15:339**–347.

56. Pannier B, Brunel P, El Aroussy W, Lacolley P, Safar ME. Pulse pressure and echocardiographic findings in essential hypertension*. J Hypertens*. *1989*;***7***:*127*–129

57. Patrick GT, Gilbert JA. On the effects of loss of sleep. Psychology Rev. 1896;**3**:469–83.

58. Pilcher JJ, Huffcutt AI. Effects of sleep deprivation on performance: a meta-analysis. Sleep. 1996; **19**:318–26.

59. Ragab A, Mahfouz RA, Waleed E, Mohammed A. Association of fractional pulse pressure to aortic stiffness and their impact on diastolic function and coronary flow reservein asymptomatic diabetic patients . Hypertension.2013;20:605-611.

60. Safar M, Chamiot-Clerc P, Dagher G, Renaud JF. Pulse pressure, endothelium function, and arterial stiffness in spontaneously hypertensive rats.*Hypertension*. 2001; **38:1416**–1421.

61. Safar ME: Systolic blood pressure, pulse pressure and arterial stiffness a cardiovascular risk factors. Curr Opin Nephrol Hypertens. 2001 March; 10 (**2**): 257-261.

62. Salomaa V, Riley W, Kark JD, Nardo C, Folsom AR. Non–insulin-dependent diabetes mellitus and fasting glucose and insulin concentrations are associated with arterial stiffness indexes: the ARIC study. *Circulation*. *1995*;***91***:*1432*–144

63. Serkan C, Umit G, Sule K. Increased aortic pulse and fractional pulse pressure in patients with cardiac syndrome. Hypertension.2006;**15**:179-184

64. Simone G, McClelland R, Gottdiener JS, Celentano A, Kronmal RA, Gardin JM. Relation of hemodynamics and risk factors to ventricularvascular interactions in the elderly: the Cardiovascular Health Study. *J Hypertens*. 2001;**19**: 1893–1903.

65. Smyth HS, Sleight P, Pickering GW. Reflex regulation of arterial pressure during sleep in man. *Circ. Res*. 1969; **24**: 109–21.

66. Somers VK, Dyken ME, Mark AL, Abboud FM. Sympathetic nerve activity

67. Staessen JA, Bieniaszewski L, O'Brien E *et al*. Nocturnal blood pressure fall on ambulatory monitoring in a large international database. *Hypertension* 1997; **29**: 30–9.

68. Tofler G, Brezinski D, Schafer A, et al. Concurrent morning increase in platelet aggregability and the risk of myocardial infarction and sudden cardiac death. N Engl J Med 1987; **316**: 1514-8.

69. Tozawa M, Iseki K, Iseki C, Takishita S. Pulse pressure and risk of total mortality and cardiovascular events in patients on chronic hemodialysis. *Kidney Int*. 2002;**61**:717–726.

70. Van Bortel LM, Struijker-Boudier HA, Safar ME. Pulse pressure, arterial stiffness, and drug treatment of hypertension. *Hypertension*. 2001; **38**: 914–921.

71. Van Dijk RA, Dekker JM, Nijpels G, Heine RJ, Bouter LM, Stehouwer CD. Brachial artery pulse pressure and common carotid artery diameter: mutually independent associations with mortality in subjects with a recent history of impaired glucose tolerance. *Eur J Clin Invest*. 2001;**31**:756–763.

72. Van Dongen HPA, Maislin G, Mullington JM, Dinges DF. The cumulative cost of additional wakefulness: dose–response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. Sleep. 2003;**26**:117–26.

73. Verdecchia P, Schillaci G, Reboldi G, Franklin SS, Porcellati C. Different prognostic impact of 24-hour mean blood pressure and pulse pressure on stroke and coronary artery disease in essential hypertension. *Circulation*. 2001;**103**: 2579–2584.

74. Viazzi F, Leoncini G, Parodi D, Ravera M, Ratto E, Vettoretti S, Tomolillo C, Sette MD, Bezante GP, Deferrari G, Pontremoli R. Pulse pressure and subclinical cardiovascular damage in primary hypertension. *Nephrol Dial Transplant*. 2002;**17**: 1779–1785.

75. Watanabe H, Ohtsuka S, Kakihana M, Sugishita Y. Coronary circulation in dogs with experimental decrease in aortic compliance. J Am Coll Cardiol. 1993;**21**:1497–1506

APPENDIX 1

Reference chart for manual blood pressure measurement (American Heart Association, 2000)

RECOMMENDATIONS	COMMENTS
Patient should be seated comfortably, with back supported, legs uncrossed, and upper arm bared.	Diastolic pressure is higher in the seated position, whereas systolic pressure is higher in the supine position. An unsupported back may increase diastolic pressure; crossing the legs may increase systolic pressure
Patient's arm should be supported at heart level.	If the upper arm is below the level of the right atrium, the readings will be too high; if the upper arm is above heart level, the readings will be too low. If the arm is unsupported and held up by the patient, pressure will be higher
Cuff bladder should encircle 80 percent or more of the patient's arm circumference.	An undersized cuff increases errors in measurement.
Mercury column should be deflated at 2 to3 mm per second.	Deflation rates greater than 2 mm per second can cause the systolic pressure to appear lower and the diastolic pressure to appear higher.
The first and last audible sounds should be recorded as systolic and diastolic pressure, respectively. Measurements should be given to the nearest 2 mm Hg.	
Neither the patient nor the person taking the measurement should talk during the procedure.	Talking during the procedure may cause deviations in the measurement

APPENDIX 2

QUESTIONNAIRE FOR A STUDY ON EFFECTS OF SLEEP DFEPRIVATION ON BLOOD PRESSURE AND BLOOD SUGAR

Questionnaire NO…….

Name …… **Age…….**

Sex …… **Address……**

Height …….. **Weight……**

Contact Phone No……..

1. What is your current occupation?

……

2. How many days on average do you work in a month?

……..

3. What is your highest level of education?

……..

4. Do you suffer from any chronic infections?

……

Tick the responses to the following questions as appropriate

HISTORY OF DRUG ABUSE

Question	**Response**
Do you currently take any tobacco products, such as cigarettes, cigars or pipes?	○ Yes ○ No
Do you currently take tobacco products daily?	○ Yes ○ No
How old were you when you first started smoking?	Age (years)……. ○ Don't know
On average how many of the following products do you smoke each day/ week?	Manufactured cigarettes…… Hand rolled cigarettes…….. Pipes full of tobacco…….. Cigars…… Number of shisha sessions……..
In the past did you ever smoke any tobacco products?	○ Yes ○ No
How long ago did you stop smoking?	○ Years ago ○ Months ago ○ Weeks ago
Do you currently use any smokeless tobacco products [such as snuff, chewing tobacco, betel]?	○ Yes ○ No

QUESTION	RESPONSE
Do you currently take any alcoholic product such as beer, wine, and spirits?	o Yes o No
During the past twelve months, how frequently have you had at least one standard alcoholic drink?	o Daily o 5-6 days per week o 3-4 days per week o 1-2 days per week o 1-3 days per month o Less than once a month
During the past one week how many standard drinks did you have each day?	Monday…… Tuesday…… Wednesday…… Thursday…… Friday…….. Saturday…….. Sunday……..
In the past did you ever take any alcoholic products?	o Yes o No
How long ago did you stop drinking?	o Years ago o Months ago o Weeks ago

HISTORY OF RAISED BLOOD PRESSURE

Question	Response
Have you ever had your blood pressure measured by a doctor or health worker?	○ Yes ○ No
Have you ever been told by a doctor or health worker that you have raised blood pressure or hypertension?	○ Yes ○ No
Have you been told in the last twelve months?	○ Yes ○ No
In the past two weeks, have you taken any drugs (medication) for raised blood pressure prescribed by a doctor or other health worker?	○ Yes ○ No
Have you ever seen a traditional healer for raised blood pressure or hypertension?	○ Yes ○ No
Are you currently taking any herbal remedy for your raised blood pressure?	○ Yes ○ No

HISTORY OF DIABETES

QUESTION	RESPONSE
Have you ever had your blood sugar measured by a doctor or health worker?	○ Yes ○ No
Have you ever been told by a doctor or other health worker that you have raised blood sugar or diabetes?	○ Yes ○ No
Have you been told in the past twelve months?	○ Yes ○ No
In the past two weeks, have you taken any drugs (medication) for diabetes prescribed by a doctor or health worker?	○ Yes ○ No
Are you currently taking insulin for diabetes prescribed by a doctor or healthworker?	○ Yes ○ No
Have you ever seen a traditional healer for diabetes or raised blood pressure?	○ Yes ○ No
Are you currently taking any herbal or traditional remedy for your diabetes?	○ Yes ○ No

HISTORY OF SLEEPING PATTERN

QUESTION	RESPONSE
How many hours on average do you sleep in a day?	
Have you ever suffered from a sleeping disorder in the past? *Either due to a medical condition or emotional state*	○ Yes ○ No
Do you have a regular sleeping pattern? *That is, specified sleeping and waking times or a minimum number of sleeping hours?*	○ Yes ○ No
Does your work involve night duties?	○ Yes ○ No
In a typical week, how many hours in total do you sleep?	
Do you suffer from any medical condition that has a great effect on your sleep pattern?	○ Yes ○ No
Are you on any medication that has affects your sleep pattern?	○ Yes ○ No
Do you consider yourself to have a healthy sleeping pattern?	○ Yes ○ No

APPENDIX III

CONSENT FORM

I.....voluntarily agree to participate in the research study on effects of sleep deprivation on blood pressure and blood sugar.

The study aims at collecting data from healthy individuals pertaining to their sleeping pattern and compares that with their blood pressure levels. The participants will be monitored for a period of eight weeks. The study poses no health risk to the participant whatsoever.

All the information collected will be used exclusively for academic purposes only at the University of Nairobi.

The researcher has explained to me the objectives of the study and has assured me that my name and details will be confidential and that the results of the study will be made known to me.

I hereby agree the results of the study to be used for academic purposes only.

RESEARCHER:

Martin Kuria Mungai - 0729 099 390

SUPERVISOR:

Dr. Frederick Bukachi - 0727804933

Kenyatta National Hospital/University of Nairobi ERC Secretariat-

(254) 020 2726300 Ext 44355/Tel: (254) 020 726300 EXT 44102, 44355

SIGNATURE DATE

....

APPENDIX IV

DATA COLLECTION SHEET

Date…….

Subject no.	*Group Test / Control*	*No. of hours slept*	*Systolic blood pressure*	*Diastolic blood pressure*	*Pulse pressure*	*Mean Arterial pulse pressure*	*Fractional pulse pressure*
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